

Erythrocyte sedimentation rate in patients with positive sputum for AFB and negative HIV serological test

Ahmad Hasan Raheem*

Abstract

The goals of this study are detection of the prevalence of ESR elevation in patients who suffering from pulmonary tuberculosis with positive sputum for acid fast bacilli and negative serological test for HIV, and showing the effect of normal ESR on diagnosis of active pulmonary tuberculosis. 37 patients of pulmonary TB with sputum positive for AFB and negative serological test for HIV, were involved in this retrospective study over 145 days, at major TB center of AL-Hilla city, Iraq. The Westergren method used for detection of ESR for all patients. Of the total 37 patients involved in this study 21(57 %) were males and 16(43 %) were females. The ages of the male patients ranged from 21 to 82 years, and the females from 23 to 75 years in addition to one girl with age of 5 years. 22(59.5 %) patient's cigarette smoker and 15(40.5 %) nonsmoker. 3-patient (8.1%) with ESR less than 20mm/hr, 13-patient (35.1%) with ESR 20-40 mm/hr, 12-patient (32.4%) with ESR 41-60mm/hr and 9-patient (24.3%) more than 60 mm/hr. According to dependent normal range in this study 7(19%) patients with normal ESR. 19 % of patients involved in this study have normal ESR, so the pulmonary TB should be expected in any patient with suggestive clinical features even when the ESR is normal specially in an endemic area as in Iraq, and it is clear from result above that the smoking is important risk factor for pulmonary TB.

Keywords: ESR, Tuberculosis, AFB, sputum, HIV

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Introduction

Tuberculosis was founded in Egypt as early as 5,000 years ago [1]. It is a widespread, and can be fatal, infectious disease caused by Mycobacterium tuberculosis bacteria [2]. In 2014, 9.6 million people around the world became sick with TB disease and there were around 1.5 million TB-related deaths worldwide [3]. Most of deaths occurred in developing countries. The total number of tuberculosis cases has been decreasing since

2006, and new cases have decreased since 2002 [4]. The prevalence of tuberculosis is widely variable in different areas; about 80% of the population in many Asian and African countries with positive tuberculin tests, while only 5–10% of the United States population tests positive [2]. More people in the developing countries suffering from tuberculosis because of an impaired immunity, largely due to high rates of HIV

infection and the corresponding development of AIDS [5].

Although the pulmonary tuberculosis is the most common form of the tuberculosis, many other parts of the body can be involved. It can spread through the air where the patient with active TB act as source of infection. Most cases of TB infections are asymptomatic and termed as latent tuberculosis. About one in ten latent infections eventually progresses to active disease which, if left untreated, kills more than 50% of those so infected.

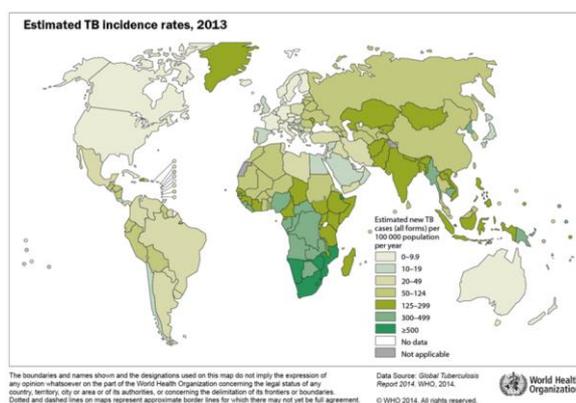


Figure 1.
Estimated TB incidence rates

The most vital point in the management of patients with TB is early diagnosis as the treatment is usually easy and available. The medical evaluation for tuberculosis include a medical history, a physical examination, a chest X-ray and microbiological examination (of sputum or some other appropriate sample). It may also include immunological tests, other scans and tissue biopsy. The medical history which concentrate on the characteristic symptoms of pulmonary TB and these include prolonged cough for three weeks or more, chest pain, dyspnoea, hemoptysis, fever, chills, excessive night sweating, anorexia, weight loss and lethargy. At the beginning

the sputum is mucoid but later on become purulent with or without blood. Extra-pulmonary infection causes a wide range of symptoms. The past medical history includes previous TB infection, past TB treatment, presence of risk factors or medical disorders that increase risk for TB infection such as diabetes mellitus, malignancy and HIV infection. Family history of pulmonary TB and living in crowded locus are important point in medical history. Depending on the sort of patient population surveyed, as few as 20%, or as many as 75% of pulmonary tuberculosis cases may be without symptoms [2]. Pulmonary TB should be suspected when the features of chest infection has persisted longer than three weeks, or when a respiratory illness in an otherwise healthy individual, resist the regular antibiotics. A physical examination: this done to evaluate general condition of the patient and cannot be used to confirm or exclude the diagnosis of TB infection. However, certain findings are expectant of TB, for example; prime weight loss and localized pulmonary signs.

Microbiological studies

Mycobacterial culture; a definitive diagnosis of tuberculosis can only be made by culturing Mycobacterium tuberculosis organisms from a specimen taken from the patient [2] (Fig. 2). This specimen is usually sputum, but may be other sample such as pus, CSF, tissue biopsy. 'A diagnosis that made by other methods may be described as probable. For a diagnosis cancelling of the tuberculosis infection, most protocols require that two separate cultures both test negative [2]. In the culture of AFB, the mycobacterium tuberculosis(MTB) need about 4-6 weeks to grow significantly on

solid media (Löwenstein-Jensen and Middlebrook media) and 1-3 weeks on liquid media (such as radioactive BACTEC system and non-radiometric MGIT)



Figure 2.
Distinctive clusters of *Mycobacterium tuberculosis* form in this culture.

Sputum examination: this represent an important source for diagnosis of pulmonary TB by detection of acid-fast bacilli in the patient's sputum. The preferred method for this is fluorescence microscopy (auramine-rhodamine staining), which is more sensitive than conventional Ziehl-Neelsen staining [6]. When there is no spontaneous production of sputum, a sample can be obtained by nebulized inhalation of a saline with or without bronchodilator solution.

Alternative sampling: in patients unable to produce sputum, possible alternative sample include gastric washings (specially in pediatric age group), laryngeal swab, bronchoscopy and fine needle aspiration. In certain cases, some more invasive investigations are needed, including tissue biopsy by mediastinoscopy or thoracoscopy.

Chest X-ray and CT

When there is active pulmonary TB, the chest X-ray can show patches of consolidation and/or cavitary lesions that can affect any part of the lungs but usually seen in the upper lobe with or without involvement of regional lymph nodes or

pleural effusions. In disseminated TB a pattern of many tiny nodules throughout the lung fields is common - the so-called miliary TB. In immunocompromised patients as in HIV infection, there may be just minor radiological changes or even completely normal chest X-ray. The characteristic features on chest radiographs may give suggestion for diagnosis of pulmonary TB but don't confirm it. However, chest X-ray may be used to exclude the possibility of pulmonary TB in a person with positive tuberculin skin test but with no symptoms of the disease. The tree-in-bud sign may appear on the chest CT-scan of some patients affected by tuberculosis, but it is not specific to tuberculosis [7].

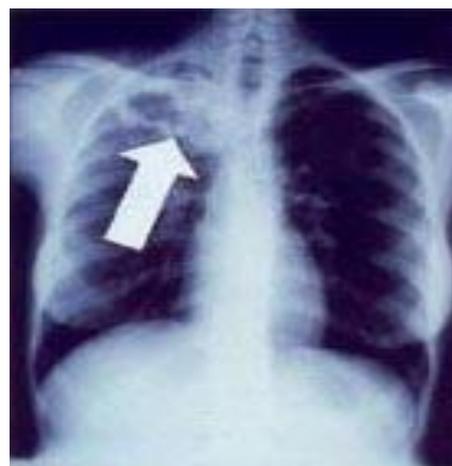


Figure 3.
Tuberculosis creates cavities visible in x-rays like this one in the patient's right upper lobe.

Tuberculin skin test

Two tests are available; the Mantoux and Heaf tests. Adenosine deaminase (ADA) test: In 2007, a systematic review of adenosine deaminase by the NHS Health Technology Assessment Programme concluded. There is no evidence to support the use of ADA tests for the diagnosis of pulmonary TB. However, there is

considerable evidence to support their use in pleural fluid samples for diagnosis of pleural TB, where sensitivity was very high, and to a slightly lesser extent for TB meningitis. In both pleural TB and TB meningitis, ADA tests had higher sensitivity than any other tests [8].

Nucleic acid amplification tests (NAAT); these are qualitative tests e.g polymerase chain reaction (PCR) and Transcription mediated amplification (TMA) that are used to detect mycobacterial nucleic acid within short period (hours to two days) of specimen collection. Full blood count and ESR; these are important tests for assessment of patients' general health, haematological changes and presence of concomitant disease.

Interferon-gamma release assays: it can detect latent TB infection by measuring the interferon-gamma release in response to mycobacterium tuberculosis, but not bacille calmette Guerin (BCG) and most non tuberculous mycobacteria.

Treatment

The treatment of TB includes administration of multiple antibiotics over a specific period of time. Social contacts need screening and even treatment if necessary. Antibiotic resistance is an increasing problem in multiple drug-resistant tuberculosis infections. Standard treatment involves 6 months' treatment with isoniazid and rifampicin, given in the first 2 months with pyrazinamide and ethambutol. Treatment should be started immediately in any patient who is smear-positive, or smear-negative but with typical radiological changes and no response to standard antibiotics. Six months of therapy is appropriate for all patients with new-onset pulmonary TB and most cases of extrapulmonary TB. However, 12 months of

therapy is indicated for meningeal and spinal TB; in these cases, streptomycin may be used instead of ethambutol. When the resistance for anti TB drug is not anticipated, patients can be considered to be non-infectious after 2 weeks of appropriate therapy [9]. Pyridoxine (vitamin-B6) is indicated for pregnant women and malnourished patients to prevent isoniazid induced peripheral neuropathy.

Method

Thirty-seven of forty-one patients of pulmonary TB with sputum positive for AFB and negative serological test for HIV, were involved in this retrospective study started from March 01, 2015 to July 23,2015, at major TB center of AL-Hilla city, Iraq. Four patients were excluded from this study because of deficient data.

Patients distribution data included; smoking state, age, sex, HIV serological test in and ESR for each patient. The ESR is measured by Westergren method that detect the sedimentation rate of red blood cells in whole blood by mixing venous blood with an aqueous solution of sodium citrate and allowing the mixture to stand in an upright standard pipet (Fig. 4), reading the millimeters of the cells descending after one hour [10]. The dependent normal range of ESR in this study is 0-22 mm/hr for men and 0-29 mm/hr for women [11].



Figure 4. Westergren pipet array on StaRRsed automated ESR analyzer

The sputum of the involved patients in this research was examined for AFB using Zhiel Neelsen stain, where patient's sputum specimen is spread on a microscope slide. A staining dye is added to the cells of the specimen, and then washed by an acid solution. The cells are then examined under a microscope (Fig. 5). If the cells retain the stain, this confirms the presence of mycobacterium. Most mycobacteria are known to be acid-fast, which means they hold onto the dye when washed in an acid solution [12].

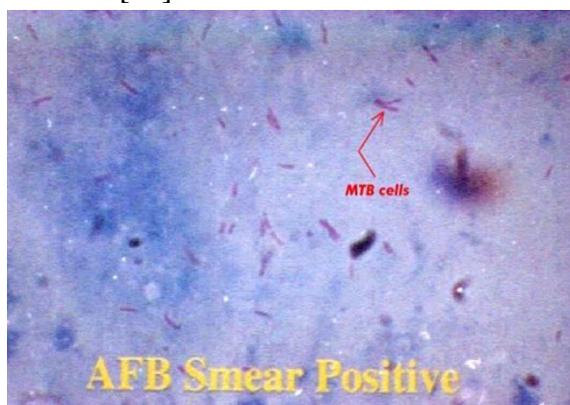


Figure 5.
positive AFB smear

The serological test for HIV that used in this study is Enzyme-Linked Immunosorbent Assays (ELISA). ELISA is the most widely used type of test to screen for HIV infection because of its relatively simple, has high sensitivity, and appropriate for large numbers of samples. More than 40 different ELISA test kits are available, but only about 10 are licensed by the FDA for use in the United States [13].

Results

Of the total thirty-seven patients involved in this study, seven patients (19%) with normal ESR according to dependent normal range in this study (Figure 6). Three patients (8.1%) with ESR less than 20mm/hr,

thirteen patients (35.1%) with ESR 20-40mm/hr, twelve patients (32.4%) with ESR 41-60mm/hr and nine patients (24.3%) more than 60 mm/hr. Unfortunately, we didn't obtain the PCV (packed cell volume) of the involved patients in this retrospective study where this may affect the real results of ESR. Twenty-one (57 %) were males and sixteen (43 %) were females (Figure 7). The ages of the male patients ranged from 21 to 82 years, and the females from 23 to 75 years in addition to one girl of 5 years old. The mean age of the total patients is 51.2 years. Twenty-two (59.5 %) patients are cigarette smoker and fifteen (40.5 %) nonsmoker (Figure 8).

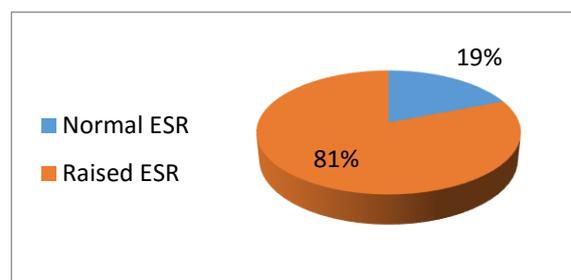


Figure 6.
Percentage of patients with normal and patients with raised ESR according to normal range of Mayo Foundation for Medical Education and Research.

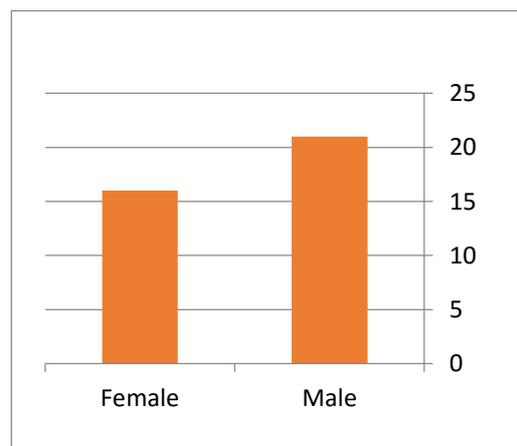


Figure 7.
No. of males and female's patients.

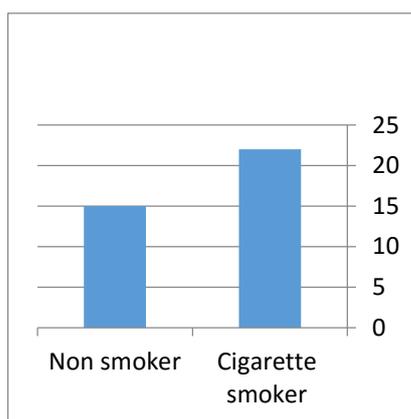


Figure 7.
No. of cigarette smoker non-smoker patients.

Discussion

The ESR is a blood test measuring the rate of fall of red blood cells in a column of anticoagulated blood in 1 hour, with the units expressed in millimeters per hour (mm/h) [14]. This test is widely used as nonspecific test for many pathological conditions such as infections, inflammatory diseases and neoplastic disorders. In general, the ESR in the women tend to be higher, and menstruation and pregnancy can elevate the ESR temporarily.

Drugs such as methyldopa, oral contraceptives, penicillamine procainamide, theophylline, and vitamin A can increase ESR, while aspirin, cortisone, and quinine may decrease it. There is another method for detection of ESR in minutes by centrifugation and this is particularly useful in emergency department. Although the ESR test is useful as it simple and cheap but we should avoid false reassurance of normal result in patient with clinical suggestion of pulmonary TB to prevent serious and avoidable complications that can result from delayed diagnosis and treatment of pulmonary TB. HIV serological test was done for all patients in this study where any impairment of immunity makes the patient liable for many sorts of infection including

TB. The very low prevalence of HIV infection in Iraq don't reluct the need of HIV screening tests specially for risky groups. TB infection an important cause of morbidity and mortality among HIV infected patients; the WHO estimates that TB accounts for up to a third of AIDS deaths worldwide. When someone is infected with TB, the likelihood of them becoming sick with the disease is increased many times if they are also HIV positive [15].

Twenty-two of total thirty-seven patients involved in this study were smoker, this high percentage (59.45%) make the smoking an important risk factor of pulmonary infection particularly pulmonary TB where the cigarette smoking can damage the respiratory mucosa and decrease resistance to infection. The crowding and alcohol ingestion, renal failure, diabetes mellitus, and many immunodeficiency disorders are other risk factors for pulmonary TB.

Conclusion and Recommendation

19 % of patients involved in this study have normal ESR, so the pulmonary TB should be expected in any patient with suggestive clinical features even when the ESR is normal specially in an endemic area as in Iraq. Cigarette smoking important risk factor of pulmonary TB and we should encourage the smoking cessation and supporting programs for avoidance of smoking specially in risky groups. Although the prevalence of HIV infection is very low in Iraq, the proper screening test for HIV infection is highly recommended.

Competing interests

The authors declare that there is no conflict of interest.

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