Diagnostic Value of Combined Pleural IL-33, ADA and Peripheral T-SPOT.TB for Tuberculous Pleurisy

Jin Fenhua
Wenzhou Medical University Second Affiliated Hospital
Wang Daohui
Wenzhou Medical University Second Affiliated Hospital
Lin Hui
Wenzhou Medical University Second Affiliated Hospital
Xia Xiaodong
Wenzhou Medical University Second Affiliated Hospital
wen huang (qq2627897841@126.com)
the second affiliated hospital of WenZhou medical university https://orcid.org/0000-0002-0010-3056

Research article

Keywords: Tuberculosis, pleural effusion, interleukin-33, adenosine deaminase, tuberculosis T cell spot detection

Posted Date: September 18th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-48549/v1

Abstract

Background To investigate the correlation between pleural fluid interleukin-33 (IL-33) and adenosine deaminase （ADA） and peripheral blood tuberculosis T cell spot detection (T-SPOT.TB), and the combined value of the three tests for the diagnosis of tuberculous pleurisy.

Method 79 patients with pleural effusion admitted from June 2017 to December 2018 were enrolled. They were divided into tuberculous pleural effusion (TPE) group (57 cases, 72.2%) and malignant pleural effusion group (17 cases,21.5%), pneumonia-like pleural effusion group (5 cases, 6.3%). Correlation between pleural fluid IL-33,pleural effusion ADA and peripheral blood T-SPOT.TB was analyzed, comparison of the three separate and combined diagnostic efficacy was also performed.

Result The levels of IL-33, ADA and peripheral blood T-SPOT.TB in patients with TPE were significantly higher than those in non-TPE (P<0.001). The level of pleural fluid IL-33 was positively correlated with pleural effusion ADA and peripheral blood T-SPOT.TB. The Area under the ROC curve（AUC）of TPE diagnosed by pleural IL-33, ADA and peripheral blood T-SPOT.TB were 0.753, 0.912 and 0.865, respectively. AUC for combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB is the largest, with a value of 0.962. Specificity is 100% and sensitivity is 88.5%.

Conclusion Combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB can improve the diagnostic efficacy of tuberculous pleurisy.

Background

Tuberculous pleurisy is a common form of extrapulmonary tuberculosis. Pleural biopsy and bacteriological testing are the gold standard for diagnosis of tuberculous pleurisy. However, it is difficult to diagnose because of the invasive operation of pleural biopsy and the difficulty in cultivating mycobacterium tuberculosis[1, 2]. With the advances in enzymology and molecular biology in recent years, enzymes and cytokines have attracted more and more attention in the pathogenesis of various immune diseases[3]. Adenosine deaminase (ADA) is present in various tissues of human body and is mainly involved in the decomposition of purine nucleosides. It has been widely used in clinical diagnosis of tuberculosis in recent years[4]. ADA testing is currently recognized as an ideal indicator for the diagnosis of tuberculous pleurisy [5]. Tuberculosis T cell spot detection (T-SPOT.TB) is a kind of interferon-γ release assay (IGRA). The number of T cells secreting interferon-γ (IFN-γ) can be used as an auxiliary method for early diagnosis of tuberculosis [6, 7]. Researches [8–10] showed that the level of interleukin-33 (IL-33) in pleural fluid was significantly higher in patients with tuberculous pleurisy than in other causes. Therefore, we speculate that IL-33 may play an important role in the production of tuberculous pleural effusion (TPE). The combined value of the three tests for the diagnosis of tuberculous pleurisy was investigated to identify the correlation between pleural fluid interleukin-33(IL-33),adenosine deaminase (ADA) and peripheral blood tuberculosis T cell spot detection (T-SPOT.TB).It is

intended to provide a reference for the clinical diagnosis of tuberculous pleurisy. The results are reported below.

1. Methods

1.1 Research object

Seventy-nine patients with pleural effusion admitted to the Department of Respiratory Medicine, Second Affiliated Hospital of Wenzhou Medical University from June to February 2018, were collected. According to the diagnosis results, the patients were divided into TPE group (57 cases, 72.2%), malignant pleural effusion group (17 cases, 21.5%), and pneumonia-like pleural effusion group (5 cases, 6.3%).

1.2 Diagnostic criteria

1.2.1 Group of TPE

Acid-fast bacilli detected in Pulmonary effusion, and/or granulomatous changes in pleural biopsy samples, exclude other causes of granulomatous pleurisy;

Exudate, pleural effusion absorption and clinical symptoms relieved by anti-tuberculosis treatment.

1.2.2 Group of non-tuberculous pleural effusion(non-TPE):

Including malignant pleural effusion group and pneumonia-like pleural effusion group.

Malignant pleural effusion(MPE) group: Imaging results consistent with primary bronchogenic carcinoma complicated with pleural effusion;lung cancer confirmed with pulmonary biopsy obtained by fiberoptic bronchoscopy or thoracoscopy; Metastatic tumor cells detected with Pleural effusion exfoliative cytology.

Pneumonia-like pleural effusion(PPE) group: presence of symptoms of cough, cough, and fever; lung exudation showed by chest imaging and absorption of pleural fluid after antibiotic treatment.

1.3 Exclusion criteria

Any one of the followings: Patients had chest trauma or received any treatment for invasive pleural examination in the previous year before hospitalization; Patients have received any anti-tumor or anti-tuberculosis treatment before; Patients who have used glucocorticoids, non-steroidal anti-inflammatory drugs, or immunosuppressants; Unknown causes of pleural effusion; pleural effusion caused by rheumatic immune diseases.

1.4 Specimen collection method

5 mL of drainage fluid was collected by ultrasound-guided thoracentesis from patients with pleural effusion, and centrifuged for 10 minutes at 3000 r/min using heparin with the concentration of 500 U/ml.

The supernatant was collected and stored in a refrigerator at eighty Celsius degrees below zero.

1.5 Detection method

The IL-33 in pleural effusion was measured by enzyme linked immunosorbent assay (ELISA). The kit was provided by abcam company (UK). The procedure was carried out strictly in accordance with the operating instructions. The levels of serum ADA and serum lactate dehydrogenase (LDH), peripheral blood T-SPOT.TB were measured in the Second Affiliated Hospital of Wenzhou Medical University in accordance with the instructions.

1.6 Statistical analysis

Data were analyzed with the statistical software SPSS(version 22.0). It was expressed as mean ± standard deviation (x ± s) for normal distributed date.Non-normally distributed data was expressed as median and interquartile range(IQR). Measurement data were compared using the independent sample T test. Pearson correlation was employed to analysis the correlations between pleural fluid IL-33, pleural effusion ADA and peripheral blood T-SPOT. The receiver operating characteristic curve (ROC curve) was plotted with the sensitivity as the Y-axis and 1-specificity as the x-axis. The optimal threshold was determined according to the Yoden index (sensitivity + specificity − 1). $P < 0.05$ was taken as a statistically significant difference.

1.7 Ethics statement

This study was approved by the institutional review board of the second affiliated hospital of WenZhou medical university (Approval No L-2020-1).Written informed consent was provided by all patients.

2. Results

2.1 Demographic characteristics

A total of 79 patients were collected, and demographic characteristics are shown in Table 1.

Table 1
Demographic characteristics of patients with pleural effusion

diagnose	N	Age(years)	Male(n,%)
TPE	57	38 ± 18	41, 72%
MPE	17	64 ± 14	8, 47%
PPE	5	60 ± 11	3, 60%
No significant difference for age and gender among those three groups.			

2.2 Levels of IL-33, ADA, LDH and T-SPOT.TB in peripheral blood

The levels of pleural fluid IL-33, ADA and peripheral blood T-SPOT.TB in patients with TPE were significantly higher than those in non-tuberculous pleural effusions, and the difference was statistically significant (P < 0.001). As shown in Table 2.

Table 2
Levels of IL-33, ADA, LDH and peripheral blood T-SPOT.TB in pleural effusions of patients

	TPE	Non-TPE	P value
ADA(U/L)	48.7 ± 14.0	20.8 ± 19.5	<0.001
LDH(U/L)	417.0 ± 188.7	562.4 ± 446.6	0.145
IL-33(ng/L)	144.60 ± 48.10	99.77 ± 35.18	<0.001
T-SPOT.TB(pg/ml)	171.0 ± 121.2	34.2 ± 47.6	<0.001
The levels of pleural fluid IL-33, ADA and peripheral blood T-SPOT.TB were higher in patients with TPE(P < 0.05)			

2.3 Correlations.

The level of IL-33 in pleural fluid was positively correlated with pleural effusion ADA and peripheral blood T-SPOT.TB(r = 0.343, 0.450,P<0.05). As shown in Fig. 1, Fig. 2.

2.4. Diagnostic value of ADA, IL-33 and peripheral blood T-SPOT.TB for tuberculous pleurisy in pleural effusion.

Table 3 shows the diagnostic value of pleural IL-33, ADA and peripheral blood T-SPOT.TB. ROC curve is shown in Fig. 3.

Table 3
Diagnostic value of IL-33, ADA and peripheral blood T-SPOT.TB in pleural effusion for tuberculous pleurisy

	Cut-off value	Sensitivity(%)	Specificity(%)	AUC(95%CI)
IL-33	155.96 ng/L	49.1	100.0	0.753(0.637–0.869)
ADA	30.55 U/L	93.0	90.9	0.912(0.804-1.000)
T-SPOT.TB	25.35 pg/ml	92.3	71.4	0.865(0.713-1.000)
AUC were 0.753, 0.912, 0.865 respectively for pleural IL-33, pleural ADA and peripheral blood T-SPOT. The sensitivities were 49.1%, 93%, 92.3% with specificity of 100%, 90.9%, 71.4% respectively using the cut-off value of 155.96 ng/L for IL-33, 30.55 U/L for ADA, 25.35 pg/ml for T-SPOT.TB respectively.				

2.5 Diagnostic value of combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB for tuberculous pleurisy.

ROC curve analysis was performed to define the diagnostic profile of combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB in identifying tuberculous pleurisy. The area under the ROC curve for combined detection the pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB was the largest at 0.962, with specificity 100%, sensitivity 88.5%. As shown in Table 4.

Table 4
Diagnostic value of combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB for tuberculous pleurisy

Combined detection	AUC	Sensitivity(%)	Specificity(%)
IL-33 + ADA	0.940	92.3	85.7
IL-33 + T-SPOT.TB	0.923	76.9	100
ADA + T-SPOT.TB	0.945	84.6	100
IL-33 + ADA + T-SPOT.TB	0.962	88.5	100

Diagnostic value of combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB for tuberculous pleurisy. Combined IL-33, ADA, TSPOT.TB, the diagnostic specificity was 100%, and the sensitivity was 88.5%.

3. Discussion

Tuberculous pleurisy is the most common cause of pleural effusion, accounting for 49.5 to 54.5% of the cause of hospitalized pleural effusion in China [11].A rapid and effective detection method for early diagnosis and treatment of patients with tuberculous pleural effusion is needed to reduce complications such as tuberculous empyema and lung damage caused by tuberculous pleural effusion [12].

IL-33 was discovered by Schmitz in 2005 and belongs to the IL-1 class cytokine superfamily. It has a homologous clover-like structures [13]. The results of this study showed that the level of IL-33 in pleural effusion was significantly higher in patients with tuberculous pleurisy than in non-tuberculous pleural effusion. The area under the ROC curve for IL-33 in TPE was 0.753, and the sensitivity was 49.1%, specificity is 100% at the best cutoff value of 155.96 ng/L. The level of pleural fluid IL-33 was positively correlated with pleural effusion ADA and peripheral blood T-SPOT.TB. Lee KS and Xuan WX and other scholars [9, 10] found that the level of IL-33 in pleural effusion of patients with tuberculous pleurisy was significantly higher than other causes of pleural effusion and serum IL-33 levels, the sensitivity was 78% and 86.96%, specificity was 65% and 90.48% respectively. It was also suggested by Lee KS and other scholars that pleural fluid IL-33 level and pleural ADA are significantly positively correlated [9]. Li D and other scholars [8] also showed that the sensitivity of IL-33 in the diagnosis of tuberculous pleurisy was 83.9%, the specificity was 87.3%, and the area under the ROC curve was 0.823. Therefore, the above evidence shows that IL-33 is related to the pathophysiology of TPE. Although we did not probe the specific mechanism of IL-33 in the pathogenesis of TPE, the significant relationship between IL-33 and tuberculous pleurisy observed in this study can be explained by the following hypothesis: IL-33 is shown to exhibit an immunomodulatory effect to some extent, such as the induction of cytokines and responsive cells. A growing number of basic studies [14–16] have shown that IL-33 can mediate and

even enhance Th1 cellular immune responses by increasing interferon-gamma (Interferon-γ, IFN-γ). On the other hand, some studies also found that IL-33 expression is up-regulated by IFN-γ and tumor necrosis factor-α (TNF-α) [17, 18]. Therefore, IFN-γ is not only an upstream regulator of IL-33, but also a downstream product of IL-33 signaling [15, 16, 19]. Therefore, in tuberculous pleurisy, IL-33 and IFN-γ may form a coupled positive feedback loop [15–20]. Therefore, IL-33 may be involved in the pathogenesis and development of tuberculous pleurisy, and its elevated level may play a role of in the stimulation of inflammation by mycobacterium tuberculosis. IL-33 has an important diagnostic value in the diagnosis of tuberculous pleurisy.

ADA is an important enzyme in the metabolism of purine nucleosides in various tissues of human body, especially lymphocytes. The pathogenesis of tuberculous pleurisy is delayed-type hypersensitivity caused by MTB infection. The tuberculosis protein of MTB enters the pleural cavity and causes pleural inflammatory reaction, which leads to lymphocyte differentiation and proliferation, resulting in increased ADA content [4]. ADA is one of the most widely studied and recommended biomarkers and has been found to have a good performance in diagnosing TPE. A meta-analysis of 63 studies [21] evaluated the value of pleural ADA activity in identifying TPE and non-TPE, demonstrating its high sensitivity and specificity (92% and 90%, respectively). ADA is one of the highly recommended biomarkers and has been found to have good performance in diagnosing TPE. The results of this study showed that the ADA level in pleural effusion was significantly higher in patients with tuberculous pleurisy than in non-tuberculous pleural effusion, the sensitivity of diagnosis of tuberculous pleurisy was 93.0%, the specificity was 90.9%, which was similar to the previous study [21].

Tuberculous pleurisy is mainly mediated by cellular immunity. After stimulation by MTB antigen, T cells get activated to secrete cytokine IFN-γ to participate in the immune response. There are corresponding specific T cells in the peripheral blood of patients [22]. The principle of T-SPOT.TB detection is to isolate MTB-specific T cells in peripheral blood, which can secret IFN-γ after in vitro culture and antigen re-stimulation, so we can diagnose the presence of MTB infection by examining the IFN-γ concentration with the corresponding antibody. Its diagnostic value is not affected by the patient's gender, age, tumor, immunosuppression, etc. It can be used not only for the diagnosis of extrapulmonary tuberculosis, but also as a tool for therapeutic effect evaluation, which has a high practical value [23]. The results of this study showed that the level of T-SPOT.TB in peripheral blood of patients with tuberculous pleural effusion was significantly higher than that of patients with non-tuberculous pleural effusion. The sensitivity of peripheral blood T-SPOT. TB for diagnose of TPE was 92.3% and the specificity was 71.4%. However, studies have shown that peripheral blood T-SPOT.TB has its own defects because it is affected by the number of peripheral blood T lymphocytes [24], especially in immunodeficient patients [25], which may cause false negative results. Moreover, peripheral blood T-SPOT.TB cannot differential MTB latent infection from active tuberculosis, which further limits its use.

This study found that the combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB could further improve the sensitivity and specificity of TPE diagnosis. The area under the ROC curve was the largest at 0.962 when combined those three, with 100% specificity, 88.5% sensitivity.

In summary, this study compared the AUC, sensitivity and specificity of pleural effusion IL-33, ADA and blood TSPOT for the diagnosis of tuberculous pleurisy. We found that IL-33 has the highest specificity of 100%. It can be used for the exclusion of tuberculous pleurisy, but the sensitivity of IL-33 is not high, only at 49.1%. However, the diagnostic sensitivity was increased to 76.9% when combined with TSPOT.TB. Combined IL-33, ADA, TSPOT.TB, the diagnostic specificity was 100%, and the sensitivity was 88.5%, suggesting that the combined detection has a higher diagnostic value for tuberculous pleurisy. It can prevent missed diagnosis, which is helpful for early detection and early treatment, so that it has important auxiliary diagnostic value for tuberculous pleurisy.

4. Conclusion

Combined detection of pleural effusion IL-33, ADA and peripheral blood T-SPOT.TB can improve the diagnostic efficacy of tuberculous pleurisy.

Abbreviations

IL-33
interleukin- 33
ADA
adenosine deaminase and
T-SPOT.TB
peripheral blood tuberculosis T cell spot detection
TB
tuberculosis
IGRA
interferon-γ release assay
TPE
tuberculous pleural effusion
PPE
pneumonia-like pleural effusion
MPE
malignant pleural effusion
ELISA
enzyme linked immunosorbent assay
LDH
lactate dehydrogenase
ROC
operating characteristic curve
SPSS
Statistical Product and Service Solutions
IQR

interquartile range

Declarations

Ethical Approval and Consent to participate

This study was approved by the institutional review board of the second affiliated hospital of WenZhou medical university (Approval No L-2020-1).Written informed consent was provided by all patients. See the attached file named Ethics Committee Consent form1, Ethics Committee Consent form2 and patients' informed consent form.

Consent for publication

Written informed consent was obtained from all subjects before the study.

Availability of data and materials

See the file named date and materials.

Competing interests

The Authors declare that there is no conflict of interest.

Funding

The authors disclosed receipt of the following financial support for the research, and publication of this article: ELISA kit of IL-33 was funded by grants of Wenzhou science and Technology Bureau (Grant No.Y20160251).

See the file named Application for scientific research project.

Authors' contributions

Huang wen and JFH researched literature and conceived the study. WDH was involved in protocol development, gaining ethical approval, patient recruitment and data analysis. LH and XXD wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Acknowledgments

Thanks to Ms. Chen haiyan, Ms.Xu anqi for their assistance in data collection.

Authors' information

The first author, JFH

Address: Department of Respiratory Medicine,
The second affiliated hospital of Wenzhou Medical University,
109, xueyuan western Road, Wenzhou city, Zhejiang province, 325027,P.R.China

E-mail:jinfenghua11@yeah.net
Tel:86-577-88002814, 13454830506(+86)

Fax:86-577- 88832693
ORCID https://orcid.org/0000-0001-8757-5170

The second author, WDH

Address: Department of Respiratory Medicine,
The second affiliated hospital of Wenzhou Medical University,
109, xueyuan western Road, Wenzhou city, Zhejiang province, 325027,P.R.China

E-mail: wenzhouw123456@126.com

Tel:86-577-88002814,

Fax:86-577- 88832693

The third author, LH ,

Address: Department of Respiratory Medicine,
The second affiliated hospital of Wenzhou Medical University,
Wenzhou city,Zhejiang province, 325027, P.R.China

E-mail:linhui22@yeah.net

Tel: 86-577-88002814,

Fax:86-577- 88832693

The fourth Author XXD

Address: Department of Respiratory Medicine,

The second affiliated hospital of Wenzhou Medical University,
109, xueyuan western Road, Wenzhou city, Zhejiang province, 325027, P.R.China

E-mail:wzdxxd@126.com
Tel:86-577-88002814,

Fax:86-577- 88832693

Corresponding Author HW,

Address: Department of nephrology,
The second affiliated hospital of Wenzhou Medical University,109, xueyuan western Road, Wenzhou city, Zhejiang province, 325027, P.R.China

E-mail:qq2627897841@126.com

Tel:86-577-88002611, 15906494505 (+86), Fax:86-577- 88832693
ID https://orcid.org/0000-0002-0100-3056

DISCLOSURES

We declare that we have no conflicts of interest. All authors made a substantial contribution to the information or material submitted for publication. All read and approved the final manuscript.

References

1. Xie Ss,Lin L, Ming L,et al. The efficacy and safety of adjunctive corticosteroids in the treatment of tuberculosis pleurisy: a systematic review and meta analysis [J]. Oncotarget,2017, 8(47):83315–83322.
2. Luo Y, Xue Y, Guo X, et al. Diagnostic value of pleural fluid T-SPOT for tuberculous pleurisy: An updated meta-analysis [J].Tuberculosis. 2020(122),101941.
3. Wang, et al. The pleural fluid lactate dehydrogenase/ adenosine deaminase ratio differentiates between tuberculous and parapneumonic pleural effusions [J]. BMC Pulmonary Medicine 2017(17):168.
4. Aggarwal AN, Agarwa lR, Sehgal IS, Dhooria S. Adenosine deaminase for diagnosis of tuberculous pleural effusion: A systematic review and meta-analysis [J]. PLOS ONE 14(3): e0213728.
5. Wu Yan-bin, Ye Z, Qin S, et al. Combined detections of interleukin 27, interferon-γ, and adenosine deaminase in pleural effusion for diagnosis of tuberculous pleurisy [J].Chinese Medical Journal. 126(17):3215–3221.
6. Feng Zhu Q, Ou, Zheng J. Application Values of T-SPOT.TB in Clinical Rapid Diagnosis of Tuberculosis [J].Iran J Public Health. 2018 Jan; 47(1): 18–23.
7. Ji, et al. Usefulness of interferon-γ release assay for the diagnosis of sputum smear-negative pulmonary and extra-pulmonary TB in Zhejiang Province, China [J].Infectious Diseases of Poverty.2017 (6):121.
8. Li D, Shen Y, Fu X,et al.Combined detections of interleukin-33 and adenosine deaminase for diagnosis of tuberculous pleural effusion[J].Int J Clin Exp Pathol,2015,8(1):888–893.
9. Lee KS, Kim HR, Kwak S,et al.Association between Elevated Pleural Interleukin-33 Levels and Tuberculous Pleurisy[J].Ann Lab Med,2013,33(1): 45–51.

10. Xuan WX, Zhang JC, Zhou Q,et al.IL-33 levels differentiate tuberculous pleurisy from malignant pleural effusions[J].Oncol Lett,2014,8(1): 449–453.
11. Doosoo Jeon. Tuberculous Pleurisy: An Update [J]. Tuberc Respir Dis (Seoul). 2014;76(4):153–9.
12. Xiaoli Lei J, Wang Z, Yang, et al. Diagnostic Value of Pleural Effusion Mononuclear Cells Count and Adenosine Deaminase for Tuberculous Pleurisy Patients in China: A Case-Control Study [J]. Front Med (Lausanne). 2019;6:301.
13. Schmitz J, Owyang A,Oldham E,et al.IL-33,an interleukin-1-like cytokine that signals via the IL-1 receptor-related protein ST2 and induces T helper type 2-associated cytokines[J].Immunity,200523(5): 479–490.
14. Blom L,Poulsen LK.IL-1 family members IL-18 and IL-33 upregulate the inflammatory potential of differentiated human Th1 and Th2 cultures[J].J Immunol,2012189(9): 4331–4337.
15. Smithgall MD, Comeau MR, Yoon BR,et al.IL-33 amplifies both Th1- and Th2-type responses through its activity on human basophils, allergen-reactive Th2 cells, iNKT and NK cells[J].Int Immunol,200820(8): 1019–1030.
16. Bourgeois E, Van LP,Samson M,et al. The pro-Th2 cytokine IL-33 directly interacts with invariant NKT and NK cells to induce IFN-gamma production[J]. Eur J Immunol. 2009;39(4):1046–55.
17. Wood IS, Wang B, Trayhurn PIL-33, a recently identified interleukin-1 gene family member, is expressed in human adipocytes[J].Biochem Biophys Res Commun,2009,384(1):105–109.
18. Masamune A, Watanabe T, Kikuta K,et al.Nuclear expression of interleukin-33 in pancreatic stellate cells[J].Am J Physiol Gastrointest Liver Physiol,2010,299(4):G821-832.
19. Xu D, Jiang HR, Kewin P,et al. IL-33 exacerbates antigen-induced arthritis by activating mast cells[J]. Proc Natl Acad Sci U S A. 2008;105(31):10913–8.
20. Préfontaine D, Lajoie-Kadoch S, Foley S, et al. Increased expression of IL-33 in severe asthma: evidence of expression by airway smooth muscle cells[J]. J Immunol. 2009;183(8):5094–103.
21. Liang QL, Shi HZ,Wang K, Qin SM,Qin XJ. Diagnostic accuracy of adenosine deaminase in tuberculous pleurisy: a meta-analysis [J]. Respir Med. 2008;102:744–54.
22. LIUXQ BIANSN. CHENGXH, etal. Utility of T-cell interferon-γ release assays for the diagnosis of female genital tuberculousis in a tertiary referral hospital in Beijing,China[J].Medicine (Baltimore),2016,95(44):e5200.
23. YANL,XIAOH,HANM,etal. Diagnostic value of T-SPOT.TB interferon-γ release assays for active tuberculosis[J]. Exp Ther Med. 2015;10(1):345–51.
24. PANL,JIAH,LIUF,etal.Risk factors for false-negative TSPOT.TB assay results in patients with pulmonary and extrapulmonaryTB[J].JInfect,201570(4): 367–380.
25. HAASMK,DALEYCL. Mycobacterial lung disease complicating HIV infection[J].Semin Respir Crit Care Med,2016,37 (2): 230–242.

Figures

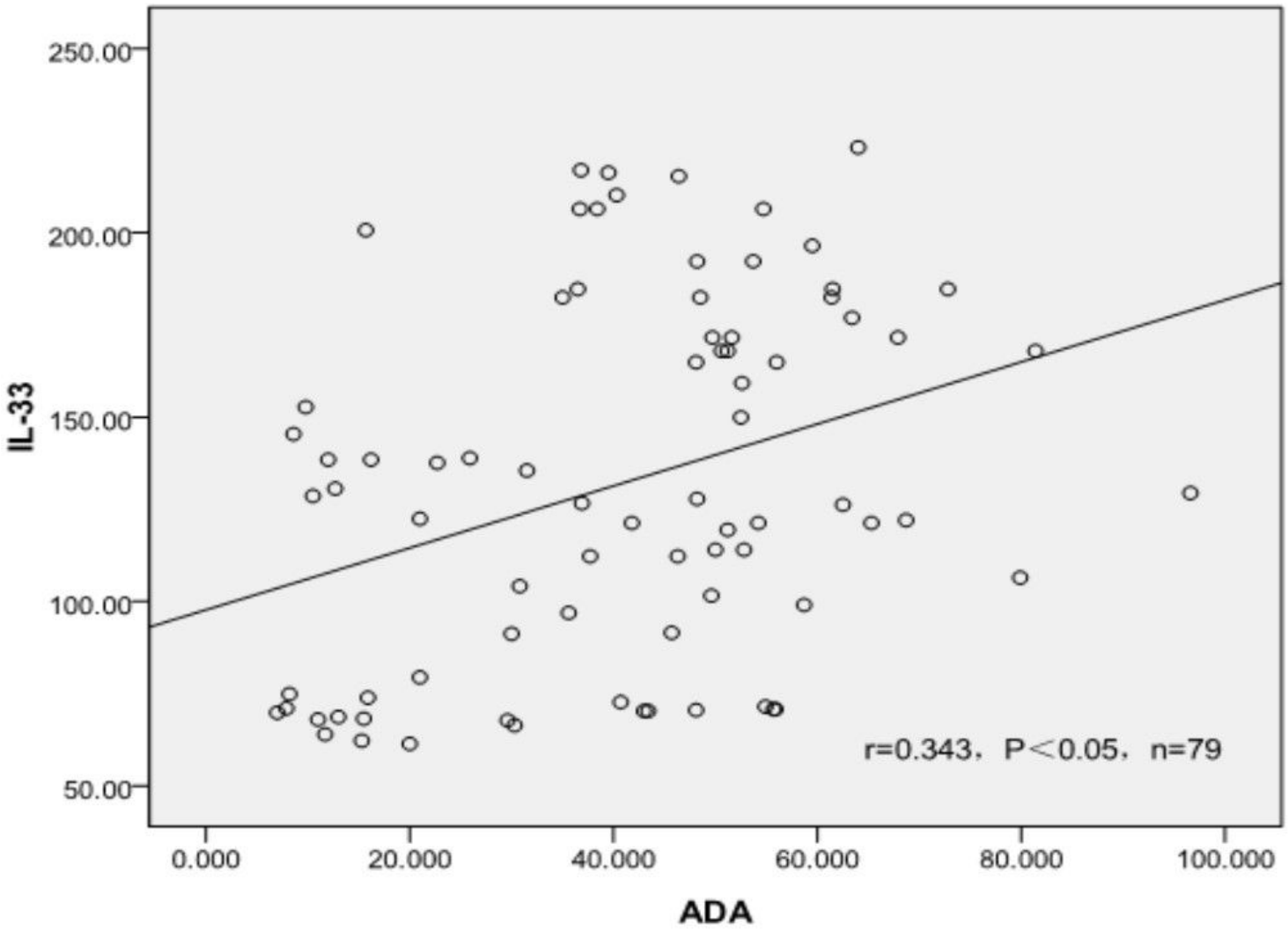

Figure 1

entitled correlation between pleural fluid IL-33 level and pleural ADA level. All patients were included (n=79).We used Pearson correlation to analysis the correlations between pleural fluid IL-33, pleural effusion ADA and peripheral blood T-SPOT. The result show that pleural fluid IL-33 level and pleural ADA level were positively linear related, (r=0.343, P□0.05)

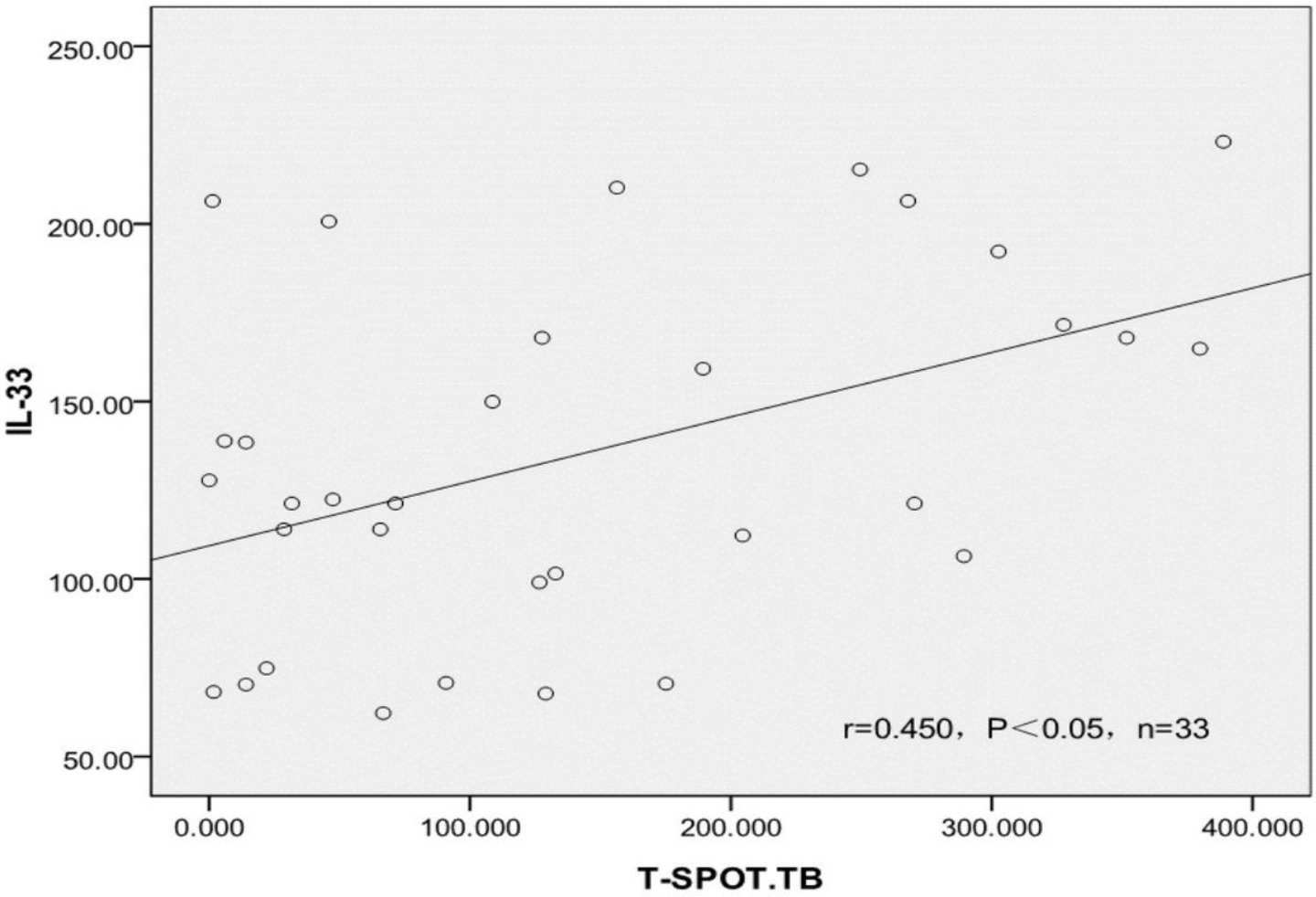

Figure 2

entitled correlation between IL-33 level in pleural fluid and peripheral blood T-SPOT.TB level.33 patients were tested for peripheral blood T-SPOT (n =33).TB and included. Pearson correlation was employed to analysis the correlations between pleural fluid IL-33, pleural effusion ADA and peripheral blood T-SPOT. The result show that pleural fluid IL-33 level and peripheral blood T-SPOT.TB were positively related, (r=0.450, P<0.05).

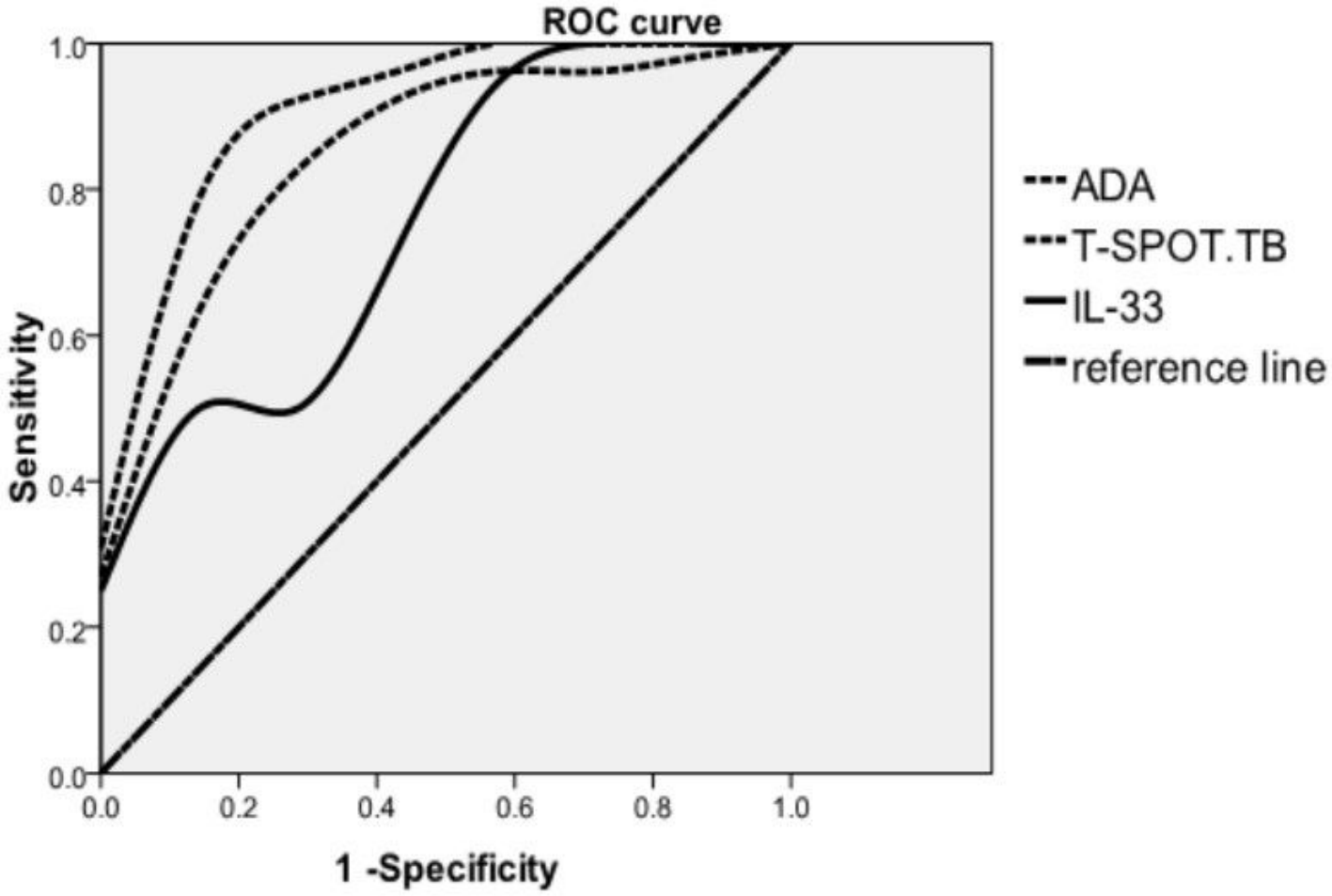

Figure 3

ROC curve of pleural effusion ADA, IL-33 and peripheral blood T-SPOT.TB. The receiver operating characteristic curve (ROC curve) was plotted with the sensitivity as the Y-axis and 1-specificity as the x-axis. AUC were 0.753, 0.912, 0.865 respectively for pleural IL-33, pleural ADA and peripheral blood T-SPOT. (n=79,79,33 for pleural IL-33, pleural ADA and peripheral blood T-SPOT respectively).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- rawdateandmaterials1.xls
- rawdateandmaterials2.xls