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Diagnostic value of neutrophil-to-lymphocyte ratio, fibrinogen-to-albumin ratio and red blood cell distribution width in tuberculosis combined with other bacterial infections

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Abstract

Objective To investigate the clinical significance of the neutrophil-to-lymphocyte ratio (NLR), fibrinogen-to-albumin ratio (FAR), and red blood cell distribution width (RDW) in pulmonary tuberculosis (PTB) associated with other bacterial lung infections.

Methods A total of 74 patients with PTB complicated with other bacterial lung infections, who were admitted to the Sixth People's Hospital of Nantong City (Nantong, China) from January 2021 to December 2023, were included in this study as the PTB with infection complication group. A comparison group of 96 patients with uncomplicated PTB, admitted to the same hospital during the same period, was used as the PTB without infection complication group. The NLR, FAR, and RDW values in peripheral blood were determined and compared between the two groups. The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic performance of these indicators for early detection of PTB complicated with other bacterial infections.

Results The NLR, FAR, and RDW values were significantly higher in the PTB with infection complication group compared to the PTB without infection complication group, with differences reaching statistical significance ($P < 0.05$). NLR value showed a positive correlation with white blood cell count, C-reactive protein levels, and D-dimer levels. ROC curve analysis indicated that the area under the curve (AUC) values for diagnosing PTB with bacterial infection using blood NLR, FAR, and RDW were 0.861, 0.818, and 0.799, respectively. The combined AUC value of these three indicators was 0.982. The validation results showed that the diagnostic sensitivity (98.6%) and specificity (89.58%) of the combination of NLR, FAR, and RDW were higher than those of each indicator alone.

Conclusion The combined assessment of blood NLR, FAR, and RDW values has high clinical diagnostic value for diagnosing PTB complicated with other bacterial infections.

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Keywords Tuberculosis, Bacterial infection, Neutrophils, Lymphocytes, Fibrinogen, Albumin, Red blood cell distribution width

Background

Pulmonary tuberculosis (PTB) is a common infectious disease of the lungs caused by *Mycobacterium tuberculosis*(*Mtb*) [1].*Mtb* infected one-third of the population in 2021, producing disease in approximately 10% and killing 1.6 million people [2].Co-infections involving tuberculosis(TB) and bacterial pathogens have been reported, particularly in populations with a high prevalence of TB [3].There is a significant increase in susceptibility to PTB and the risk of death among individuals aged 65 and over [4]. Elderly patients with PTB have poor physique, low immunity, and chronic consumption of PTB, so they are more likely to be complicated by pulmonary bacterial infection [5].Distinguishing between TB and co-infections involving bacterial pathogens presents a significant clinical challenge [6]. Failure to differentiate these conditions may result in poorer health outcomes, including increased healthcare costs, antimicrobial resistance, and higher mortality rates [3, 7]. Clinical observations indicate that PTB is often complicated with pulmonary bacterial infections, but they are difficult to identify using conventional diagnostic methods. This is especially true for patients with bacterial-negative PTB, which presents diagnostic challenges due to atypical imaging findings and prominent fever, along with abnormal laboratory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), D-dimer(DD), and white blood cell count(WBC). Currently, diagnosis is primarily based on empirical anti-infective treatment or a combination of anti-tuberculosis and anti-infective therapies, followed by assessment of lesion absorption through chest X-ray and computed tomography scans. This approach may result in irrational use of drugs use and delayed patient recovery [8, 9].Therefore, there is a pressing need to develop a rapid and accurate diagnostic test for TB. Neutrophil-to-lymphocyte ratio (NLR), fibrinogen-to-albumin ratio (FAR), and red blood cell distribution width (RDW) have been identified as emerging biomarkers for evaluating the severity of inflammation [10–12]. Given that these ratios are easily and rapidly measured, a growing number of studies have focused on these indicators. Significant alterations in NLR, FAR, and RDW have been well-documented in various common acute and chronic diseases, including neoplasms [13–15], cardiovascular diseases [16, 17]. These biomarkers have garnered attention as potential diagnostic indicators capable of aiding in risk assessment and clinical decision-making.However, fewer studies have systematically examined the value of NLR, FAR, and RDW in the differential diagnosis of TB with concurrent bacterial infection. Therefore, this study aims to investigate the diagnostic value of NLR, FAR, and RDW in patients with TB and concurrent bacterial infection, and to provide a more accurate and reliable foundation for the differential diagnosis and individualized treatment of these patients.

Methods

Case selection

This study included 74 PTB patients complicated with bacterial infection, admitted to the Sixth People's Hospital of Nantong City (Nantong, China) between January 2021 and December 2023. In addition, 96 patients diagnosed with PTB without complications during the same period were included as the uncomplicated group. The inclusion criteria were as follows: [1] diagnosed with PTB based on clinical, radiographic, and microbiological findings; and [2] for the complication group, confirmed bacterial lung infection according to the Infectious Diseases Society of America/American Thoracic Society criteria [18]. The exclusion criteria were: [1] co-infections with viruses (e.g., HIV, HBV, HCV, influenza) or fungi (e.g., invasive candidiasis, aspergillosis); [2] a history of malignancies or immunosuppressive therapy (e.g., long-term corticosteroids, chemotherapy); [3] severe organ failure, such as end-stage renal disease or decompensated liver cirrhosis; and [4] missing critical clinical or laboratory data.

Severity classification

Severity classification was based on the Acute Physiology and Chronic Health Evaluation (APACHE) II score, which includes acute physiology score, age score, and chronic health score, with a total score of 0–71 points. Higher scores indicate more severe conditions. Patients were classified into two groups: a severe group (APACHE II score > 15, $n = 21$) and a non-severe group (APACHE II score ≤ 15, $n = 53$). This cutoff was chosen based on clinical practice [19], where an APACHE II score above 15 is commonly associated with increased disease severity and worse prognosis in critically ill patients.The study protocol was approved by the Ethics Committee of the Sixth People's Hospital of Nantong City (NTLYLL2024009). All patients provided written informed consent prior to participation in the study.

Sample size calculation

The sample size was estimated using PASS software (NCSS, LLC, Kaysville, UT, USA) to ensure adequate statistical power (≥ 80%) for detecting differences in NLR, FAR, and RDW between groups with an alpha level of

0.05. The calculation was based on preliminary data, with an expected effect size of 0.6 for NLR differences. The estimated minimum sample size required was 70 patients per group. To account for potential dropout, we recruited 74 and 96 patients in the complication and uncomplicated groups, respectively.

Baseline matching

To minimize potential bias, a propensity score matching (PSM) approach was applied, matching patients in both groups based on age, gender, and key laboratory parameters. The standardized mean difference (SMD) was used to assess the balance of covariates before and after matching.

Laboratory analysis

Fasting blood samples (5mL) were collected from the antecubital vein of patients in both groups in the early morning, placed in a procoagulation tube, and centrifuged at 3,000 rpm for 10 minutes to obtain the serum. The serum (supernatant) was then collected and stored at -80 °C for later measurement of albumin(AIB) levels using a Beckman AU5800 Biochemical Analyzer (Beckman Coulter Inc., Brea, CA, USA). Neutrophils, lymphocytes, and RDW were measured using a Mindray BC-6900 Automated Blood Cell Analyzer (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). Fibrinogen (FIB) levels were measured using a Sysmex® CS5100™ Automated Blood Coagulation Analyzer (Sysmex Corporation, Kobe, Japan). The NLR and FAR values were calculated based on the test results.

Machine learning algorithms to construct PTB without infection complication and PTB with infection complication diferential diagnostic models

We used the R package "autoReg" to perform statistical analysis on the expression levels of NLR, FAR, and RDW in patients with PTB with and without infection complications. Specifically, subgroup analysis was conducted using the presence or absence of infection complications as the observation indicator. Normally distributed variables were expressed as mean ± standard deviation, and intergroup differences were analyzed using the t-test ($P < 0.05$). Non-normally distributed variables were presented as median (IQR), with intergroup differences assessed using the Wilcoxon test ($P < 0.05$). Based on these analyses, we constructed a logistic regression model using the R package "glmnet" and performed univariate, multivariate, and stepwise logistic regression analyses using "autoReg". Additionally, we utilized the R package "mlr3" to develop 15 machine learning models. To comprehensively evaluate the diagnostic performance of these models, we assessed them using 19 evaluation indicators derived from the confusion matrix. The results from multiple models and indicators were visualized using the Origin 2021 for heatmap representation.

Data analysis

Data were analyzed using the SPSS version 17.0 software (IBM Corporation, Armonk, NY, USA). Normally distributed data are expressed as the mean ± standard deviation. Comparisons between two groups were performed using a paired t-test, and correlations between variable were assessed by Pearson correlation analysis. Categorical variables were compared using the chi-square (χ^2) test. Rates were compared using Fisher's exact test. Logistic regression analysis was performed to calculate the probability of joint diagnosis using NLR, FAR, and RDW. The Receiver Operating Characteristic (ROC) curve was plotted, and the area under the curve (AUC) was calculated to evaluate the diagnostic performance of NLR, FAR, and RDW in detecting PTB complicated with bacterial infection. P value < 0.05 was considered statistically significant.

Results

Comparison of general clinical data between two groups

There was no statistically significant difference between the PTB with infection complication group and the PTB without infection complication group in terms of age, sex ratio, hypertension, diabetes mellitus, and smoking history with t/x^2 values of 0.019, 1.935, 3.534, 0.554, and 0.003, respectively, $P > 0.05$)(Table 1).

Correlation analysis of blood NLR, FAR, RDW values and various clinical indicators

RDW value was positively correlated with CRP, DD, ESR, and FER values in 170 patients in the PTB without infection complication group and PTB with infection complication group($P < 0.05$).NLR value was positively correlated with WBC, CRP, and DD values($P < 0.05$). FAR value was positively correlated with WBC, PLT, CRP, DD, ESR, and FER values ($P < 0.05$). NLR value was highly positively correlated with WBC values ($r = 0.614$, $P < 0.01$),and procalcitonin (PCT) value was not correlated with RDW, NLR, and FAR values ($P > 0.05$)(Table 2).

Comparison of NLR, FAR, and RDW values between the two groups

The NLR, FAR, and RDW values in the PTB with infection complication group were 6.204(4.328,9.348),0.145(0.120,0.192),and 14.400(13.200,15.625),respectively, while in the PTB without infection complication group, the values were 2.726(2.159, 3.821), 0.095(0.071, 0.126), and 12.800(12.200, 13.400), respectively. These differences were statistically significant ($P < 0.001$) (Table3).

Table 1 Comparison of clinical characteristics between the PTB with infection complication group and PTB without infection complication group

Data	Group			
	PTB without infection complication group (number = 96)	PTB with infection complication group (number = 74)	t/x^2	*P*
Age(year)	62.52 ± 7.638	67.51 ± 8.10	0.019	0.891
Sex				
Male	69(71.9)	60(81.1)	1.935	0.206
Female	27(28.1)	14(18.9)		
Pulse(times/min)	80.18 ± 12.77	82.04 ± 13.70	0.914	0.367
Breathing(times/min)	17.90 ± 2.38	18.62 ± 2.83	1.772	0.078
Systolic pressure(mmHg)	126.27 ± 15.09	127.15 ± 24.31	0.273	0.785
Diastolic pressure(mmHg)	78.01 ± 9.98	76.05 ± 15.69	-0.936	0.351
Hypertension				
Yes	19(19.8)	24(32.4)	3.534	0.075
No	77(80.2)	50(67.6)		
Diabetes				
Yes	20(20.8)	19(25.7)	0.554	0.468
No	76(79.2)	55(74.3)		
Smoking				
Yes	23(24.0)	18(24.3)	0.003	0.958
No	73(76.0)	56(75.7)		
Drink				
Yes	15(15.6)	12(16.2)	0.011	0.917
No	81(84.4)	62(83.8)		
Hemoptysis				
Yes	26(27.0)	16(21.6)	0.676	0.414
No	70(73.0)	58(78.3)		
Fever				
Yes	14(14.6)	14(18.9)	0.567	0.451
No	82(85.4)	60(81.1)		

Table 2 Correlations of NLR, FAR, and RDW with clinical characteristics of the patients

Index	RDW		NLR		FAR	
	r	*p*	*r*	*p*	*r*	*p*
WBC	0.149	0.138	0.614	< 0.001	0.381	< 0.001
HB	-0.4 99	< 0.001	-0.257	0.009	-0.291	0.03
PLT	-0.003	0.976	0.205	0.039	0.437	< 0.001
CRP	0.355	< 0.001	0.555	< 0.001	0.584	< 0.001
DD	0.262	0.008	0.318	0.001	0.299	0.002
ESR	0.318	0.001	0.163	0.104	0.676	< 0.001
PCT	0.164	0.101	0.122	0.223	0.135	0.178
FER	0.200	0.045	0.132	0.101	0.398	< 0.001

Note: WBC, white blood cell count; HB, hemoglobin; PLT, platelet; CRP, C-reactive protein; DD, D-dimer; ESR, erythrocyte sedimentation rate; PCT, procalcitonin,; FER, Ferritin

Table 3 Comparison of laboratory indicators between the PTB with infection complication group and PTB without infection complication group

Group	*n*	RDW(%)	NLR	FAR
PTB with infection complication group	74	14.400(13.200,15.625)	6.204(4.328,9.348)	0.145(0.120,0.192)
PTB without infection complication group	96	12.800(12.200,13.400)	2.726(2.159,3.821)	0.095(0.071,0.126)
Z		-6.709	-8.059	-7.091
P		< 0.001	< 0.001	< 0.001

Table 4 Comparison of NLR, FAR, and RDW values between the severe group and non-severe group

Index	Severe group(number = 21)	Non-severe group(number = 53)	Z	*P*
RDW(%)	15.600(14.500,16.900)	14.100(12.900,15.100)	-3.455	< 0.001
NLR	9.878(7.171,13.918)	5.081(3.829,8.203)	-3.999	< 0.001
FAR	0.186(0.144.0.268)	0.138(0.113,0.167)	-3.903	< 0.001

Table 5 ROC curve of diagnostic efficacy of the NLR, FAR, and RDW in patients with PTB complicated with other bacterial infections

Index	Cut-off Value	Sensitivity/%	Specificity/%	Youden index/%	AUC	Positive likelihood ratio(%)	Negative likelihood ratio(%)	95% confidence interval
RDW	12.850	86.50	69.79	56.29	0.799	2.86	19.34	0.730–0.869
NLR	4.261	78.40	83.33	61.73	0.861	4.70	25.92	0.803–0.919
FAR	0.107	89.20	66.66	55.86	0.818	2.67	16.20	0.755–0.881
Combineddiagnosis		98.60	89.58	88.18	0.982	9.46	1.56	0.968–0.996

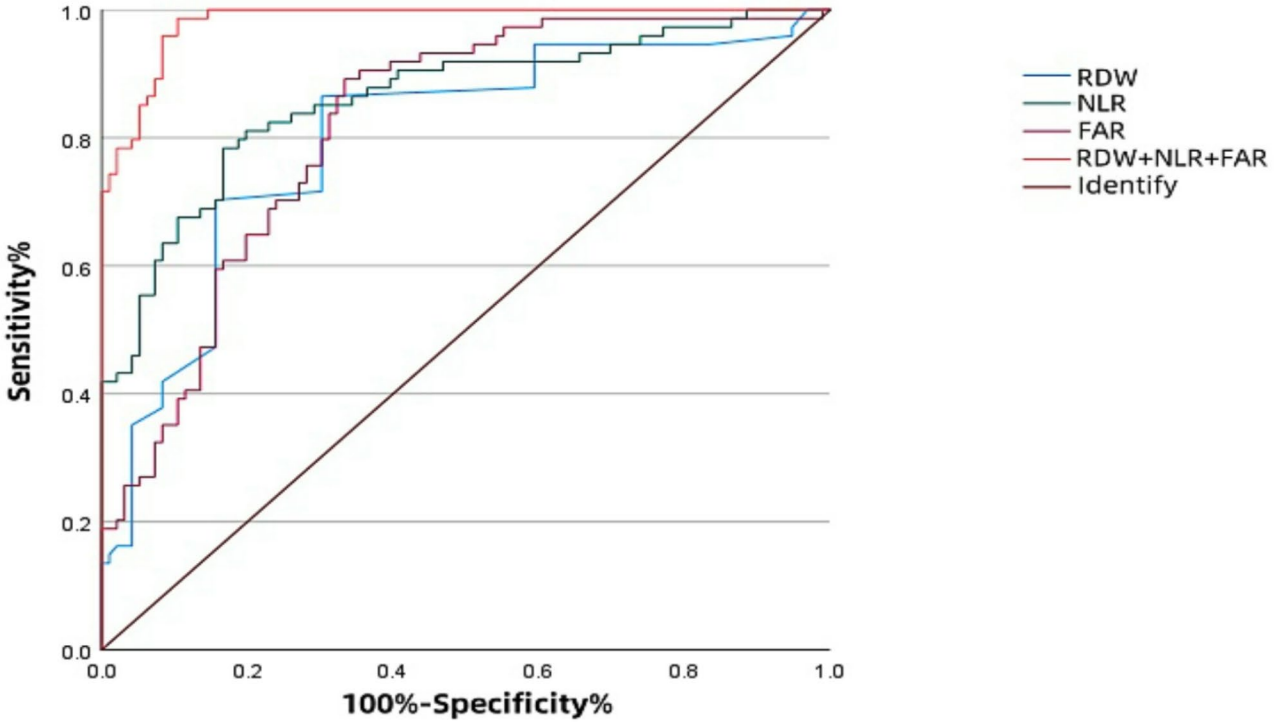

Fig. 1 ROC curve of the diagnostic efficacy of NLR, FAR, and RDW in patients with PTB complicated with other bacterial infections

Serum NLR, FAR, and RDW values in the severe group and non-severe group

The NLR, FAR, and RDW values in the severe group were higher than those in the non-severe group($P < 0.05$,Table 4).

Clinical significance of NLR, FAR, and RDW values in the diagnosis of PTB complicated with other bacterial infections

The results of the ROC curve showed that the AUC value of NLR was 0.861, its Youden index was 0.617, sensitivity was 0.784, and specificity was 0.833; the AUC value of FAR was 0.818, its Youden index was 0.559, sensitivity was 0.892, and specificity was 0.667; the AUC value of RDW was 0.799, its Youden index was 0.563, sensitivity was 0.865, and specificity was 0.698. Additionally, the AUC value of the combination of NLR, FAR and RDW was 0.982, its Youden index was 0.882, sensitivity was 0.986, and specificity was 0.896 (Table 5; Fig. 1).

P TB with infection complication group and PTB without infection complication group diferential diagnostic model based on 15 machine learning algorithms

We performed univariate, multivariate, and stepwise logistic regression analyses on the expression levels of NLR, FAR, and RDW in patients with PTB with and without infection complications using the R package "autoReg" to identify potential models for distinguishing

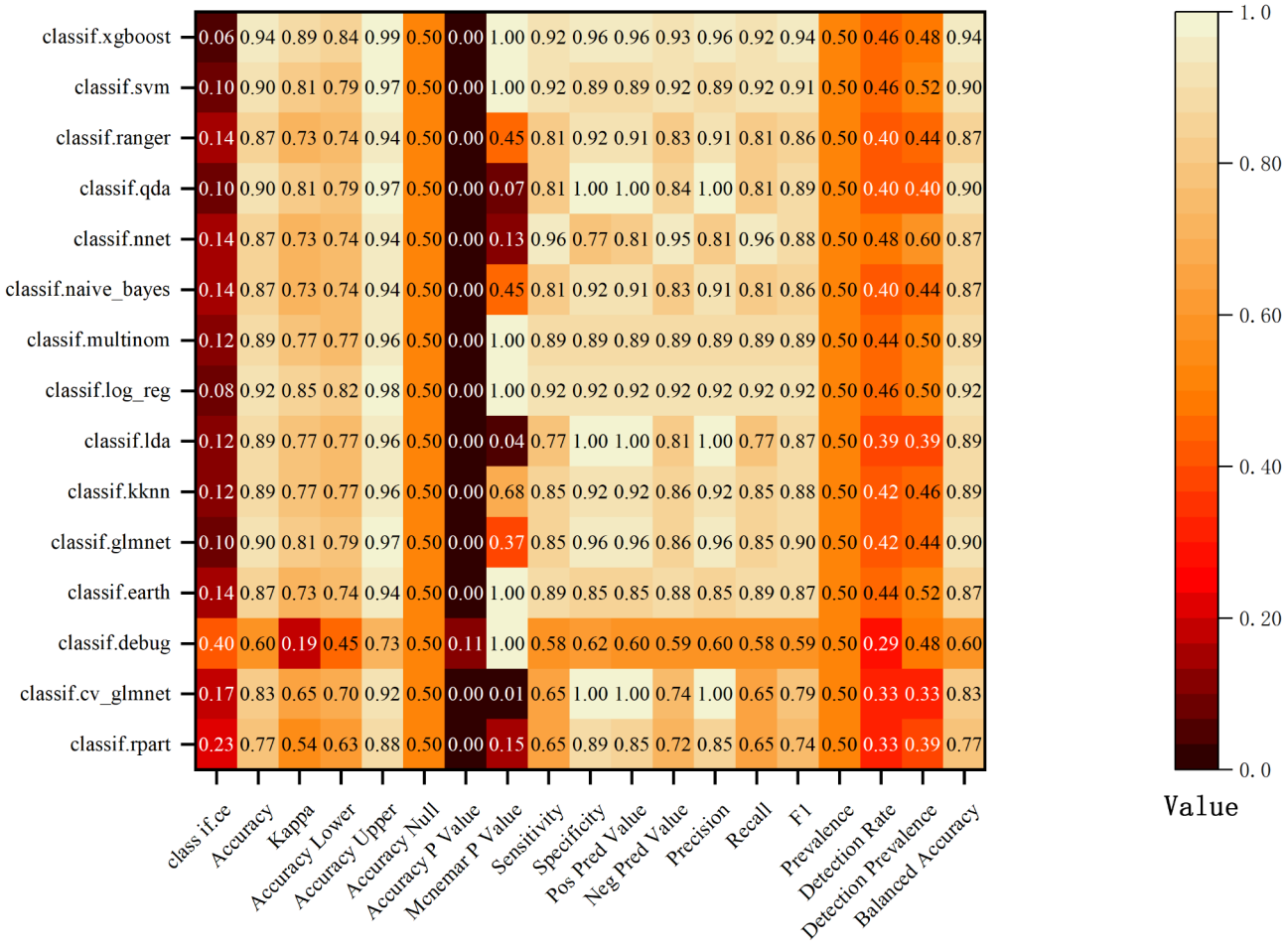

Fig. 2 Performance of 15 machine learning models for the combined diagnosis of pulmonary tuberculosis with other bacterial infections using NLR, FAR, and RDW

between these two groups. These three indicators were then incorporated into the machine learning model. Table S1 provides detailed results for 15 machine learning models and 19 diagnostic performance indicators, while Fig. 2 presents a heatmap of the data.Among the models evaluated, Extreme Gradient Boosting (XGBoost) was selected as the optimal model due to its superior diagnostic performance (Classif. ce = 0.057692, Accuracy = 0.94231, Kappa = 0.88462, Accuracy Lower = 0.84053, Accuracy Upper = 0.98794, Accuracy Null = 0.50000, Accuracy *P* Value = 0.00002, McNamara *P* Value = 1.0000, Sensitivity = 0.92308, Specificity = 0.96154, Positive Predictive Value = 0.96000, Negative Predictive Value = 0.92593, Precision = 0.96000, Recall = 0.92308, F1 = 0.94118, Prevalence = 0.50000, Detection Rate = 0.46154, Detection Prevalence = 0.48077, and Balanced Accuracy = 0.94231).

Discussion

Currently, PTB remains one of the major infectious diseases posing a serious threat to global public health. When the airway of elderly patients with PTB is reconstructed after repeated inflammation, the mucosal barrier is destroyed and the function of clearing bacteria is reduced, which leads to the susceptibility of pulmonary bacterial infection in elderly patients with PTB. However, its clinical signs are often atypical, especially similar to the clinical signs and symptoms of primary TB infection, which is easy to be ignored, resulting in prolonged course of disease, affecting the quality of life of patients, and may endanger the lives of patients.Bacterial culture is considered the gold standard for diagnosing bacterial infections, but it has certain limitations, primarily it is costly and time-consuming [20, 21]. Co-infections in elderly patients with TB often lead to misdiagnosis or underdiagnosis due to the lack of effective diagnostic and therapeutic approaches. As such, This search for biomarkers to enable the early and rapid diagnosis of PTB combined with another bacterial infection remains a central concern for clinicians.

The NLR is the ratio of peripheral blood neutrophil count to lymphocyte count.Neutrophils and lymphocytes not only reflect the role of neutrophils in infection, but

also reflect the changes in lymphocyte counts in vivo to identify the type of pathogens in time.The NLR is a low-cost, routinely used, reproducible assay available from leukocyte counts and has been shown to be a marker of systemic inflammatory response [22]. This study showed that the NLR value in the PTB with infection complication group was significantly higher than that in the PTB without infection complication group ($P<0.05$), and the NLR value in the severely ill patients in the PTB with infection complication group was higher than that in the non-severely ill patients($P<0.05$), which was also consistent with the results of a study by Nagai et al. [23], suggesting that NLR was related to PTB complicated with bacterial infection complication. The NLR is a simple and effective indicator of body inflammation. When bacterial infection occurs in the body, its level can rapidly increase to resist bacterial invasion. In the process of infection, dendritic cells can present antigens to natural killer T cells, leading to local extravasation of neutrophils, thereby promoting the entry of natural killer T cells into tissues and affecting peripheral blood lymphocyte counts [24].During the inflammatory response to TB, neutrophils and other inflammatory cells, such as macrophages, accumulate in large numbers to counteract the invasion of *Mtb* [25]. Studies have shown that the number of neutrophils in patients with PTB is significantly increased and is associated with disease severity [26]. When TB patients are co-infected with other bacteria, the existing inflammatory response is further intensified, leading to the release of more neutrophils to the infection site for antimicrobial action [27, 28]. TB infection can impair the immune system, leading to reduced lymphocyte function [29]. Bacterial infections may cause immunosuppression or immune tolerance. In cases of long-term chronic inflammation, lymphocyte function may be suppressed [30].Therefore, the NLR can better dynamically reflect the infection status.The NLR is a reliable predictor of inflammation and increases with the progression of some chronic diseases. Studies have shown that an increased NLR may be a predictor of clinical outcomes in a variety of diseases, including *Mycoplasma pneumoniae* pneumonia [31], large lymph node masses [32], etc. When the NLR was used alone as a variable, the AUC of the NLR for the diagnosis of PTB with bacterial infection complication was 0.861 ($P<0.001$), the sensitivity was 78.4%, and the specificity was 83.33%. These results suggest that the NLR can be used as an early independent factor for the diagnosis of PTB with bacterial infection complication, with high sensitivity and specificity.

RDW is a parameter that reflects the heterogeneity of the red blood cell volume. Previous studies have suggested that RDW may be a laboratory indicator of infection or inflammation [33, 34]. Mao et al.. reported that when the respiratory tract was infected by various pathogens, the RDW value would change abnormally, which was found to be related to the changes of WBC, PLT and creatinine. It has been suggested that the RDW value may reflect the course of respiratory diseases [35]. A study by Wang et al.. found that RDW may be a promising indicator for predicting severe liver inflammation in autoimmune hepatitis. And it is positively correlated with the severity of liver inflammation [36]. This study found that the RDW value of the PTB with infection complication group was significantly higher than that of the PTB without infection complication group ($P<0.05$), the RDW value of the severely ill patients in the PTB with infection complication group was higher than that of the non-severely ill patients in the PTB with infection complication group ($P<0.05$). During bacterial infection, the inflammatory response is excessively activated, and a large number of pro-inflammatory factors released during this process reduce the maturation of red blood cells by inhibiting the maturation factor of red blood cells, so that a large number of immature red blood cells are released into the blood, the heterogeneity of red blood cell size is increased, and ultimately the RDW value in peripheral blood is increased [37]. Bacterial infections can enhance oxidative stress, leading to excessive production of reactive oxygen species (ROS). These ROS can damage the erythrocyte membrane, reduce its deformability, and shorten its lifespan [38, 39]. TB patients often experience anemia, which may be exacerbated by chronic inflammation. Chronic inflammation inhibits iron utilization by regulating hepcidin in the liver, resulting in ineffective erythropoiesis [40]. To compensate for the loss of red blood cells, the bone marrow releases erythrocytes of varying shapes into circulation, leading to an increased RDW. In addition, the RDW value was positively correlated with CRP, DD, ESR, and FER ($P<0.05$). RDW had a sensitivity of 86.5%, a specificity of 69.79%, and an AUC of 0.799 in the screening of early PTB with other bacterial infection complication. These findings suggested that RDW can be used as a potential inflammatory index to evaluate the changes of PTB with other bacterial infection complication. However, its specificity is low for early screening. Therefore, whether RDW can be used to evaluate the severity and prognosis of PTB with other bacterial infection complication requires follow-up multi-center studies, including a larger number of patients. In view of the fact that RDW is a simple, convenient, low cost and easy to detect clinical indicator, it is worth further study to determine its potential value and provide reference for clinicians.

This is the first retrospective study of FAR in TB. The FIB not only plays a key role in the process of coagulation, but also has an important roles in the inflammatory response and tumor metastasis and progression [41]. The ALB enhances catabolism to combat inflammation.The

FAR is a ratio of FIB and ALB levels that can be used as a potential prognostic biomarker to predict the risk of various diseases.In this study, we found that FAR values were significantly higher in the PTB with infection complication group than in the PTB without infection complication group.The FAR was higher in severely ill patients than in non-severely ill patients. This finding is consistent with that reported by Torun et al. [42].The reason may be that when a bacterial infection occurs, in order to fight against bacteria, the inflammatory response in the body is rapidly activated, resulting in a rapid increase in the content of FIB [43]. Furthermore, the ALB also plays a role in the regulation of inflammatory cells. In the inflammatory state, the increase of microvascular permeability affects the distribution of intravascular and extravascular ALB, which leads to the decrease of the serum ALB concentration [44].Patients with PTB often exhibit coagulation abnormalities, which may be exacerbated by concurrent bacterial infections, leading to a further increase in FIB levels. Studies have shown that FIB synthesis in the septic liver occurs at a significantly higher rate than ALB synthesis, indicating a shift in hepatic protein metabolism toward pro-inflammatory protein production during inflammation [45], This finding is consistent with the results of the present study.The FAR also plays an important role in the prognosis of many diseases in clinical practice. For example, in a cross-sectional study of 650 patients with acute coronary syndrome after percutaneous coronary intervention, the results showed that the AUC of the ROC curve of the FAR predicting left ventricular systolic dysfunction (LVSD) was 0.735. Thus, admission FAR is an independent predictor of LVSD in acute coronary syndromes patients undergoing percutaneous coronary intervention [46]. A study by Wang et al.. showed that FAR measured before admission may be a useful indicator for assessing acute kidney injury, with an AUC of the ROC curve of 0.685 [47]. Another study showed that the FAR was closely related to the occurrence of diabetic retinopathy (DR) in type 2 diabetes mellitus (T2DM) patients, and the AUC of the ROC curve of the FAR predicting the progression of DR was 0.708 [48].In addition, ROC curve analysis showed that FAR had a sensitivity of 89.20%, a specificity of 66.66%, and an AUC of 0.818 in the diagnosis of PTB with other bacterial infection complication, and its diagnostic efficacy was higher than that of RDW and lower than that of NLR. In addition, Pearson correlation analysis revealed that the FAR value was positively correlated with the WBC, PLT, CRP, DD, ESR, and FER values ($P<0.05$). The above results indicate that the FAR is correlated with the laboratory indicators commonly used in the clinical assessment of infection. From the above findings, it can be concluded that NLR, FAR and RDW have some predictive value for the occurrence of PTB with bacterial infection complication. However, the combined AUC of the three factors for predicting PTB with bacterial infection complication was 0.982, with a sensitivity of 98.60% and specificity of 89.58%. The AUC of the ROC curve, sensitivity and specificity of NLR, FAR combined with RDW were higher than those of each alone, suggesting that NLR, FAR combined with RDW had a higher efficacy in predicting the incidence of PTB with bacterial infection complication. These three indicators provide insights into the body's physiological state from different perspectives. The NLR primarily reflects the immune response of leukocytes, the FAR integrates inflammation and nutritional status, and the RDW is associated with red blood cell production and distribution. By combining these indicators, a more comprehensive assessment of a patient's health status can be achieved. This approach is particularly valuable in complex diseases, such as cancer and infections, where a single indicator may not fully capture disease severity or prognosis.In clinical practice, blood routine, biochemistry and coagulation function are routinely tested on admission, which is economical, simple and easy, and the NLR, FAR and RDW are easy to measure. In conclusion, combined biomarkers have higher diagnostic power than individual biomarkers. Clinically, it is helpful to evaluate the risk of PTB with bacterial infection complication early, so as to provide timely clinical intervention and treatment.In this study, the ROC analysis was employed to assess the diagnostic performance of the NLR, the FAR, and RDW.

Machine learning methods utilize a large amount of manually labeled data to train models to learn the features of manually labeled data, and have proven their superiority in disease diagnosis, classification, and prognosis judgment [49].Previous research has demonstrated that models integrating multiple clinical and laboratory measures improve classification accuracy [50].The XGboost model performs well with a diagnostic accuracy of 0.93, sensitivity of 0.92, specificity of 0.96, and F1 score of 0.94.This demonstrates the potential diagnostic value of XGBoost model in distinguishing pulmonary tuberculosis complicated with bacterial infection.The 19 diagnostic indicators identified in this study contribute to the development of diagnostic models for future PTB cases, both with and without bacterial complications, providing a valuable reference for clinicians in diagnosing PTB complicated with other bacterial infections.

This study is a retrospective study based on prospective data. It has the limitations of single center and small sample size. This study included 74 patients with pulmonary tuberculosis complicated with bacterial infection, particularly in the severe group (21 cases) and non severe group (53 cases).The limited sample size may reduce statistical power, potentially affecting the stability and generalizability of the results [51]. Therefore, expanding the

sample size is essential for further validation.In addition, the subjects included in this study were not stratified by morbidity mechanism, and the results may be different. Future studies need to further study the changes of NLR, RDW and FAR values. The NLR, RDW and FAR are calculation indexes in blood routine analysis, which are cheap, simple and practical, and can be used as a new combination index in blood analysis and detection report, and can be popularized in medical institutions. Especially in primary medical institutions, it is very important to help identify and diagnose bacterial infections and reduce medical expenses.

Conclusion

In summary, the NLR, FAR and RDW indicators have some clinical reference value for the differential diagnosis of PTB combined with other bacterial infection complication.Additionally, the diagnostic value of the three combined tests is higher. Clinicians should closely monitor the changes in the NLR, FAR and RDW indexes to reduce the misdiagnosis rate and omission rate, increase the understanding of the disease condition of the patient, and to provide reference for the clinical use of drugs.

Abbreviations

PTB	Pulmonary tuberculosis
Mtb	*Mycobacterium tuberculosis*
TB	Tuberculosis
NLR	Neutrophil-to-lymphocyte ratio
FAR	Fibrinogen/albumin ratio
RDW	Red blood cell distribution width
AUC	Area under the curve
ROC	Receiver operating characteristic
LVSD	Left ventricular systolicdysfunction
ESR	Erythrocyte sedimentation rate
CRP	C-reactive protein
APACHE	Acute Physiology and Chronic Health Evaluation
ALB	Albumin
WBC	White blood cell
HB	Hemoglobin
PLT	Platelet
CRP	C-reactive protein
DD	D-dimer
PCT	Procalcitonin
FER	Ferritin
ROS	Reactive oxygen species
DR	Diabetic retinopathy
T2DM	Type 2 diabetes mellitus
XGBoost	Extreme Gradient Boosting

Supplementary Information

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Supplementary Material 1

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None.

Author contributions

HY F and HM Z designed the study; HY F and HM L collected data; WQ S and HY F analyzed and interpreted data; HY F and HM L drafted the article; HY Z and HM Z critically revised the article. All authors approved the final version of the manuscript.

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Data availability

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

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from Ethics Committee of the Sixth People's Hospital of Nantong, NTLYLL2024009, and written informed consent was obtained from all participants prior to inclusion in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Abebe F. Synergy between Th1 and Th2 responses during Mycobacterium tuberculosis infection: A review of current Understanding. Int Rev Immunol. 2019;38(4):172–9.
2. Preda M, Tănase BC, Zob DL, Gheorghe AS, Lungulescu CV, Dumitrescu EA et al. The bidirectional relationship between pulmonary tuberculosis and lung Cancer. Int J Environ Res Public Health. 2023;20(2).
3. Attia EF, Pho Y, Nhem S, Sok C, By B, Phann D, et al. Tuberculosis and other bacterial co-infection in Cambodia: a single center retrospective cross-sectional study. BMC Pulm Med. 2019;19(1):60.
4. Olmo-Fontánez AM, Scordo JM, Schami A, Garcia-Vilanova A, Pino PA, Hicks A, et al. Human alveolar lining fluid from the elderly promotes Mycobacterium tuberculosis intracellular growth and translocation into the cytosol of alveolar epithelial cells. Mucosal Immunol. 2024;17(2):155–68.
5. Resende M, Ferreira CM, Barbosa AM, Cardoso MS, Sousa J, Saraiva M, et al. Myeloid HIF-1α regulates pulmonary inflammation during experimental Mycobacterium tuberculosis infection. Immunology. 2020;159(1):121–9.
6. Heidary M, Shirani M, Moradi M, Goudarzi M, Pouriran R, Rezaeian T, et al. Tuberculosis challenges: resistance, co-infection, diagnosis, and treatment. Eur J Microbiol Immunol (Bp). 2022;12(1):1–17.
7. Shimazaki T, Taniguchi T, Saludar NRD, Gustilo LM, Kato T, Furumoto A, et al. Bacterial co-infection and early mortality among pulmonary tuberculosis patients in Manila, the Philippines. Int J Tuberc Lung Dis. 2018;22(1):65–72.
8. Yu H, Yang A, Derrick S, Mak JYW, Liu L, Fairlie DP, et al. Artificially induced MAIT cells inhibit M. bovis BCG but not M. tuberculosis during in vivo pulmonary infection. Sci Rep. 2020;10(1):13579.
9. Ordonez AA, Wang H, Magombedze G, Ruiz-Bedoya CA, Srivastava S, Chen A, et al. Dynamic imaging in patients with tuberculosis reveals heterogeneous drug exposures in pulmonary lesions. Nat Med. 2020;26(4):529–34.
10. Wang RH, Wen WX, Jiang ZP, Du ZP, Ma ZH, Lu AL, et al. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index

(SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Front Immunol. 2023;14:1115031.
11. Zhou XJ, Lu K, Liu ZH, Xu MZ, Li C. U-shaped relationship found between fibrinogen-to-albumin ratio and systemic inflammation response index in osteoporotic fracture patients. Sci Rep. 2024;14(1):11299.
12. Chen J, Wu Y, Zhao H, Ruan G, Qin S. Ratio of hemoglobin to red cell distribution width: an inflammatory predictor of survival in AIDS-related DLBCL. Front Immunol. 2024;15:1354325.
13. Zou H, Liu SH, Yang R, Wu XJ, Cao YP, Huang HF. Combination of Neutrophil-to-Lymphocyte ratio and red cell distribution width with serum tumor markers for the differential diagnosis of breast Cancer and its association with pathological features and molecular types. Clin Breast Cancer. 2022;22(4):e526–35.
14. Di Raimondo C, Caposiena Caro RD, Spallone D, Silvaggio D, Lombardo P, Del Duca E, et al. Baseline neutrophil/lymphocyte ratio (NLR) and red blood cell distribution width (RDW) correlate with advanced stages in cutaneous squamous cell carcinoma. Int J Dermatol. 2022;61(2):175–9.
15. Fu Y, Yu Y, Zhou Y, Li T, Xie Y, Wang Y, et al. The fibrinogen-albumin ratio as a novel prognostic factor for elderly patients with osteosarcoma. Med (Baltim). 2023;102(36):e34926.
16. Makkar K, Sharma YP, Batta A, Hatwal J, Panda PK. Role of fibrinogen, albumin and fibrinogen to albumin ratio in determining angiographic severity and outcomes in acute coronary syndrome. World J Cardiol. 2023;15(1):13–22.
17. Bodolea C, Hiriscau EI, Buzdugan EC, Grosu AI, Stoicescu L, Vesa Ş, et al. The association between peripheral blood cells and the frailty syndrome in patients with cardiovascular diseases. Endocr Metab Immune Disord Drug Targets. 2020;20(9):1419–33.
18. Olson G, Davis AM. Diagnosis and treatment of adults with Community-Acquired pneumonia. JAMA. 2020;323(9):885–6.
19. Tian Y, Yao Y, Zhou J, Diao X, Chen H, Cai K, et al. Dynamic APACHE II score to predict the outcome of intensive care unit patients. Front Med (Lausanne). 2021;8:744907.
20. Panhwar S, Keerio HA, Ilhan H, Boyacı IH, Tamer U, Principles. Methods, and Real-Time applications of Bacteriophage-Based pathogen detection. Mol Biotechnol. 2024;66(11):3059–76.
21. Li W. Prospective application of Aptamer-based assays and therapeutics in bloodstream infections. Mini Rev Med Chem. 2020;20(10):831–40.
22. Avcil S. Evaluation of the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume as inflammatory markers in children with attention-deficit hyperactivity disorder. Psychiatry Clin Neurosci. 2018;72(7):522–30.
23. Nagai Y, Yokogawa N, Shimada K, Sugii S. Utility of the neutrophil-to-lymphocyte ratio for predicting bacterial infection in patients with rheumatoid arthritis receiving Tocilizumab. Rheumatol Int. 2020;40(12):2039–46.
24. Zhao L, Yang X. Cross talk between natural killer T and dendritic cells and its impact on T cell responses in infections. Front Immunol. 2022;13:837767.
25. Kinsella RL, Kimmey JM, Smirnov A, Woodson R, Gaggioli MR, Chavez SM, et al. Autophagy prevents early Proinflammatory responses and neutrophil recruitment during Mycobacterium tuberculosis infection without affecting pathogen burden in macrophages. PLoS Biol. 2023;21(6):e3002159.
26. Ndlovu LN, Peetluk L, Moodley S, Nhamoyebonde S, Ngoepe AT, Mazibuko M, et al. Increased neutrophil count and decreased neutrophil CD15 expression correlate with TB disease severity and treatment response irrespective of HIV Co-infection. Front Immunol. 2020;11:1872.
27. Gopalakrishnan A, Dietzold J, Verma S, Bhagavathula M, Salgame P. Toll-like receptor 2 prevents Neutrophil-Driven immunopathology during infection with Mycobacterium tuberculosis by curtailing CXCL5 production. Infect Immun. 2019;87(3).
28. Sankar P, Ramos RB, Corro J, Mishra LK, Nafiz TN, Bhargavi G, et al. Fatty acid metabolism in neutrophils promotes lung damage and bacterial replication during tuberculosis. PLoS Pathog. 2024;20(10):e1012188.
29. Ma Z, Li S, Liu Y, Li C, Wang X, Tang X, et al. Serum lymphocytes and cytokines: diagnostic value and influence on the immune status in patients with pulmonary tuberculosis. J Bras Pneumol. 2023;49(5):e20230154.
30. Feng X, Classon C, Terán G, Yang Y, Li L, Chan S, et al. Atrophy of skin-draining lymph nodes predisposes for impaired immune responses to secondary infection in mice with chronic intestinal nematode infection. PLoS Pathog. 2018;14(5):e1007008.
31. Li D, Gu H, Chen L, Wu R, Jiang Y, Huang X, et al. Neutrophil-to-lymphocyte ratio as a predictor of poor outcomes of Mycoplasma pneumoniae pneumonia. Front Immunol. 2023;14:1302702.
32. Romano A, Pavoni C, Di Raimondo F, Tarella C, Viviani S, Rossi A, et al. The neutrophil to lymphocyte ratio (NLR) and the presence of large nodal mass are independent predictors of early response: A subanalysis of the prospective phase II PET-2-adapted HD0607 trial. Cancer Med. 2020;9(23):8735–46.
33. Bommenahalli Gowda S, Gosavi S, Ananda Rao A, Shastry S, Raj SC, Menon S, et al. Prognosis of COVID-19: red cell distribution width, platelet distribution width, and C-Reactive protein. Cureus. 2021;13(2):e13078.
34. Erken E, Ulgen C, Sarisik FN, Erken N, Gungor O, Altunoren O. Hematological parameters and clinical features in patients with advanced chronic kidney disease. Yonago Acta Med. 2020;63(4):353–9.
35. Mao S, Zang D, Wu L, Shi W, Wang X. Diagnostic and prognostic value of red blood cell distribution width in children with respiratory tract infections. Clin Lab. 2019;65(5).
36. Wang H, Wang J, Huang R, Xia J, Zuo L, Yan X, et al. Red blood cell distribution width for predicting significant liver inflammation in patients with autoimmune hepatitis. Eur J Gastroenterol Hepatol. 2019;31(12):1527–32.
37. Omer IM, Mohammed BAA. A study of red cell distribution width and neonatal sepsis at Soba university hospital, Khartoum, Sudan. Sudan J Paediatr. 2021;21(1):42–7.
38. Bandeira Junior G, Baldisserotto B. Fish infections associated with the genus Aeromonas: a review of the effects on oxidative status. J Appl Microbiol. 2021;131(3):1083–101.
39. Gwozdzinski K, Pieniazek A, Gwozdzinski L. Reactive oxygen species and their involvement in red blood cell damage in chronic kidney disease. Oxid Med Cell Longev. 2021;2021:6639199.
40. de Mendonça EB, Schmaltz CA, Sant'Anna FM, Vizzoni AG, Mendes-de-Almeida DP, de Oliveira RVC, et al. Anemia in tuberculosis cases: A biomarker of severity? PLoS ONE. 2021;16(2):e0245458.
41. Kwaan HC, Lindholm PF. Fibrin and fibrinolysis in Cancer. Semin Thromb Hemost. 2019;45(4):413–22.
42. Torun A, Çakırca TD, Çakırca G, Portakal RD. The value of C-reactive protein/albumin, fibrinogen/albumin, and neutrophil/lymphocyte ratios in predicting the severity of CoVID-19. Rev Assoc Med Bras (1992). 2021;67(3):431-6.
43. Yakovlev S, Strickland DK, Medved L. Current view on the molecular mechanisms underlying Fibrin(ogen)-Dependent inflammation. Thromb Haemost. 2022;122(11):1858–68.
44. Pérez MC, Fernández-Sarmiento J, Bustos JD, Ferro-Jackaman S, Ramírez-Caicedo P, Nieto A, et al. Association between the lactate-albumin ratio and microcirculation changes in pediatric septic patients. Sci Rep. 2024;14(1):22579.
45. Omiya K, Sato H, Sato T, Wykes L, Hong M, Hatzakorzian R, et al. Albumin and fibrinogen kinetics in sepsis: a prospective observational study. Crit Care. 2021;25(1):436.
46. Wang X, Hu Y, Luan H, Luo C, Kamila K, Zheng T, et al. Predictive impact of fibrinogen-to-albumin ratio (FAR) for left ventricular dysfunction in acute coronary syndrome: a cross-sectional study. Eur J Med Res. 2023;28(1):68.
47. Xu W, Ouyang X, Lin Y, Lai X, Zhu J, Chen Z, et al. Prediction of acute kidney injury after cardiac surgery with fibrinogen-to-albumin ratio: a prospective observational study. Front Cardiovasc Med. 2024;11:1336269.
48. Chen X, Zhao J, You Y, Li Z, Chen S. The ratio of fibrinogen to albumin is related to the occurrence of retinopathy in type 2 diabetic patients. Diabetes Metab Syndr Obes. 2023;16:1859–67.
49. Zhang Z, Sejdić E. Radiological images and machine learning: trends, perspectives, and prospects. Comput Biol Med. 2019;108:354–70.
50. Wang J, Jiang F, Cheng P, Ye Z, Li L, Yang L, et al. Construction of novel multi-epitope-based diagnostic biomarker HP16118P and its application in the differential diagnosis of Mycobacterium tuberculosis latent infection. Mol Biomed. 2024;5(1):15.
51. Daniël Lakens; Sample Size Justification. Collabra: Psychol 5 January. 2022;8(1):33267.

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