ORIGINAL RESEARCH

# A Novel Differentiation Nomogram Model for Brucellar Spondylitis and Tuberculous Spondylitis

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**Background:** Tuberculous spondylitis (TS) and brucellar spondylitis (BS) exhibit certain similarities in clinical presentation and imaging characteristics, making differential diagnosis challenging. Developing a reliable differential diagnosis model can assist clinicians in distinguishing between these two conditions at an early stage, allowing for targeted prevention and treatment strategies. **Methods:** Patients diagnosed with TS and BS were retrospectively collected and randomized into training and validation cohorts (ratio 7:3). The least absolute shrinkage and selection operator (LASSO) regression was used to reduce data dimensionality and select variables. Multivariate logistic regression was used to build predictive models. A nomogram was constructed to provide a visual representation of the model. Receiver operating characteristic (ROC) curve, calibration plots and decision curve analysis (DCA) were used to measure the predictive performance of the nomogram.

**Results:** A total of 183 patients included (101 cases of TB, 82 cases of BS) our study. Our results showed that these variables including time from symptom onset to admission, anorexia, adenosine deaminase (ADA) and psoas abscess were important to differentiate TS and BS. The area under the curve (AUC) of ROC curve was 0.820 [95% *CI* (0.749, 0.892)] and 0.899 [95% *CI* (0.823, 0.976)] for the training and validation cohort, respectively. The results of calibration curve and DCA confirmed that the nomogram performed well in differentiating TS patient from BS.

**Conclusion:** The combination of time from symptom onset to admission, anorexia, ADA and psoas abscess demonstrated good differential properties for TS and BS. We developed a new nomogram model that can effectively differentiate TS and BS based on these four characteristics, which could be a valid and useful clinical tool for clinicians to aid in early differential diagnosis and targeted treatment. **Keywords:** spinal infectious diseases, spinal tuberculous, brucellosis, nomograms

### Introduction

Tuberculous spondylitis (TS), also known as Pott's disease, is a chronic spinal infection caused by *Mycobacterium tuberculosis*. It often occurs secondary to pulmonary tuberculosis and accounts for more than half of all bone and joint tuberculosis cases.<sup>1,2</sup> Beyond the systemic toxicity symptoms of tuberculosis, patients typically experience low back pain and restricted mobility.<sup>3,4</sup> Brucellosis, a common zoonotic disease caused by *Brucella* infections, can affect multiple organ systems, with the musculoskeletal system being particularly susceptible.<sup>5–7</sup> In China, the incidence of brucellar spondylitis (BS) among brucellosis patients is reported to be 16.6%.<sup>8</sup> Both TS and BS share overlapping clinical presentations and imaging features, complicating their differentiation. Although blood culture, tissue culture, and histopathological examination are considered gold standards for diagnosis, these methods are limited by low positivity rates, as well as significant demands on resources and expertise, posing

challenges for accurate diagnosis and differential diagnosis.<sup>2,9</sup> The timely and accurate differentiation of TS from BS is challenging due to delayed imaging manifestations, prolonged blood cultures, and the complexity of serologic diagnostics.<sup>10</sup>

The Xinjiang Uygur Autonomous Region, particularly its southern areas, experiences a high incidence of TS and BS, posing a significant public health threat. Despite the pressing need, existing research has primarily focused on comparing imaging features, with limited studies directly comparing clinical characteristics and laboratory markers distinguishing these two diseases. Moreover, predictive differentiation models remain scarce.<sup>2,11,12</sup> Developing a reliable differential diagnostic model could aid clinicians in early identification of these diseases, facilitating targeted preventive and therapeutic interventions. Thus, it would optimize treatment outcomes, delay disease progression, and improve patients' quality of life.

This study aims to develop a differential diagnosis model based on clinical data from patients with tuberculous spondylitis and brucellar spondylitis hospitalized at the First People's Hospital of Kashi Prefecture. By employing a nomogram-based approach, known for its simplicity and clinical utility, the model incorporates a range of clinical and laboratory factors to deliver an intuitive and personalized risk assessment tool. This tool is expected to enhance diagnostic accuracy and provide clinicians with a reliable foundation for informed decision-making.

#### **Methods**

#### Study Design

A retrospective study was conducted on patients diagnosed with TS and BS who were hospitalized in the Department of Spine Surgery at the First People's Hospital of Kashi Prefecture between January 2020 and June 2023. The included patients were randomly divided into a training cohort and a validation cohort in a 7:3 ratio. The training cohort was used to construct the model, while the validation cohort was used to assess the model's discriminatory accuracy and performance. The study adhered to the principles of the Declaration of Helsinki and received approval from the Ethics Committee of the First People's Hospital of Kashi Prefecture. Informed consent was obtained from all subjects and/or their legal guardians for participation in this study.

Inclusion criteria for TS: Patients aged 18 years or older who met one of the following: a. Positive culture or acid-fast staining of biopsy or surgical specimen for *Mycobacterium tuberculosis*; b. Tuberculous granuloma visible on histologic examination; c. Confirmation of clinical treatment follow-up showing effective anti-tuberculosis treatment. Inclusion criteria for BS: Patients aged 18 years or older who met one of the following: a. Positive culture of blood, bone marrow, or tissue for *Brucella*; b. Agglutination test titer of  $\geq 1/160$ ; c. Confirmation of clinical treatment. Exclusion criteria: a. Patients with incomplete or missing information; b. Patients with repeated hospitalizations or non-first-time diagnoses.

### Data Collection

All information was obtained from the hospital's electronic medical record system.

- a. Demographic characteristics: gender, age, body index (BMI).
- b. Clinical characteristics: time from symptom onset to admission (≤3 months, 4–12 months, >1 year), season of admission (spring: March, April, May; summer: June, July, August; autumn: September, October, November; winter: December, January, February), hypertension, presence of fever, night sweats, anorexia, and muscle weakness.
- c. Initial laboratory tests: hemoglobin (Hb), platelet (PLT), peripheral white blood cell count (WBC), neutrophils (N), monocytes (Mono), lymphocytes (L), prothrombin time (PT), international normalized ratio (INR), prothrombin time activity (PTA), activated partial thromboplastin time (APTT), fibrinogen (Fib), D-dimer, fibrinogen degradation products (FDP), erythrocyte sedimentation rate (ESR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), globulin (GLO), albumin/globulin ratio (A/G ratio), total bilirubin (TBIL), direct bilirubin (DBIL), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), adenosine deaminase (ADA), creatinine (Cr), urinary creatinine (Ur), serum potassium (K), sodium (Na), chloride (Cl), and calcium (Ca).
- d. Imaging data according to initial Magnetic Resonance Imaging (MRI) findings: lesion site (cervical, thoracic, lumbar, thoracolumbar, or lumbosacral), number of affected vertebrae, and presence or absence of psoas, para-vertebral, or epidural abscesses.

## Data Analysis and Diagnostic Model Building

Only the initial laboratory and examination data after admission were extracted for all patients. Multiple imputation was used to fill in variables with a missing ratio of <20%. To eliminate computational errors from different data magnitudes, a linear normalization method (min-max scaling) was applied to adjust the measurements to the range of [0,1], ensuring equal weight for each feature when processed by the classifier. A Least Absolute Shrinkage and Selection Operator (LASSO) regression model was used to select variables, with ten-fold cross-validation determining the optimal penalty term coefficient  $\lambda$ . Features with non-zero coefficients were selected as important features. Variables selected by LASSO regression were further analyzed by multivariate logistic regression, with variables having P < 0.05 included in the final nomogram, a visual display of the model.

R studio 4.1.2 software was utilized to construct the nomogram. The training cohort employed the receiver operating characteristic (ROC) curve to calculate the area under the curve (AUC), the calibration curve to assess the agreement between the predicted probability of TS and BS discrimination and the actual discrimination rate, and the clinical decision curve (DCA) to evaluate the model's clinical benefit ratio. The internal validation cohort used AUC, calibration curves, and DCA curves to assess the model's stability, accuracy, and clinical benefit ratio. The Hosmer-Lemeshow test was employed to analyze the goodness of fit between the predicted and observed values. Continuous variables were presented as mean  $\pm$  SD or median and interquartile range (IQR), depending on data characteristics. Categorical variables were described as frequencies and percentages (%). For comparisons between the TS and BS groups, an unpaired *t*-test, Wilcoxon rank sum test, Pearson's chi-square test, or Fisher's exact test were utilized, selected based on specific circumstances. Statistical analysis, LASSO regression feature screening, model construction, and evaluation were conducted using R studio 4.1.2, and statistical differences between the two groups were considered significant when P < 0.05.

### Results

A total of 183 patients were included in the study, comprising 101 cases of TS (45 males and 56 females) and 82 cases of BS (59 males and 23 females) (Figure 1). The average age of patients with BS was  $52.0\pm13.1$  years, compared to  $53.7\pm15.9$  years for patients with TS. Additionally, 95.1% of BS patients had a disease duration of less than one year, whereas only 58.4% of TS patients had a disease duration of under one year. Statistically significant differences (P < 0.05) were observed between the two groups in gender, BMI, time from symptom onset to admission, N, L, ALT, AST, TBIL, DBIL, GGT, ADA, Cl, lesion site, number of vertebrae affected, as well as the presence of psoas and paravertebral abscesses (Table 1).

Figure 2A presents the coefficient profiles of 45 features in the LASSO regression model as a function of the log  $(\lambda)$ . As the log $(\lambda)$  value decreases, the number of features with non-zero coefficients increases. Figure 2B presents the selection of the tuning parameter  $(\lambda)$  in the LASSO regression model using 10-fold cross-validation. The optimal  $\lambda$  value, identified at one standard deviation (indicated by the vertical dashed line on the right side), resulted in the identification of 14 features with non-zero coefficients. Covariance analyses indicated low covariance for each indicator (Figure S1).

The variables identified by LASSO regression were analyzed using multivariate logistic regression. Results indicated that time from symptom onset to admission (P < 0.001), anorexia (P = 0.002), ADA (P = 0.022), and psoas abscess (P = 0.019) were statistically significant (Table 2). A nomogram was created to visualize the differential diagnostic model using these four variables. For each patient's variable in the nomogram, a vertical line was drawn upward to intersect the score line segment, giving the score for that indicator. The scores of all variables were then summed to obtain the total score. Finally, a vertical line was drawn downward from the total score axis to determine the corresponding probability of identifying as tuberculous spondylitis (Figure 3). For instance, if a patient has a symptom onset-to-admission time exceeding 1 year, no anorexia, an ADA level of 20.0 U/L, and the presence of a psoas abscess, the total score for this patient would be 172.5 points (calculated as 47+17.5+33+75= 172.5), corresponding to a TS risk of 0.979 (Figure 4).



Figure I The flowchart of patient selection.

The Hosmer-Lemeshow test showed  $x^2 = 2.7536$ , P = 0.9489 for the training cohort and  $x^2 = 3.043$ , P = 0.932 for the validation cohort, indicating an excellent fit between the predicted and observed values. The AUC of the model and the internal validation cohort were 0.820[95% CI (0.749,0.892)] and 0.899[95% CI (0.823,0.976)], respectively,

Variables	Levels	BS (N=82)	TS (N=101)	P value
Gender, %	Male	59 (72%)	45 (44.6%)	<0.001
	Female	23 (28%)	56 (55.4%)	
Age (years)	Mean ± SD	52.0 ± 13.1	53.7 ± 15.9	0.427
BMI (kg/cm <sup>2</sup> )	Mean ± SD	24.5 ± 4.8	22.4 ± 3.5	0.001
Time, %	≤3 months	51 (62.2%)	31 (30.7%)	<0.001
	4~12 months	27 (32.9%)	28 (27.7%)	
	>1 year	4 (4.9%)	42 (41.6%)	
Season, %	Spring	16 (19.5%)	28 (27.7%)	0.137
	Summer	18 (22%)	30 (29.7%)	
	Autumn	26 (31.7%)	19 (18.8%)	
	Winter	22 (26.8%)	24 (23.8%)	
Hypertension, %	Yes	8 (9.8%)	15 (14.9%)	0.418
	No	74 (90.2%)	86 (85.1%)	
Fever, %	Yes	37 (45.1%)	43 (42.6%)	0.845
	No	45 (54.9%)	58 (57.4%)	
Anorexia, %	Yes	40 (48.8%)	39 (38.6%)	0.218
	No	42 (51.2%)	62 (61.4%)	
Night sweats, %	Yes	45 (54.9%)	49 (48.5%)	0.479
	No	37 (45.1%)	52 (51.5%)	
Muscle weakness, %	Yes	20 (24.4%)	35 (34.7%)	0.179
	No	62 (75.6%)	66 (65.3%)	
Hb (g/L)	Mean ± SD	127.1 ± 15.7	126.6 ± 18.4	0.857

(Continued)

Variables	Levels	BS (N=82)	TS (N=101)	P value
PLT (10 <sup>9</sup> /L)	Mean ± SD	290.0 ± 114.3	316.0 ± 105.5	0.112
WBC (10 <sup>9</sup> /L)	Mean ± SD	6.1 ± 1.8	6.3 ± 2.2	0.439
N (10 <sup>9</sup> /L)	Mean ± SD	3.4 ± 1.3	4.2 ± 2.0	0.004
Mono (10 <sup>9</sup> /L)	Mean ± SD	0.5 ± 0.2	0.5 ± 0.2	0.751
L (10 <sup>9</sup> /L)	Mean ± SD	2.0 ± 0.8	1.5 ± 0.5	<0.001
PT (s)	Mean ± SD	12.3 ± 1.1	12.1 ± 0.9	0.158
INR	Mean ± SD	1.0 ± 0.1	1.0 ± 0.1	0.331
PTA (%)	Mean ± SD	88.9 ± 16.5	91.1 ± 13.3	0.321
APTT (s)	Mean ± SD	28.1 ± 3.2	27.8 ± 3.5	0.504
Fib (g/L)	Mean ± SD	4.5 ± 1.1	4.8 ± 2.4	0.300
D-dimer (ug/mL)	Mean ± SD	1.3 ± 1.3	1.6 ± 5.0	0.539
FDP (ug/mL)	Mean ± SD	4.7 ± 4.6	5.4 ± 13.1	0.612
ESR (mm/h)	Mean ± SD	40.7 ± 21.1	40.5 ± 22.6	0.955
ALT (U/L)	Mean ± SD	35.5 ± 33.9	20.7 ± 12.9	<0.001
AST (U/L)	Mean ± SD	30.4 ± 31.1	22.5 ± 11.7	0.033
ALB (g/L)	Mean ± SD	33.9 ± 3.9	34.9 ± 4.5	0.131
GLO (g/L)	Mean ± SD	34.7 ± 5.4	34.4 ± 5.4	0.745
A/G Ratio	Mean ± SD	1.0 ± 0.2	1.0 ± 0.2	0.212
TBIL (umol/L)	Mean ± SD	8.7 ± 4.3	6.9 ± 3.3	0.002
DBIL (umol/L)	Mean ± SD	3.1 ± 2.2	2.4 ± 1.2	0.005
GGT (U/L)	Mean ± SD	59.2 ± 48.8	41.2 ± 45.3	0.011
ALP (U/L)	Mean ± SD	126.3 ± 57.6	113.6 ± 82.8	0.223
ADA (U/L)	Mean ± SD	27.0 ± 16.4	16.6 ± 8.1	<0.001
Cr (mg/d)	Mean ± SD	56.7 ± 14.3	63.3 ± 41.7	0.145
Ur (mg/d)	Mean ± SD	6.9 ± 7.1	6.4 ± 4.8	0.571
K (mmol/L)	Mean ± SD	4.0 ± 0.4	4.1 ± 0.5	0.372
Na (mmol/L)	Mean ± SD	139.4 ± 3.2	139.9 ± 3.0	0.277
CI (mmol/L)	Mean ± SD	103.2 ± 3.6	104.4 ± 3.9	0.034
Ca (mmol/L)	Mean ± SD	2.1 ± 0.1	2.2 ± 0.2	0.343
Segments (n)	Mean ± SD	2.4 ± 0.9	3.1 ± 2.1	0.004
Location, %	с	5 (6.1%)	3 (3%)	0.021
	т	9 (11%)	28 (27.7%)	
	L	42 (51.2%)	44 (43.6%)	
	T+L	6 (7.3%)	12 (11.9%)	
	L+S	20 (24.4%)	14 (13.9%)	
Psoas abscess, %	Yes	3 (3.7%)	16 (15.8%)	0.015
	No	79 (96.3%)	85 (84.2%)	
Paravertebral abscess, %	Yes	22 (26.8%)	51 (50.5%)	0.002
	No	60 (73.2%)	50 (49.5%)	
Epidural abscess, %	Yes	8 (9.8%)	16 (15.8%)	0.321
	No	74 (90.2%)	85 (84.2%)	

Table I (Continued).

Abbreviations: TS, tuberculous spondylitis; BS, brucellar spondylitis; BMI, body mass index; Time, time from symptom onset to admission; Hb, hemoglobin; PLT, platelet; WBC, white blood cell count; N, neutrophil; Mono, monocyte; L, lymphocyte; PT, prothrombin time; INR, international normalized ratio; PTA, prothrombin time activity; APTT, activated partial thromboplastin time; Fib, fibrinogen; FDP, fibrinogen degradation products; ESR, erythrocyte sedimentation rate; ALT, aminotransferase; AST, aspartate aminotransferase; ALB, albumin; GLO, globulin; A/G ratio, albumin globulin ratio; TBIL, total bilirubin; DBIL, direct bilirubin; GGT, transpeptidase; ALP, alkaline phosphatase; ADA, adenosine deaminase; Cr, creatinine; Ur, urinary creatinine; K, serum potassium; Na, sodium; Cl, chloride; Ca, calcium; C, cervical; T, thoracic; L, lumbar; T+L, thoracolumbar; L+S, lumbosacral.



Figure 2 Cross-validation(A) and variable selection of LASSO regression(B).

demonstrating strong discrimination (Figure 5). The calibration curves for both the model and validation cohort indicate high agreement between actual observations, demonstrating good consistency, calibration, and stability (Figure 6). The decision curves show that the model achieves net benefit over "no treatment" or "treat all" scenarios at almost any probability threshold in both the training and validation cohorts, indicating good clinical applicability (Figure 7).

Variables	β	SE	Z	Р	OR(95% CI)	
Gender	Gender					
Male	-	-	-	-	-	
Female	1.724	0.769	1.525	0.127	3.23(0.716,14.57)	
BMI	-0.161	0.107	-1.497	0.134	0.852(0.690,1.051)	
Time	Time					
≤3 months	-	-	-	-	-	
4~12 months	0.274	0.848	0.324	0.746	1.316(0.250,6.931)	
>1 year	3.956	1.148	3.447	<0.001	52.247(5.511,495.316)	
Season						
Spring	-	-	-	-	-	
Summer	2.180	1.157	1.885	0.060	8.842(0.917,85.305)	
Autumn	-0.622	0.945	-0.658	0.511	0.537(0.084,3.424)	
Winter	0.049	1.000	0.049	0.961	1.05(0.148,7.46)	
Anorexia						
Yes	-2.914	0.934	-3.120	0.002	0.054(0.009,0.338)	
No	-	-	-	-	-	

 Table 2 Predictors for TS by Multivariate Logistic Regression Analysis of the

 Training Cohort

(Continued)

Table 2 (Continued).

Variables	β	SE	z	P	OR(95% CI)
N	0.023	0.246	0.095	0.924	1.024(0.633,1.656)
L	-1.283	0.800	-1.604	0.109	0.277(0.058,1.329)
ALT	-0.037	0.030	-1.217	0.224	0.964(0.909,1.023)
TBIL	-0.163	0.117	-1.390	0.165	0.85(0.676,1.069)
ADA	-0.095	0.041	-2.284	0.022	0.91(0.839,0.987)
Segments	0.542	0.294	1.842	0.065	1.719(0.966,3.061)
Location					
С	-	-	_	_	-
т	3.238	2.090	1.549	0.121	25.472(0.424,1530.886)
L	0.473	1.689	0.280	0.780	1.605(0.059,43.987)
T+L	1.572	2.028	0.775	0.438	4.816(0.09,256.621)
L+S	0.468	1.897	0.247	0.805	1.597(0.039,65.725)
Psoas abscess					
Yes	3.925	1.674	2.344	0.019	50.631(1.903,1347.197)
No	-	-	-	-	-
Paravertebral abscess					
Yes	1.579	0.949	1.664	0.961	4.848(0.755,31.128)
No	-	-	-	-	-

**Abbreviations:**  $\beta$ , Regression Coefficient; SE, Standard Error; Z, Z value; P, P value; OR(95% Cl), Odds Ratio and 95% Confidence Interval; BMI, body mass index; Time, time from symptom onset to admission; N, neutrophil; L, lymphocyte; ALT, aminotransferase; TBIL, tot al bilirubin; ADA, adenosine deaminase; C, cervical; T, thoracic; L, lumbar; T+L, thoracolumbar; L+S, lumbosacral.

### Discussion

Since infectious spondylitis can lead to severe consequences and even pose a threat to patients' lives, early diagnosis and prompt treatment are critical to preventing disease progression. Bacterial culture remains the gold standard for



Figure 3 Nomogram for differentiating between TS and BS.

Abbreviations: ADA, adenosine deaminase; TS, tuberculous spondylitis.



Figure 4 Application example of a nomogram for predicting the risk of TS. Abbreviations: ADA, adenosine deaminase; TS, tuberculous spondylitis.



Figure 5 ROC curves of the nomogram. (A) training cohort; (B) validation cohort.

diagnosing TS and BS.<sup>13,14</sup> However, this method has significant limitations, including a low positivity rate, prolonged culture time, complex procedures, and difficulty in obtaining specimens.<sup>3,15,16</sup> Moreover, inadequate medical resources in some primary hospitals and underdeveloped regions of China further hinder timely and accurate diagnosis and treatment, increasing the risk of complications and making treatment more challenging. In the absence of microbiological evidence, a comprehensive evaluation of systemic symptoms, laboratory findings, and imaging features assists in differentiating TS from BS at an early stage.<sup>17</sup> However, the widespread use of antibiotics has reduced the prevalence of typical clinical presentations, and the substantial overlap in symptoms between TS and BS complicates differential diagnosis, often



Figure 6 Calibration curves of the nomogram. (A) training cohort; (B) validation cohort.



Figure 7 Decision curve analysis of the nomogram. (A) training cohort; (B) validation cohort.

necessitating the expertise of experienced clinicians.<sup>18,19</sup> Therefore, it is crucial to develop a simple and reliable method that combines demographic characteristics, clinical manifestations, and common laboratory findings. This approach would assist clinicians in differentiate between TS and BS, minimize misdiagnosis, alleviate patient suffering and enable timely intervention.

In this study, we developed a differential diagnosis model to distinguish between TS and BS. Initial laboratory and examination results obtained at the time of admission were selected to minimize heterogeneity and enhance model performance, incorporating a total of 45 variables. Key variables were identified using LASSO regression, and a predictive model was constructed and visualized through logistic regression. This model identified four predictors

closely associated with TS: time from symptom onset to admission, anorexia, ADA levels, and psoas abscess. Validation results showed that the model exhibited strong discriminatory and calibration performance. Decision curve analysis (DCA) further confirmed that the model effectively differentiates between TS and BS, providing a net clinical benefit with high applicability. Additionally, the data required for the model are relatively easy to obtain, enabling timely and accurate diagnostic support for clinicians. This makes the model particularly well-suited for primary hospitals, aiding in the accurate diagnosis of tuberculosis and brucellar spondylitis.

Several studies have indicated that individuals aged between 50 and 60 years are more likely to develop infectious spondylitis.<sup>20–22</sup> The mean age of patients in both groups in this study was over 50 years, which is consistent with previous findings, suggesting that infectious spondylitis is more prevalent among middle-aged and older populations. The significant differences in age, gender, and ethnicity between the patient groups may have influenced the study results. The notable gender disparity between TS and BS patients in this study is in line with a previous study conducted in a northwestern Chinese population, where the authors attributed the difference to potential sampling error.<sup>12</sup> In the BS group, the population engaged in animal husbandry and farming in southern Xinjiang is predominantly male, with increased exposure to diseased animals, thereby raising the risk of infection. The BMI of patients in the TS group was significantly lower than that of the BS group, which aligns with the findings of the previously mentioned study. Another study also showed that the BMI of patients with tuberculous epididymitis was significantly lower than that of patients with bacterial epididymitis.<sup>23</sup> This may be explained by the fact that the BS group in this study predominantly consisted of men, who generally have a higher BMI than women. Additionally, TS patients in this study typically had a longer disease duration, which may lead to increased body depletion and malabsorption of nutrients due to symptoms such as prolonged low-grade fever and night sweats, thereby reducing their BMI.

Considering the different transmission routes and mechanisms of infection, *Mycobacterium tuberculosis* is primarily transmitted through the respiratory tract and is typically associated with reduced immune defenses and increased susceptibility to infection.<sup>13</sup> Its infection process is generally insidious, progressing slowly over time. In our study, we observed that the time from symptom onset to admission was significantly longer in TS, with over 40% of TS patients reporting a disease duration exceeding one year, compared to the shorter disease course observed in BS. In contrast, *Brucella* is primarily transmitted through contact with infected animals or the consumption of contaminated animal products. Its acute or subacute onset, characterized by systemic effects such as fever, anorexia, and joint pain, often prompts patients to seek medical attention at an earlier stage.<sup>11</sup> These findings align with those of Bosilkovski et al<sup>24</sup> who demonstrated that the median duration from symptom onset to diagnosis in BS was 45 days. Similarly, AlQahtani et al<sup>25</sup> reported a longer symptom duration in TS compared to BS. Most BS patients in our study also presented in the acute or subacute phases, further supporting the view that BS generally has a shorter disease course.<sup>26</sup> This contrast highlights the gradual onset and chronic progression of TS. Nevertheless, further research is needed to explore the specific role of this indicator in differentiating between these two diseases to better guide clinical practice.

Magnetic resonance imaging (MRI), a well-established technique widely used in spine imaging, has become the test of choice for spinal infections due to its excellent sensitivity, specificity, and accuracy.<sup>18,27</sup> In our study, more than half of the BS cases involved the lumbar vertebrae, while over 70% of TS cases involved the thoracolumbar vertebrae. Consistent with our findings, Turunc et al<sup>28</sup> also reported that thoracic vertebra involvement and psoas abscess formation were more common in TS than in BS. Additionally, Li et al<sup>18</sup> and Colmenero et al<sup>29</sup> found that thoracic vertebra involvement was more frequent in TS than in BS. Previous studies have demonstrated that MRI is highly accurate in differentiating TS from BS.<sup>30</sup> Our study further confirms that the presence of a psoas abscess is an important predictor for distinguishing TS from BS, consistent with previous findings.<sup>12,31</sup>

Adenosine deaminase (ADA) is a key enzyme in purine metabolism, predominantly located in the thymus, spleen, and lymphoid tissues. It converts adenosine to inosine and plays a crucial regulatory role in the development and maturation of the immune system as well as in the activity of immune cells.<sup>32,33</sup> Additionally, ADA is involved in the proliferation and differentiation of lymphocytes. When pathogens trigger a cell-mediated immune response, T cells are activated and release ADA. Monitoring ADA levels can thus serve as an indirect indicator of the immune system's status and T-cell activity.<sup>34</sup> Consequently, ADA assays in body fluids, such as pleural effusion and cerebrospinal fluid, have been widely used as an adjunctive diagnostic test for tuberculous pleurisy and meningitis.<sup>34–37</sup> This study showed that

ADA levels below 14.95 U/L (cut-off value) were more indicative of TS, whereas levels exceeding this threshold were more suggestive of BS. This discrepancy may be attributed to higher peripheral blood lymphocyte levels in BS compared to TS, leading to a concomitant increase in ADA levels. Currently, there are no reports on the application of ADA in diagnosing tuberculous spondylitis, and further in-depth studies are warranted.

In a related study, a diagnostic model differentiating TS from BS was developed and integrated into an Excel-based calculator.<sup>12</sup> This model incorporated imaging and laboratory data and utilized machine learning algorithms. While this represents an innovative approach, our study offers a distinct advantage by focusing on clinical features and laboratory markers that are more accessible in resource-limited settings. Our nomogram demonstrates superior diagnostic accuracy, highlighting the robustness and reliability of our model despite its simpler methodology. Furthermore, the intuitive and user-friendly nature of our nomogram facilitates its potential integration into routine clinical practice, offering a practical tool for primary hospitals, particularly in underdeveloped regions. By identifying TS from BS early, the model could assist clinicians in focusing on targeted diagnostic tests, such as specific serologies, thereby enhancing diagnostic efficiency. It may also provide preliminary support for initiating empiric therapy based on predictions while awaiting definitive results from cultures or serologies. This approach could help prevent disease progression and ensure appropriate treatment.

This study has the following limitations: (1) it is a retrospective study; (2) it is a single-center study with a small sample size; (3) there is a lack of an external dataset to validate the model. Future prospective studies with larger sample sizes and involving multiple centers are needed for further validation.

#### Conclusions

In conclusion, we developed a differential diagnostic model to distinguish between tuberculous spondylitis and brucellar spondylitis. Our findings identified key variables, including the duration from symptom onset to admission, anorexia, ADA levels, and the presence of a psoas abscess, as significant contributors to the differentiation. The nomogram model demonstrated robust discrimination and reliable predictive performance, suggesting its potential utility in clinical practice.

### **Data Sharing Statement**

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

# **Ethics Approval**

This study was approved by the Ethics Committee of the First People's Hospital of Kashi Prefecture, identified by the approval code: [2024] KUAISHENYAN No.60. Informed consent was obtained from all subjects and/or their legal guardians for participation in this study.

### **Author Contributions**

Maimaitiyibubaji Abudukadier, Yuxin Zhang and Maozhao Li have contributed equally to this work, and shared first authorship. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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### Disclosure

The authors declare no competing interests.

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