Diagnostic utility of serum adenosine deaminase level in the diagnosis of pulmonary tuberculosis

Abdelsadek H. Alaarag^a, Osama I. Mohammad^a, Naglaa M. Farag^b

Aim of the work This study was conducted to evaluate the role of serum adenosine deaminase (ADA) level in the diagnosis of pulmonary tuberculosis (TB) and its relationship with clinical, radiological, and laboratory parameters.

Patients and methods This study was performed on 70 individuals: 60 patients with tuberculous and nontuberculous pulmonary diseases and 10 apparently healthy individuals as a control group. The participants were divided into four groups: group I included 30 patients with active pulmonary TB who were subdivided into group IA, which included 20 patients with sputum smear-positive pulmonary TB, and group IB, which included 10 patients with sputum smearnegative pulmonary TB (culture positive); group II included 10 patients with tuberculous pleural effusion; group III included 20 patients with nontuberculous lung diseases (five cases with pneumonia, five cases with pyogenic lung abscess, five cases with bronchiectasis, three cases with lung cancer, and two cases with mesothelioma); and group IV included 10 apparently healthy individuals as a control group. Patients were subjected to history taking, clinical examination, plain chest radiography posterior-anterior view, three consecutive sputum smears for acid-fast bacilli (AFB), sputum culture for AFB using BACTEC TB-460 system in group IB, laboratory investigations, tuberculin skin test, serum ADA level evaluation in all participants, and pleural ADA level evaluation in cases of tuberculous pleural effusion.

Introduction

Tuberculosis (TB) is an infectious bacterial disease caused by Mycobacterium tuberculosis, which most commonly affects the lungs. It is transmitted from person to person through droplets from the throat and lungs of people with the active respiratory disease. In healthy people, infection with M. tuberculosis often causes no symptoms, as the person's immune system acts to 'wall off' the bacteria. The symptoms of active TB of the lung are coughing, sometimes with sputum or blood, chest pain, weakness, weight loss, fever, and night sweats. TB is treatable with a 6-month course of antibiotics [1]. A positive acid-fast bacilli (AFB) smear and/or culture of Mycobacterium spp. is the gold standard for the diagnosis of TB. Although smear positivity correlates well with infectivity, much of the transmission occurs before the level of bacilli reach 10 000/ml in the sputum. Infection is a sophisticated process and certainly occurs from paucibacillary and smear-negative cases, which are more common in HIV seropositives [2]. Chest radiograph provides only a probable diagnosis; they are sometimes difficult to differentiate from other causes of lung shadows, such pneumonia and malignancies [3]. as

Results Serum ADA showed high percentage positivity (90%) in the diagnosis of pulmonary TB, followed by tuberculin skin test (83.3%), chest radiography (73.3%), erythrocyte sedimentation rate (70%), sputum for AFB (66.6%), toxic symptoms (53.3%), and hemoptysis (36.3%). Serum ADA sensitivity and specificity at cut-off point 30.15 μ /l were 95 and 86.7%, respectively, with a positive predictive value of 90.5%, negative predictive value of 92.2%, and accuracy of 91.4%.

Conclusion Serum ADA level shows higher percentage positivity compared with clinical, radiological, and laboratory parameters in the diagnosis of pulmonary TB. *Egypt J Bronchol* 2016 10:133–139 © 2016 Egyptian Journal of Bronchology

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 $\ensuremath{\textit{Keywords:}}\xspace$ pulmonary tuberculosis, serum adenosine deaminase, tuberculous pleural effusion

^aDepartment of Chest Diseases, Faculty of Medicine, Benha University, Banha, ^bAbbassia Chest Hospital, Cairo, Egypt

Correspondence to Osama I. Mohammad, Department of Chest Diseases, Faculty of Medicine, Benha Faculty of Medicine, Banha, Egypt. Tel: + +20 127 364 6430;

e-mail: osama.thorax@yahoo.com

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Erythrocyte sedimentation rate (ESR) is a nonspecific investigation, which may become rapid in a large variety of clinical conditions ranging from anemia to any chronic infectious, inflammatory, or malignant disease. ESR has absolutely no diagnostic value for TB diagnosis as a standalone criterion. However, in conjunction with other clinical parameters, its raised value can indicate a possibility of TB [2]. Adenosine deaminase (ADA) is an enzyme of purine. It is needed for the breakdown of adenosine from food and for the turnover of nucleic acids in tissues. Moreover, it regulates lymphocyte metabolism and is important for lymphocytic differentiation and growth. It is present in lymphocytes in high concentration [4]. Its activity appears to be necessary for an effective immune response as shown by many studies, such as in combined immunodeficiency disease and in typhoid fever. Besides this, increased activity of

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serum ADA has also been demonstrated in tuberculous pleural effusion, peritoneal TB, AIDS, and cancer [5].

Patients and methods

This prospective study was performed on 70 individuals: 60 patients who were admitted in the Chest Department Benha University Hospitals and Abbassia Chest Hospital during the period between October 2012 and October 2013 and 10 apparently healthy individuals who served as a control group. The study gained approval of local ethical committee of chest department, Benha University. The participants were divided into four groups. Group I included 30 patients with active pulmonary TB. Their ages ranged from 13 to 65 years, with a mean age of 37.6 years. There were 26 male and four female patients. This group was further subdivided into two groups: group IA included 20 patients with sputum smear-positive pulmonary TB, and group IB included 10 patients with sputum smear-negative culture-positive pulmonary TB. Group II included 10 patients with tuberculous pleural effusion, eight male and two female. Their ages ranged from 18 to 55 years, with a mean age of 35 years. Group III included 20 patients with nontuberculous lung diseases. Their ages ranged from 20 to 76 years, with a mean age of 52.35 years. This group included five patients diagnosed with pneumonia, five patients diagnosed with pyogenic lung abscess, five patients with bronchiectasis, diagnosed three patients diagnosed with lung cancer, and two patients diagnosed with mesothelioma. Group IV included 10 apparently healthy individuals as a control group, six male and four female. Their ages ranged from 26 to 57 years, with a mean age of 36.1 years.

Inclusion criteria for group I: group Ia – sputum smearpositive pulmonary TB: (a) two or more initial sputum smear examinations positive for AFB, and (b) one sputum smear examination positive for AFB +radiographic abnormalities consistent with active pulmonary TB [6]. Group Ib – sputum smearnegative pulmonary TB: (a) two sets (taken at least 2 weeks apart) of at least two sputum specimens negative for AFB; radiographic abnormalities consistent with active pulmonary TB; lack of clinical response despite a full course of broad spectrum antibiotic administration; a decision by physician to treat with a full course of anti-TB chemotherapy; and (b) sputum-negative culturepositive for *M. tuberculosis* [6].

Inclusion criteria for group II: cytological examination of pleural fluid that was highly rich in lymphocytes and

confirmed by means of pleural biopsy that revealed caseating granuloma [7].

Exclusion criteria for group I: extrapulmonary TB, diabetes mellitus, being on corticosteroids, presence of hepatic or renal impairment, and being on antituberculous treatment.

Patients were subjected to the following:

Full history taking, full clinical examination, plain chest radiography posterior-anterior view, three consecutive sputum smears for AFB, sputum culture for AFB using BACTEC TB-460 (Becton Dickinson, Sparks, MD, USA) system in group IB [8], laboratory investigations (complete blood count, ESR, fasting blood sugar, serum glutamic oxaloacetic transaminase, serum glutamic oxaloacetic transaminase, serum urea, and creatinine), tuberculin skin test using the Mantoux technique [9], serum ADA evaluation, and pleural ADA level in group II. ADA estimation was carried out using the sensitive colorimetric method described by Guisti and Galanti [10] with BIOSIC kit cod ADAo16 (Diazyme General Atomics, California, USA). Other investigations that were carried out for the diagnosis of individual cases were as follows: CT of the chest for 13 cases, CT-guided biopsy for two cases, bronchoscope for one case, Abram's needle biopsy for one case, open pleural biopsy for one case, and medical thoracoscopy in 10 cases.

Data management and analysis

The collected data were revised, coded, tabulated, and introduced into a PC using statistical package for social science (15.0.1 for Windows, 2001; SPSS Inc., Chicago, Illinois, USA).

Results

For results, see Tables 1-9. There was no statistical significant difference between the studied groups as regarding to sex distribution. Regarding to age there was a highly statistical significant difference between group I and group III, on the other hand there is no statistical significant difference between group I and both groups II and IV. The most prominent presenting symptoms in group I were cough and expectoration in 100% of them, in group II the most prominent presenting symptoms were cough and dyspnea in 100% of patients. While in group III cough is the most prominent presenting symptom in 100% of patients followed by expectoration in 90% and dyspnea in 85% of them. There was no statistical significant difference between group IA and both groups IB and group II as regarding to serum ADA.

On the other hand there was a highly statistical significant difference between group IA and both groups III and IV as regarding to serum ADA. Regarding also to serum ADA there was no statistical significant difference between group IB and group II, on the other hand there was a highly statistical significant difference between group IB and both groups III and IV as regarding to serum ADA. There was a highly statistical significant difference between group II and both groups III and IV as regarding to serum ADA. Ratio of ADA activity in the pleural fluid to serum in group II was 2.3:1. The best cut-off value obtained from the ROC (receiver operator characteristic) curve method for serum ADA is 30.15. At this point sensitivity was 95% and specificity 86.7% with positive predictive value (PPV) 90.5%, negative predictive value (NPV) 92.9% and accuracy is 91.4%. Serum ADA shows high percent positivity 90% followed by tuberculin skin test 83.3%, chest x-ray 73.3%, ESR 70%, sputum AFB 66.6%, toxic symptoms 53.3% and hemoptysis 36.3%.

Discussion

TB continues to be a major cause of morbidity and mortality worldwide. The diagnosis is usually based on clinical presentation, radiographic findings, and positive tuberculin test. However, clinical and radiographic features are variable and the latter test may be falsely negative. Under such circumstances, antituberculous therapy is started empirically. It therefore becomes imperative to find some rapid and useful tests for the diagnosis of TB [11]. ADA is an enzyme that catalyzes the hydrolytic and irreversible deamination of adenosine to inosine, as well as deoxyadenosine to deoxyinosine. The determination of ADA concentration in pleural fluid is currently used

Table 1	Statistical	analysis	between	the studied	groups	as regards sex

	Group I [n (%)]	Group II [n (%)]	Group III [n (%)]	Group IV [n (%)]	Total [n (%)]
Sex					
Male	26 (86.7)	8 (80.0)	16 (80.0)	6 (60)	56 (80)
Female	4 (13.3)	2 (20.0)	4 (20.0)	4 (40)	14 (20)
Total	30 (100)	10 (100)	20 (100)	10 (100)	70 (100)
P ₁ =group I vs	. group II	P ₁ 2	>0.05 (NS)		
P_2 =group I vs. group III $P_2>0$		>0.05 (NS)			
P ₃ =group I vs. group IV		P ₃ :	>0.05 (NS)		

There was no statistically significant difference between the studied groups as regards sex distribution. NS, nonsignificant.

Table 2 Statistical analysis between the studied dioups as regards at	Table 2	Statistical an	alvsis between	the studied	groups as regards ag
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	Group I	Group II	Group III	Group IV
Age				
Range	13–65	18–55	20–76	26–57
Mean±SD	37.6±14.87	35.0±11.29	52.35±15.48	36.1±11.97
P ₁ =group I vs. group II	P ₁ >0.0	P ₁ >0.05 (NS)		
P ₂ =group I vs. group III	P ₂ <0.0	P ₂ <0.01 (HS)		
P ₃ =group I vs. group IV	P ₃ >0.0	05 (NS)		

There was a highly statistically significant difference between groups I and III as regards age. However, there was no statistically significant difference between group I and both groups II and IV as regards age. HS, highly significant; NS, nonsignificant.

Table 3	Statistical co	omparison	between	the studied	groups	as regards	presenting	symp	toms

Group I (<i>N</i> =30) [<i>n</i> (%)]	Group II (<i>N</i> =10) [<i>n</i> (%)]	Group III (<i>N</i> =20) [<i>n</i> (%)]	Group IV (<i>N</i> =10) [<i>n</i> (%)]	Total (N=70) [n (%)]
30 (100)	10 (100)	20 (100)	0 (0.0)	60 (85.7)
30 (100)	2 (20)	18 (90)	0 (0.0)	50 (71.4)
21 (70)	10 (100)	17 (85)	0 (0.0)	48 (68.6)
11 (36.7)	0 (0.0)	6 (30)	0 (0.0)	17 (24.3)
16 (53.3)	3 (30)	4 (20)	0 (0.0)	23 (32.9)
9 (30)	5 (50)	12 (60)	0 (0.0)	26 (37.1)
	Group I (<i>N</i> =30) [<i>n</i> (%)] 30 (100) 30 (100) 21 (70) 11 (36.7) 16 (53.3) 9 (30)	Group I (N=30) [n Group II (N=10) [n (%)] 10 (100) 30 (100) 10 (100) 30 (100) 2 (20) 21 (70) 10 (100) 11 (36.7) 0 (0.0) 16 (53.3) 3 (30) 9 (30) 5 (50)	Group I (N=30) [n Group II (N=10) [n Group III (N=20) [n (%)] 10 (100) 20 (100) 30 (100) 10 (100) 20 (100) 30 (100) 2 (20) 18 (90) 21 (70) 10 (100) 17 (85) 11 (36.7) 0 (0.0) 6 (30) 16 (53.3) 3 (30) 4 (20) 9 (30) 5 (50) 12 (60)	Group I (N=30) [n (%)]Group II (N=10) [n (%)]Group III (N=20) [n (%)]Group IV (N=10) [n (%)]30 (100)10 (100)20 (100)0 (0.0)30 (100)2 (20)18 (90)0 (0.0)21 (70)10 (100)17 (85)0 (0.0)11 (36.7)0 (0.0)6 (30)0 (0.0)16 (53.3)3 (30)4 (20)0 (0.0)9 (30)5 (50)12 (60)0 (0.0)

The most prominent presenting symptoms in group I were cough and expectoration in 100% of them. In group II, the most prominent presenting symptoms were cough and dyspnea in 100% of patients. In group III, cough was the most prominent presenting symptom in 100% of patients, followed by expectoration in 90% and dyspnea in 85% of them.

 Table 4 Comparison between group IA versus other groups as regards serum ADA

	Serum ADA	(U/I)		
Variables	Range	Mean±SD	t	Ρ
Group IA	29–48.5	36.97±4.92	-	-
Group IB	30.1–62	39.89±9.56	1.114	0.275 (NS)
Group II	30.4–37	34.03±2.12	1.8	0.083 (NS)
Group III	12.4–30.2	22.13±4.39	10.07	0.001 (HS)
Group IV	7–20	14.99±4.5	11.85	0.001 (HS)

There was no statistically significant difference between group IA and both groups IB and II as regards serum ADA. In contrast, there was a highly statistically significant difference between group IA and both groups III and IV as regards serum ADA.

ADA, adenosine deaminase; HS, highly significant; NS, nonsignificant.

 Table 6 Comparison between group II versus other groups as regard serum ADA

	Serum ADA (U/I)					
Variables	Range	Mean±SD	t	Р		
Group II	30.4–37	34.03±2.12	-	-		
Group III	12.4–30.2	22.13±4.39	8.06	0.001 (HS)		
Group IV	7–20	14.99±4.5	12.1	0.001 (HS)		

There was a highly statistically significant difference between group II and both groups III and IV as regards serum ADA. ADA, adenosine deaminase; HS, highly significant.

for the diagnosis of tuberculous pleurisy. There are also studies showing high levels of ADA in serum and bronchoalveolar lavage (BAL) of patients with pulmonary TB [12]. As regards the presenting symptoms in the studied groups (Table 3), the most prevalent complaint was cough, as it was found in all 60 (100%) patients, followed by expectoration in 50 (83.3%) patients, dyspnea in 48 (80%) patients, chest pain in 29 (43.3%), toxic manifestations in 23 (38.3%) patients, and hemoptysis in 19 (28.3%) patients. This result is in accordance with that of Hassanein and colleagues, who studied the role of ADA in the diagnosis of pulmonary TB. Their study included 50 individuals: 20 patients with sputum positive for AFB, 10 patients with bronchogenic carcinoma, 10 patients with pneumonia, and 10 normal healthy individuals. The study showed that the most prevalent complaint among the 50 individuals was cough in all 40 (100%) patients, followed by expectoration in 31 (62%) patients, hemoptysis in 16 (32%) patients, chest pain in 15 (30%) patients, and toxic manifestations in 14 (28%) patients. This indicates that cough is the most common symptom in all chest diseases and is the most common symptom that brings the patients to physicians to seek medical advice [13]. In this study, the ADA level in the studied groups was as follows (Tables 4-6): ADA level in group IA ranged from 29 to 48.5 μ /l, with a mean of 36.97±4.92; in group IB it ranged from 30.1 to $62 \mu/l$, with a mean of 39.89 ± 9.56 ;

Table 5 Comparison between groups IB versus other groups as regard serum ADA

Variables	Serum ADA (I Range	U/I) Mean±SD	t	Р
Group IB	30.1–62	39.89±9.56	_	_
Group II	30.4–37	34.03±2.12	1.89	0.075 (NS)
Group III	12.4–30.2	22.13±4.39	7.04	0.001 (HS)
Group IV	7–20	14.99±4.5	7.45	0.001 (HS)

There was no statistically significant difference between groups IB and II as regards serum ADA. However, there was a highly statistically significant difference between group IB and both groups III and IV with regard to serum ADA.

ADA, adenosine deaminase; HS, highly significant; NS, nonsignificant.

Table 7 ADA activity in pleural fluid and the serum in group II

	Pleural fluid ADA	Serum ADA	Ratio
TB effusion (N=	=10)		
Range	56–120	30.4–37	
Mean±SD	79.1±19.81	34.03±2.12	2.3 : 1

The ratio of ADA activity in the pleural fluid to serum in group II was 2.3:1.

ADA, adenosine deaminase; TB, tuberculous pleural.

in group II it ranged from 30.4 to 37 μ /l, with a mean of 34.03±2.12; in group III it ranged from 12.4 to $30.2 \,\mu/$ l, with a mean of 22.13±4.39; and in group IV it ranged from 7 to $20 \,\mu/l$, with a mean of 14.99±4.50. There was a highly statistically significant difference between group I (IA and IB) and both groups III and IV (P < 0.01) as regards the level of serum ADA. There was also a highly statistically significant difference between group II and both groups III and IV (P < 0.01). This is in agreement with the findings of Verma and colleagues, who studied the role of ADA activity in pulmonary TB and other common respiratory diseases. The study was conducted on 53 cases of active pulmonary TB; ADA level in this group ranged from 31.42 to 45.80, with a mean of 39.97 $\pm 2.24 \,\mu/l$. In 14 cases of tuberculous pleural effusion the ADA level ranged from 37.28 to 43.28, with a mean of 40.19±1.57. In 33 cases of nontuberculous lung diseases the ADA level ranged from 22.42 to 32.12, with a mean of 25.80±1.41, and in 35 healthy individuals the ADA level ranged from 12.84 to 19.46, with a mean of 16.2±2.85. The study revealed that the serum ADA activity was higher in patients with tuberculous pulmonary and pleural diseases and nontuberculous pulmonary diseases than in controls. activity highest in tuberculous ADA was pleuropulmonary diseases. In the same study, the pleural fluid ADA activity was higher in pyogenic pleural effusion than in tuberculous pleural effusion

Table 8 Sensitivity specificity, PPV, NPV, and accuracy of serum ADA in the diagnosis of tuberculosis

Variables	%
AUC	0.998
Best cut-off value	30.15
Sensitivity	95
Specificity	86.7
PPV	90.5
NPV	92.9
Accuracy	91.4

The best cut-off value obtained from the receiver operator characteristic curve method for serum ADA was 30.15. At this point the sensitivity was 95% and specificity was 86.7%, with a positive predictive value of 90.5%, negative predictive value of 92.9%, and accuracy of 91.4%.

ADA, adenosine deaminase; AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

[14]. Similar results were obtained by Hassanein et al. [13], who assessed the role of ADA in serum and BAL fluid in the diagnosis of pulmonary TB and proved that patients with pulmonary TB had significantly higher ADA level in serum and BAL fluid compared with patients with nontuberculous lung diseases (lung cancer and pneumonia) and normal individuals. The results of the present study are also in accordance with those of Rao and colleagues, who studied the value of serum ADA activity in the diagnosis of pulmonary TB in India. They conducted the study on 142 cases and found that the mean ADA in pulmonary TB patients was 40.48 and 41.3 μ /l in TB pleural effusion, whereas it was $28.4 \,\mu/l$ in patients with nontuberculous chest diseases and 17.4 μ /l in the healthy group. The authors in their study stated that, as the determination of ADA is not costly or time consuming, it should be performed routinely, particularly if the diagnosis is in doubt, clinically suggestive but sputum AFB-negative, as well as to differentiate pulmonary TB from nontuberculous pulmonary diseases [7].

The results of the present study are also in agreement with those of Chander and Shrestha, who studied the diagnostic value of serum ADA level in sputum smearnegative pulmonary TB patients in Nepalese population. The study was conducted on 262 cases that were divided into three groups: group I included 142 cases of sputum smear-negative pulmonary TB with a mean ADA level of $42.26\pm21.22 \mu/l$; group II included 40 cases of COPD with a mean ADA level of $23.31\pm8.22 \mu/l$; and group III included 88 individuals as a healthy control group with a mean ADA level of $18.88\pm6.67 \mu/l$. Their results showed high statistically significant difference between group I and both groups II and III. They stressed that the overall assessment of the uses of serum ADA levels as a diagnostic

 Table 9 Percentage positivity of different parameters in the diagnosis of pulmonary tuberculosis

	N=30 [n (%)]
ТТ	25 (83.3)
ESR	21 (70)
Radiography	22 (73.3)
Sputum AFB	20 (66.6)
Serum ADA	27 (90)
Toxic symptoms	16 (53.3)
Hemoptysis	11 (36.3)

The percentage positivity of different parameters in the diagnosis of pulmonary TB. Serum ADA shows high percentage positivity (90%), followed by tuberculin skin test (83.3%), chest radiography (73.3%), ESR (70%), sputum AFB (66.6%), toxic symptoms (53.3%), and hemoptysis 36.3%.

ADA, adenosine deaminase; AFB, acid-fast bacilli; ESR,

erythrocyte sedimentation rate; TT, tuberculin test.

biochemical marker in smear-negative pulmonary TB patients showed promising results. Our study and all previous studies confirm the importance of ADA as a diagnostic tool in all forms of TB, pulmonary (smear positive and smear negative) and extrapulmonary as in tuberculous pleural effusion [15]. Increased serum ADA levels in pulmonary TB may be due to the stimulation of cell-mediated immunity. A fully functioning cell-mediated immune response is dependent on normal lymphocyte metabolism, which in part is regulated by the purine salvage enzyme ADA [16]. In a study by Conde and colleagues, the serum ADA levels decreased to normal levels after 1 month of the initiation of effective treatment in patients with pulmonary TB. They suggested that the decrease in serum ADA levels could be due to the normalization of altered lymphocytes turnover induced by TB [17]. Thora et al. [18] showed the raised activity of ADA in the newborn sera, 6 weeks after Bacillus Calmette-Guérin (BCG) vaccination. Alatas and colleagues determined the role of serum ADA activity in the diagnosis and follow up of pulmonary TB and monitoring the efficiency of therapy. A significant difference was observed in ADA activity before and after treatment, also from old TB patients and healthy controls. They stated that ADA activity is increased in pulmonary TB patients, which is a helpful parameter for monitoring therapy [19]. As shown in Table 7, ADA activity in pleural fluid and the serum in group II was evaluated. ADA level in pleural effusion ranged from 56 to $120 \,\mu/l$ with a mean of 79.1±19.8, and serum ADA ranged from 30.4 to $37 \,\mu/l$ with a mean of 34.03±2.12. The ratio of pleural fluid ADA compared with serum ADA was 2.3:1. This means that the level of pleural fluid ADA was significantly higher than that of serum ADA level; this is due to localized intrapleural production of ADA from increased

number of lymphocytes in tuberculous pleural effusion. Therefore, the measurement of ADA level in tuberculous pleural effusion has a utility in the diagnosis of TB when other clinical and laboratory tests are negative [20] (Table 8) The best cut-off value obtained for serum ADA in the diagnosis of TB was 30.15; at this point the sensitivity was 95% and specificity was 86.7%, with a positive predictive value of 90.5%, negative predictive value of 92.2%, and accuracy of 91.4%. This result is in agreement with that of Jhamaria and colleagues, who studied serum ADA in the differential diagnosis of pulmonary TB and common nontubercular respiratory disease. Their study included 20 healthy controls, 102 cases of pulmonary TB, 20 cases of suppurative lung diseases, and 18 cases of lung malignancy. In their study, using the cut-off point of $33 \,\mu/l$ in the diagnosis of TB, sensitivity and specificity were 98 and 100%, respectively. In the same study, if $33 \,\mu/l$ was taken as the cut-off point, none of the patients of nontuberculous diseases and malignancy showed value above this limit, whereas only two patients of tuberculous diseases showed values lower than $33 \,\mu/l$ [21]. Lamsal and colleagues studied the diagnostic utility of ADA activity in pleural fluid and serum of tuberculous and nontuberculous respiratory disease patients. Their study included 32 cases of active pulmonary TB, 29 cases of tuberculous pleural effusion, 13 cases of nontuberculous respiratory diseases, and 32 healthy individuals as a control group. Using the cut-off point of $25 \,\mu/l$ in serum in the diagnosis of TB, the sensitivity and specificity were 72.41 and 81.53%, respectively [20]. Similar results were obtained by Rao *et al.* [7], who used $33 \mu/l$ as a cut-off point for serum ADA in the diagnosis of TB; the sensitivity and specificity were 98.06 and 95.35%, respectively. Agarwal et al. [16] reported high specificity and sensitivity of serum ADA in the diagnosis of smearnegative culture-positive pulmonary TB taking 33 μ /l as a cut-off point. Hassanein et al. [13] used a cut-off point of $26.2 \,\mu/l$ in the diagnosis of pulmonary TB, with a sensitivity and specificity of 95 and 83.3%, respectively, with a positive predictive value of 79.2%. Chander and Shrestha [15] in their study in sputum smear-negative pulmonary TB found that, with a cut-off value of $30 \,\mu/l$, the serum ADA test showed a high specificity of 91.25% and a sensitivity of 83.10% in smear-negative pulmonary TB patients when compared with either the nontuberculous chest diseases or the healthy controls. A previous study had shown that, taking $30 \,\mu/l$ as a cutoff value, the specificity and sensitivity of ADA level as a diagnostic test of pulmonary TB came to nearly 100% [22] (Table 9). The percentage positivity of different parameters in the diagnosis of pulmonary TB was determined. Serum ADA showed high percentage positivity (90%), followed by tuberculin skin test (83.3%), chest radiography (73.3%), ESR (70%), sputum for AFB (66.6%), toxic symptoms (53.3%), and hemoptysis (36.3). These results are in accordance with those of Rao *et al.* [7], who studied the sensitivity of various tests in the diagnosis of pulmonary TB; serum ADA showed high percentage positivity (88%), followed by chest radiography (76%), ESR (72%), sputum for AFB (63%), and tuberculin test (61%).

Conclusion

Serum ADA level increases in patients with all forms of TB either pulmonary (smear positive and smear negative) or extrapulmonary as in tuberculous pleural effusion when compared with patients with nontuberculous lung diseases such as pneumonia, bronchiectasis, lung abscess, and lung cancer or normal individuals. Serum ADA level shows higher percentage positivity compared with clinical, radiological, and laboratory parameters in the diagnosis of pulmonary TB.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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