RELATIONSHIP BETWEEN ERYTHROCYTE SEDIMENTATION RATE (ESR) AND TIME TO SPUTUM SMEAR CONVERSION IN ACTIVE PULMONARY TUBERCULOSIS/LARYNGEAL TUBERCULOSIS

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ABSTRACT

BACKGROUND

Tuberculosis has been a major case of suffering and death since time immemorial. Thought to be one of the oldest human diseases, the history of Tuberculosis is at least as old as mankind. The aim of this study is to identify the relationship between erythrocyte sedimentation rate and time to sputum smear conversion in active pulmonary/laryngeal tuberculosis. The study on Relationship between ESR and time to sputum smear conversion in active pulmonary tuberculosis/laryngeal tuberculosis was conducted among 50 patients who attended as outpatients at Meenakshi Hospital, Avadi, Chennai – 600055.

MATERIALS AND METHODS

The dependent variable chosen was the time during which the patient continued to have positive sputum smears once specific treatment was initiated, i.e. from the day of diagnosis and initiation of treatment until the day a second negative sputum stain was obtained. During this period, a sample was obtained every 7 days.

The secondary quantitative variables were age, haemoglobin and ESR. Secondary qualitative variables were sex, toxic habits, initial sputum quantification and site of tuberculosis.

Study Design- The present study included adult patients above 15 years and patients with pulmonary tuberculosis/laryngeal tuberculosis and positive sputum smears at the time of diagnosis with documentation of acid fast bacilli through Ziehl–Neelsen staining of sputums. In our study of 50 cases, 6 cases had laryngeal tuberculosis along with pulmonary tuberculosis – 4 cases were male and have lesions in the interarytenoid region and 2 cases were female and had lesion in ® arytenoid. None of the patients in our study was diagnosed with diabetes. With the identification of granulomatous inflammation, caseating granuloma, acid fast bacilli on HPE of the biopsied laryngeal tissue, diagnosis was confirmed. Exclusion criteria included moribund state, seropositive HIV antibodies, seizure disorders, hepatic and renal disorder.

RESULTS

The observation and results are depicted in the form of histogram, pie charts and tabular column. In our study for the age group of (51–60) years, the mean time of sputum conversion in weeks was highest (5.85) weeks. Patients with ESR > 71, the mean time of sputum conversion was 6.5 weeks. Radiologically, lesions with cavitations the mean sputum conversion time was 5.52 weeks and lesions without cavitations it was 3.83 weeks. In Sputum Quantification, 3+ score patients had a mean sputum conversion time of 6 weeks.

According to our study, sputum smear conversion is the best indicator of treatment response. ESR can be taken as a possible predictor of the time during which the patient will remain sputum smear positive.

CONCLUSION

- Sputum smear conversion is the best indicator of treatment response.
- The older the patient, the longer the time to conversion.
- There is direct relationship between ESR and conversion period. A high ESR prolongs the sputum smear conversion.
- Presence of cavitation radiologically was associated with a longer time to conversion.
- Presence of abundant AFB in sputum is associated with a longer conversion period.
- ESR can be taken as a possible predictor of the time during which the patient will remain sputum smear positive.

KEYWORDS

ESR, Sputum Smear Conversion, Relationship.

HOW TO CITE THIS ARTICLE: Haridas PV, Sugeetha KV. Relationship between erythrocyte sedimentation rate (ESR) and time to sputum smear conversion in active pulmonary tuberculosis/laryngeal tuberculosis. J. Evolution Med. Dent. Sci. 2016;5(84):6234-6238, DOI: 10.14260/jemds/2016/1409

Financial or Other, Competing Interest: None.
Submission 07-09-2016, Peer Review 29-09-2016,
Acceptance 07-10-2016, Published 18-10-2016.
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DOI: 10.14260/jemds/2016/1409

BACKGROUND

The World Health Organisation (WHO) estimates that there are almost 13.7 million people living with Tuberculosis and that the disease kills more young people and adults than any other infectious disease in the world.

Sputum Smear Positive (SSP) Pulmonary/Laryngeal tuberculosis, patients are the most significant source of infection for tuberculosis, because when they cough or sneeze they expel droplet of Nuclei which carry infections Bacilli.

When SSP patients are initiated on multidrug anti-tuberculosis treatment, there is a multifold reduction in bacillary load expelled in sputum.

Smear conversion is defined as new smear positive pulmonary TB cases who become smear negative after a period of anti-TB treatment and are no longer infectious.

The most important symptoms in the diagnosis of pulmonary tuberculosis are: Cough of more than 3 weeks, expectoration of sputum, weight loss. Other respiratory symptoms like haemoptysis, chest pain or breathlessness and constitutional symptoms like fever/night sweats, tiredness and loss of weight may also be present. Physical findings are usually non-specific.

All patients with clinical features suspicious of pulmonary tuberculosis sputum for diagnostic sputum smear microscopy was done. The isolation of Mycobacterium tuberculosis is the gold standard for the diagnosis of tuberculosis.

A single specimen of sputum will miss about 25% of microscopically smear positive cases and about 50% of culture positive cases. So it is suggested that at least 3 specimens of sputum is to be examined for AFB: a first spot specimen, an early morning home specimen; a second spot specimen, an early morning specimen collected after awakening have the highest yield in demonstrating AFB, since they represent secretions accumulated overnight.

The Chest Radiograph and Diagnosis of Pulmonary Tuberculosis

No chest x-ray pattern is absolutely typical of pulmonary tuberculosis. The chest x-ray findings associated with pulmonary tuberculosis may be of either classical or typical pattern.

Radiographic manifestations of parenchymal tuberculosis is divided into Primary and Post-Primary phases depending on clinical stage of disease.

MATERIALS AND METHODS

Patients who attended the Meenakshi Hospital, Avadi, from July 2015 to December 2015 with respiratory symptoms suggestive of tuberculosis aetiology were subjected for sputum examination on three occasions.

Cases were defined as all patients with pulmonary tuberculosis and positive sputum smears at the time of diagnosis with documentation of Acid-Fast Bacilli (AFB) through Ziehl-Neelsen (ZN) straining of sputum.

The dependent variable chosen was the time during which the patient continued to have positive sputum smears once specific treatment was initiated, i.e. from the day of diagnosis and initiation of treatment until the day a second negative sputum stain was obtained. During this period, a sample was obtained every 7 days.

The secondary quantitative variables selected were age, haemoglobin and erythrocyte sedimentation rate.

The secondary qualitative variables studied were sex, toxic habits (Tobacco, alcohol), tuberculosis, initial sputum quantification (Numerous of few AFBs) and site of tuberculosis (Pulmonary).

Classification of Extent of Lesions Radiologically

The extent of lesions in the x-rays of the 50 patients taken up for the study were classified based on the classification of the National Tuberculosis Association of the U.S.A, which is as follows.

Minimal

Minimal lesions include those which are of slight-to-moderate density, but which do not contain demonstrable cavitation. They may have density, but they do not contain demonstrable cavitation. They may involve a small part of one or both lungs, but the total extent regardless of distribution should not exceed the volume of lungs, but the total extent regardless of distribution should not exceed the volume of lungs on one side which is present above the second chondrosternal junction and the spine of the fourth or the body of the fifth thoracic vertebra.

Moderately Advanced

Moderately advanced lesions may be present in one or both lungs, but the total extent should not exceed the following limits: disseminated lesions of slight-to-moderate density which may extend throughout the total volume of one lung or the equivalent in both lungs; dense and confluent lesions which are limited in extent to one-third the volume of one lung; total diameter of cavitation if present must be less than 4 cms.

Far Advanced

Lesions more extensive than 'moderately advanced.'

RESULTS

The following data is obtained from the present series of 50 cases taken from those who attended as outpatients at Meenakshi Hospital, Avadi, Chennai.

Age	No. of Patients	Percentage
10 - 20	2	4%
21 - 30	6	12%
31 - 40	10	20%
41 - 50	20	40%
51 – 60	8	16%
61 – 71	2	4%
> 70	2	4%

Table 1: Age Wise Distribution

In the above table, there are two patients in the age group 10-20 (4%) years, 6 patients in the age group 21-30 (12%) years, 10 patients in the age group 31-40 (20%), 20 patients in the age group 41-50 (40%), 8 patients in the age group 51-60 (16%) and two patients in 61-70 (4%) and two patients above 70 years of age.

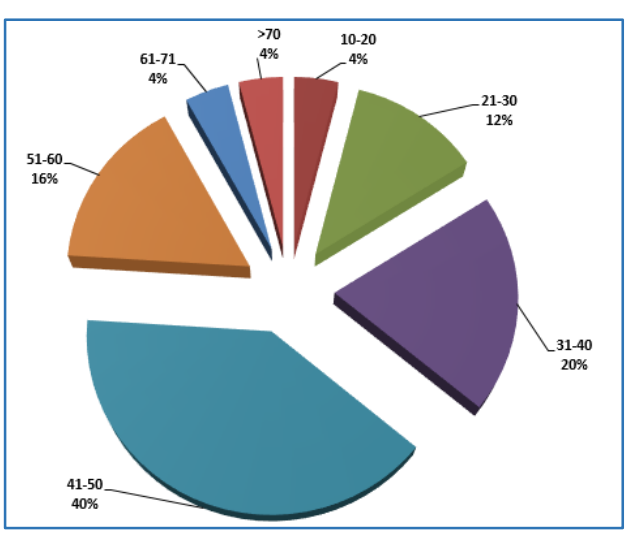

Fig. 1: Age Wise Distribution

Sex	No. of Cases	Percentage
Male	42	84%
Female	8	16 %
Table 2: Sex Distribution		

The above Table shows 42 cases (84%) of male patients and 8 (16%) cases of female patients in the study.

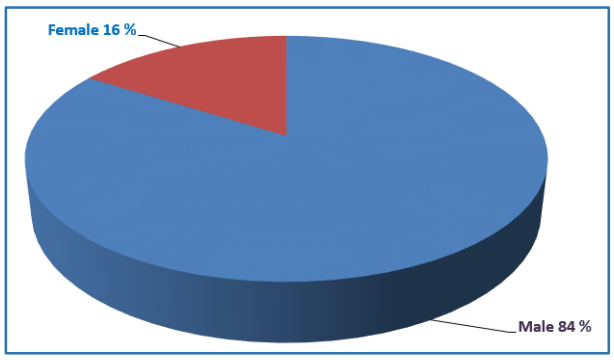

Fig. 2: Sex Distribution

Age	Mean Time of Sputum Conversion in Weeks
11 - 20	3.5
21 – 30	4
31 – 40	4.6
41 – 50	5.35
51 – 60	5.85
61 – 70	6
> 70	7
Table 3: Age: Mean Time of Sputum Conversion in Weeks	

The above table shows patients in age group (11-20 years) had a mean time of sputum conversion of 3.5 weeks, (21-30 years) had a mean time of sputum conversion of 4 weeks, (31-40 years) had a mean time of sputum conversion of 4.6 weeks, (41-50 years) had a mean time sputum conversion of 5.35 weeks, (51-60 years) had a mean time of sputum conversion of 5.85 weeks and (61-70 years) had a mean time of sputum conversion of 6 weeks and above 70 years had a meantime of sputum conversion of 7 weeks.

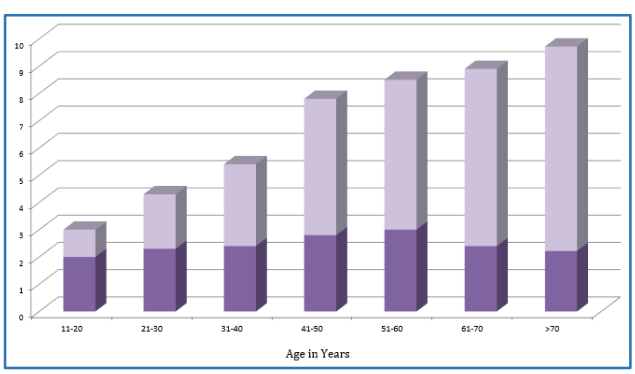

Fig. 3: Age: Mean Time of Sputum Conversion in Weeks

ESR	No. of Cases	Mean Time of Sputum Conversion in Weeks
11 - 20	4	3.5
21 – 30	4	3.5
31 – 40	4	4.25
41 – 50	10	5
51 – 60	14	5.07
61 – 70	6	6.3
> 71	8	6.5
Table 4: ESR: Mean Time of Sputum Conversion in Weeks		

ESR	Mean Time of Sputum Conversion in Weeks
< 60	4.26
> 60	6.40

Patients with ESR between 11 and 20 had a mean sputum conversion time of 3.5 weeks. Patients with ESR between 21 and 30 had a mean time of sputum conversion of 3.5 weeks. Patients with ESR between 31 and 40 had a conversion time of 4.25 weeks. For those with ESR between 41 and 50 had a sputum conversion of 5 weeks. Those whose ESR was between 51 and 60 had a sputum conversion of 5.07 weeks. Patients with ESR between 61 and 70 had a sputum conversion time of 6.3 weeks and those above 71 had a sputum conversion time of 6.5 weeks.

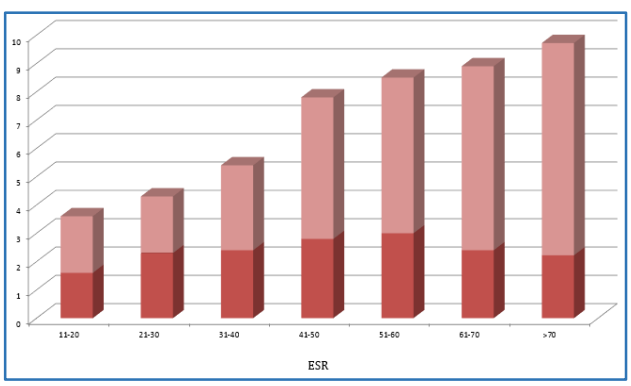

Fig. 4: ESR: Mean Time of Sputum Conversion in Weeks

Radiological Classifications	Number of Patients	Percentage
Lesions with cavitations	38	76%
Lesions without cavitations	12	24%
Table 5: Radiological Lesions		

The above table shows 38 (76%) patients of the study had radiologically moderate lesions with cavitations and 12 (24%) patients had lesions without cavitations.

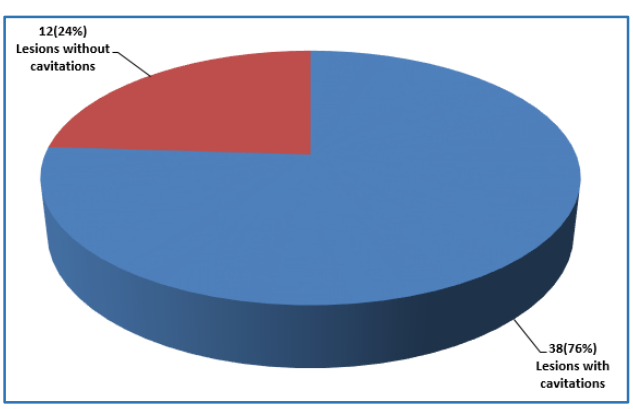

Fig. 5: Radiological Lesions

Radiological Lesions	Mean Sputum Conversion Time in Weeks
Lesions with cavitations	5.52 wks.
Lesions without cavitations	3.83 wks.

Table 6: Radiological Lesions and Mean Sputum Conversion Time in Weeks

The above table shows patients with moderate lesions with cavitations radiologically had a mean sputum conversion time of 5.52 weeks and patients with minimal lesion without cavitations had a mean sputum conversion time of 3.83 weeks.

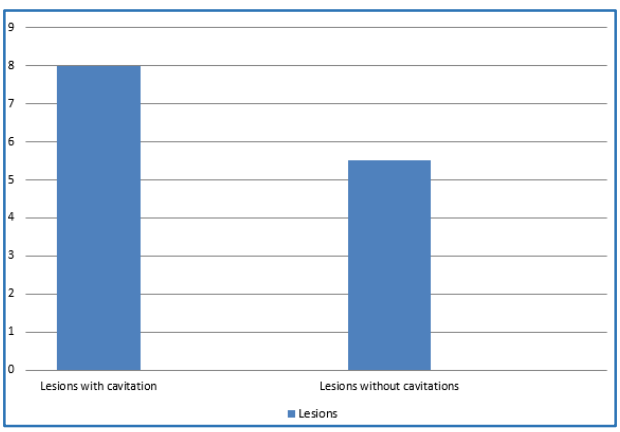

Fig. 6: Radiological Lesions and Mean Sputum Conversion Time in Weeks

Habit	Percentage
Smoking	20 (80%)
Alcohol Intake	15 (60%)
Both	15 (60%)

Table 7: Habits

The above table shows 20 (80%) patients were smoker and 15 (60%) patients were alcoholic, while 15 (60%) were both smokers and alcoholic.

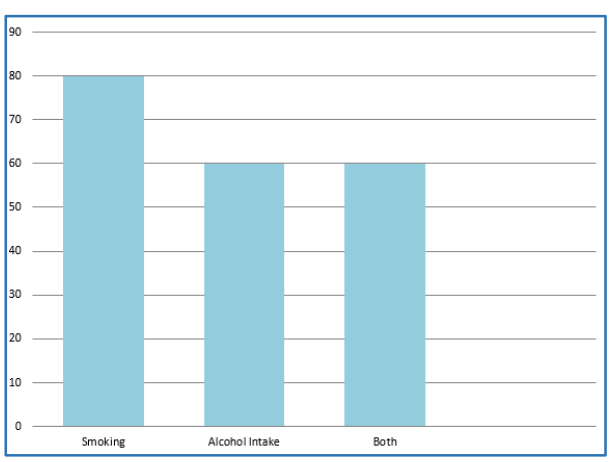

Fig. 7: Habits

Sputum Quantification	Sputum Smear Conversion Time
Scanty	- No Case Reported
1 +	3.5 Weeks
2 +	5 Weeks
3 +	6 Weeks

Table 8: Sputum Quantification

The above table shows the sputum quantification. Patients with 1+ score had a mean sputum conversion time of 3.5 weeks. Patients with 2+ score had a mean sputum conversion of 5 weeks and 3+ score patients had a mean sputum conversion time of 6 weeks.

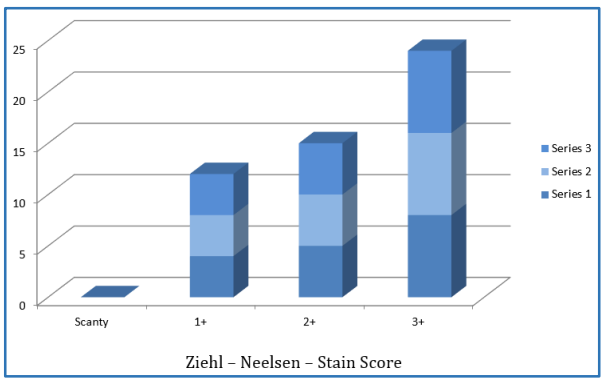

Fig. 8: Sputum Quantification

Sputum Quantification	Number of Patients	Percentage
Scanty	No case reported	0%
1+	18	36%
2+	20	40%
3+	12	24%

Table 9: Sputum Grading Distribution

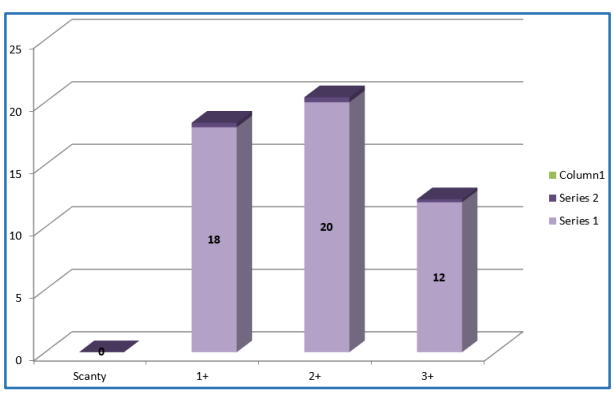

Fig. 9: Sputum Grading Distribution

DISCUSSION

There is currently consensus on the need to isolate TB patients, but not on when to suspend isolation. Once effective treatment has been initiated, the duration of infectiousness and the consequent period of isolation are still subjects of discussion.

When bacilli are exposed in vitro to either isoniazid or Rifampicin alone, the number of viable bacilli diminishes by more than 90% in 2 weeks. In vivo, this means a decrease of 10^7 to 10^4 viable bacilli per mL. When patients initiate effective therapy, the concentration of bacilli diminish rapidly. All patients must be considered to be infectious, while their sputum remain positive.

As the specificity of AFB in sputum in the diagnosis of TB is over 98%, more aggressive complementary tests are normally not necessary. Sputum smear conversion is the best indicator of treatment response.

Tuberculosis is a major pulmonary disease and infects a third of the world's population[1] and is the leading cause of death in adults due to infectious disease.[2] WHO has a working definition of a 'Case' as a person excreting tubercle bacilli in

sputum. This definition identifies excretors of tubercle bacilli as a clear priority for chemotherapy and as the target of case finding.[3]

In the present study, the mean period during which the patients presented a positive smear once anti-tuberculosis treatment initiated was 4.63 wks.

The risk of progression from infection to disease depends greatly on the capacity of the immune systems to stop multiplication of bacilli.[4]

The quantitative factors that demonstrate a positive association, i.e. that the quantity is related to a greater period of time with positive sputum smears were age and ESR[5] (Table I, III and IV).

A study by Walker D, McNerney R, Foster S[6] of a total of 166 acid-fast bacilli positive suspects who had three sputum smears examined sequentially, 128 (77.1%) were found on the first smear, a further 25 (15%) on the second smear and 13 (7.9%) additional cases were identified on the third smear. The economic analysis shows that the incremental cost of performing a third test having already done two increases rapidly with only a small gain in terms of additional cases of tuberculosis identified.

A policy of examining two samples should be considered in resource-poor settings if the remaining steps of the national diagnostic algorithm can be adhered to with respect to smear negative suspects.

In a study by Kivihya-Ndugga LE and Van Cleeff MR,[7] it was shown that using fluorescence and light microscopy collecting two smears rather than three would only marginally reduce sensitivity and would slightly improve the specificity of diagnosis of tuberculosis.

A study by Menzies D et al[8] suggested that animal and in vitro evidence suggest that patients with active tuberculosis remain contagious at least 2 weeks after the initiation of therapy. It has also been predicted that after 2 weeks of therapy almost all smear positive patients will remain culture positive and more than one half will remain smear positive.

A Domínguez-Castellano[9] in his study has concluded that old age is associated with a longer time to sputum smear conversion.

He has also documented that as ESR increases the time to sputum smear conversion also increases.

In our study the older the patient the longer the time to conversion - a finding documented by Liu et al.[10] The direct relationship between ESR and the conversion period could make this reactant. A possible predictor of the time during which the patient will remain sputum smear positive.

In radiographic pattern found in our study, cavitation (Table V and VI) was the pattern associated with a longer time to conversion. The most frequent radiographic pattern of tuberculosis found is upper lobe involvement and 90% of patients with cavitation are smear positive.

In most studied cavitary disease appears as the risk factor that most prolongs the period to sputum negativisation. Of all the radiographic patterns found in our study, cavitation was the pattern associated with a longer time to conversion.

In the final analysis, we can indicate that high ESR seem to be associated with a longer time to sputum smear conversion in patients with active pulmonary tuberculosis.

Older patients and patients with cavitary disease seem to be associated with a longer time to sputum smear conversion.[11]

The presence of abundant AFB in sputum (Table VIII) at diagnosis, a high Ziehl-Neelsen stain score is associated with prolonged smear conversion duration, a study confirmed by Telzak EE, et al.[12]

CONCLUSION

- Sputum smear conversion is the best indicator of treatment response.
- The older the patient, the longer the time to conversion.
- There is direct relationship between ESR and conversion period. A high ESR prolongs the sputum smear conversion.
- Presence of cavitation radiologically was associated with a longer time to conversion.
- Presence of abundant AFB in sputum is associated with a longer conversion period.
- ESR can be taken as a possible predictor of the time during which the patient will remain sputum smear positive.

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