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Research Article

**ANALYSIS OF BACTEC TEST OF CSF IN CNS  
TUBERCULOSIS**Dr. Faisal Atta<sup>1</sup>, Dr. Armghan Khalid<sup>2</sup>, Dr. Ussama Iftikhar<sup>2</sup><sup>1</sup>Rural Health Centrer Roda Khushab<sup>2</sup>Rural Health Centre Renala Khurd, District Okara**Article Received:** July 2020**Accepted:** August 2020**Published:** September 2020**Abstract:**

**Introduction:** In Pakistan, tuberculosis is generalized and wide spread. There have been two prevalence surveys conducted in 1960-62 and 1974-78 with similar results. According to these surveys 54% of the entire population is infected and this infection rate goes as high as 80% in age groups of 20-29 years and above. **Objectives:** The main objective of the study is to analyze Bactec test of CSF in CNS Tuberculosis. **Methodology of the study:** This descriptive study was conducted at Services Hospital Lahore during June 2019 to February 2020. We follow the following procedure for the analysis of TB in local population of Pakistan. The collected blood vials were tested every 2nd day for the first 2 weeks and weekly thereafter for a total of 6 weeks. The Bactec TB medium (12B) is an enriched middle-brook 7H9 broth base. Mycobacteria utilize a <sup>14</sup>C labelled substrate (fatty acid) present in the medium and release <sup>14</sup>CO<sub>2</sub> into the atmosphere above the medium. **Results:** A total 100 patients were included in the study. Out of these 100 patients 30 (30.94%) patients were male and 70 (70.05%) were females with male to female ratio of 1.03:1. This study was conducted in age groups 2 month to 14 years. Maximum number of cases 32(60.37%) were between 1-5 years. **Conclusion:** It is concluded that Polymerase Chain Reaction is the method for Rapid diagnosis of Tuberculous Meningitis. PCR was done on CSF and it was positive in 50.94% compared to Bactec and conventional smear and culture which showed positivity of only 15.09% & 3.77% respectively.

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**INTRODUCTION:**

In Pakistan, tuberculosis is generalized and wide spread. There have been two prevalence surveys conducted in 1960-62 and 1974-78 with similar results. According to these surveys 54% of the entire population is infected and this infection rate goes as high as 80% in age groups of 20-29 years and above<sup>1</sup>. According to these surveys infection rate in children from 0-14 years of age was 25% in 1960-62 and 22% in 1974-78, 1.6% of the population above 10 years of age had chest radiograph suggestive of active cavitory or non cavitory pulmonary tuberculosis and 0.3% were sputum positive on microscopy and/or culture<sup>2</sup>.

No age is immune to tuberculosis. It may affect any age ranging from intrauterine to upper limit of paediatric age. Incidence of infection increases as the age advances<sup>3</sup>. Tuberculosis can affect any tissue or system of body. Common presentations of tuberculosis are primary complex, tuberculous lymph adenitis and progressive primary disease. Due to introduction of BCG vaccination just after birth the clinical pattern of tuberculosis has changed<sup>4</sup>.

Neurotuberculosis is one of the serious complications of primary tuberculous infection. Tuberculous meningitis is its most dreaded form and is the main cause of death and disability in children<sup>5</sup>. CNS tuberculosis accounted for 65.5% of the total death. Tuberculous meningitis usually arises from the formation of a metastatic caseous lesion in the cerebral cortex or meninges that develops during the lymphohematogenous dissemination of the primary infection.

Tuberculous meningitis (TBM) the most dangerous form of extra pulmonary tuberculosis, occurs in 7-12% of tuberculosis patients in developing countries<sup>6</sup>. In 1985, 5% of 4000 extra pulmonary cases of tuberculosis in the USA were due to tuberculous meningitis. Tuberculous meningitis remains a common treat to health. Outcome in tuberculous meningitis is strongly associated with the stage of disease at presentation. The incidence of residual neurological handicap or death rises steeply where appropriate treatment is not initiated until after the emergence of reduced conscious level and focal neurological signs. Delay in diagnosis is directly related to poor outcome<sup>7</sup>.

**Objectives**

The main objective of the study is to analyze Bactec test of CSF in CNS Tuberculosis

**METHODOLOGY OF THE STUDY**

This descriptive study was conducted at Services Hospital Lahore during June 2019 to February 2020.

Definite information on tuberculous infection in children can be obtained only on recovery and identification of the organism from the patient. Specimen processing. Specimens such as sputum and pus which are often viscous and contain a large number of different microbial species must be liquefied and decontaminated. Urine, spinal, synovial and other fluids read no decontamination. Sodium hydroxide in the final concentration of 2% in diluted specimen is the most commonly used liquefying agent and digestant. The decontaminated specimen is concentrated by centrifugation. The supernatant is discarded and the sediment is used for culture and smear preparation<sup>8</sup>.

**1. Staining**

Acid fast bacilli can be demonstrated in the smear by either the conventional Ziehl-Neelsen carbol fuchsin stain or the fluorochrome staining technique. False negative results are commonly due to the presence of less than 10,000 bacilli per ml of specimen.

**1. Culture of Mycobacterium tuberculosis**

Traditionally two types of media are used for culture:

i. Egg based media e.g Lowenstein Jensen (L.J) medium.

ii. Agar based media, e.g Middle brook medium.

The growth of typical mycobacteria is slow and takes about 6-8 weeks for the colonies to appear. Thereafter the same length of time is required for complete identification and sensitivity testing.

**Rapid diagnostic tests for tuberculosis**

In TBM treatment cannot be delayed for want of a definitive diagnosis and therapy is often begun on a presumptive basis of the findings of cytology and biochemistry of CSF. Thus there is a crying need for rapid diagnosis of tuberculosis.

The tests available can be classified as:

**Indirect test:**

They usually measure product of the host response infection. These include:

i. Adenosine deaminase in CSF.

ii. Bromide partition.

iii. Antibody to mycobacterial antigen in CSF.

**Direct tests:**

They measure the product of the infecting organism. These include:

i. Biochemical identification of mycobacterial products like 3 (2 ketoethyl) indole by electron capture gas chromatography.

ii. Tuberculostearic acid by gas chromatography.

iii. Mass spectroscopy.

iv. Polymerase chain reaction.

v. Bactec system for rapid recovery of mycobacteria.

vi.ELISA for detecting mycobacterial antigen in CSF.

vii. Latex particle agglutination.

#### Bactec 460 Radiometric system

Radiometric detection of growth of M.Tuberculosis in vitro was first described by Middle Brook et al in Cooperation with Johnson laboratories. Bactec radiometric system uses fatty acid substrates like palmitic acid or formic acid labelled with radioactive carbon. As the mycobacteria metabolise these fatty acids, radioactive carbon dioxide is released which is measured as a marker of bacterial growth. Drug susceptibility studies with Bactec system generally show excellent correlation (98%) with conventional method of testing. The Bactec system used now a day's yields culture and susceptibility results in as little as 7 to 10 days and is more sensitive for sputum cultures than traditional media<sup>9</sup>.

#### Analysis

These vials were tested every 2nd day for the first 2 weeks and weekly thereafter for a total of 6 weeks. The Bactec TB medium (12B) is an enriched middle-brook 7H9 broth base. Mycobacteria utilize a 14C labelled substrate (fatty acid) present in the medium and release  $^{14}\text{CO}_2$  into the atmosphere above the medium. When the 12B medium vials

with growth were tested on the Bactec 460 instrument, the  $^{14}\text{CO}_2$  is aspirated from the vial and its radioactivity is determined quantitatively in terms of numbers on a scale from 0 to 999 numbers. These numbers are designated as Growth Index (GI). The GI numbers are displayed by the Bactec 460 instrument and are also printed out along with identifying rack and both numbers. The daily increase in the GI output is directly proportional to the rate and amount of growth in the medium. The Bactec instrument also introduces fresh 5%  $\text{CO}_2$  in air into the medium head space every time a vial is tested. This enhances the growth of mycobacteria. The instrument automatically tests 60 vials at the rate of approximately one vial per minute and stops at the end of the run<sup>10</sup>.

#### RESULTS:

A total 100 patients were included in the study. Out of these 100 patients 30 (30.94%) patients were male and 70 (70.05%) were females with male to female ratio of 1.03:1. This study was conducted in age groups 2 month to 14 years. Maximum number of cases 32(60.37%) were between 1-5 years. Next common age group was 6-10 years, 11(20.75%). There were 3(5.66%) and 7(13.20%) patients of age <1 year and >10 years respectively (Table VII, Graph II). The median age is 3 years.

**Table 01: Results of Smear, Culture, PCR and Bactec Test**

	Smear		AFB culture		Bactec Test		PCR	
	(Z-N staining)		(L-J Medium)		12 B Medium			
	No.	% age	No.	% age	No.	% age	No.	% age
I	2	6.25%	2	6.25%	4	12.50%	18	56.25%
II	0	0	0	0	4	22.22%	8	44.44%
II	0	0	0	0	0	0	1	33.33%
Total	2	3.77%	2	3.77%	8	15.09%	27	50.94%

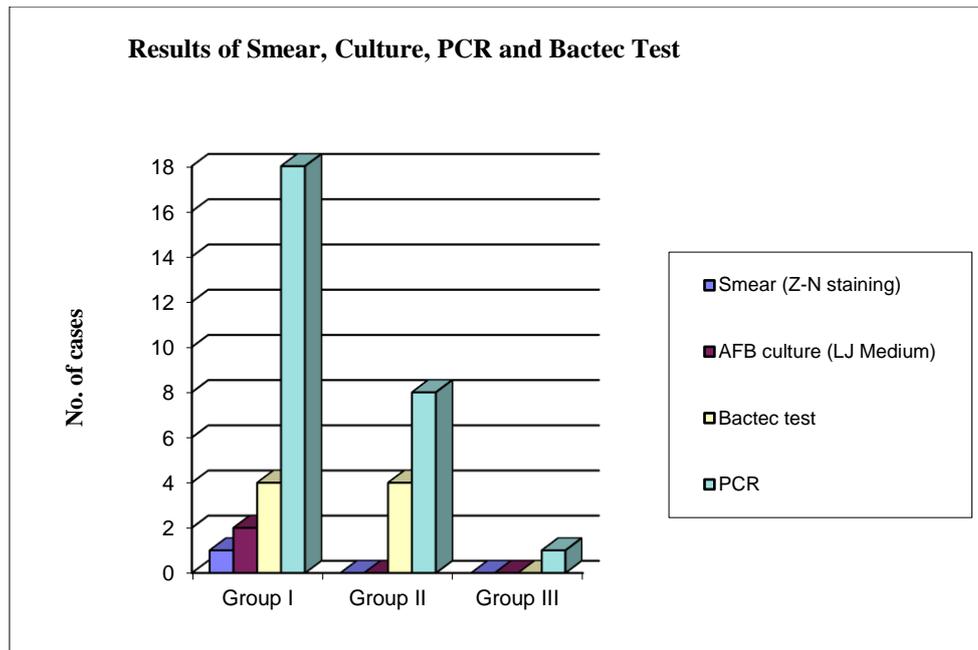
Smear Vs Culture  $p > 0.05$

Smear Vs Bactec  $P < 0.05$

AFB culture Vs Bactec  $P < 0.05$

PCR Vs Smear, Culture, Bactec

$P < 0.05$  (using Z score for proportion)



**Figure 01: Result of Smear, Culture, PCR and Bactec test**

Bactec test was positive in 4 of 32 (12.5%) highly probable cases and 4 of 18(22.22%) probable cases. Total 8 of 53 (15.09%) cases had Bactec positive. Most common X-ray chest finding was lymphadenitis total 10 of 53 (18.86%) case had positive X-ray chest findings. Two patients had miliary shadows. CT scan was done in 14 of 32(43.75%) highly probable of cases and 8 of 18 (44.44%) probable cases and 1 of 3(33.33%) possible cases.

#### DISCUSSION:

Tuberculosis is the world's leading cause of death from a single infection's agent. In developing countries like Pakistan tuberculosis continuous to be major health problem. The factors responsible for failure to control tuberculosis in Pakistan are low socioeconomic conditions, lack of health education, non-compliance and drug resistance. For the same reason mortality is high in developing countries. The reported tuberculosis rates among children less than 15 years of age in the United States increased by 40% from 1985 to 1993<sup>9</sup>.

The most severe complication of tuberculosis is infection of the central nervous system, which is invariably fatal if appropriate therapy is not administered promptly. Outcome of tuberculous meningitis is strongly associated with the stage of disease at presentation. In this study 66.03% children presented in Stage III and 32.07% in Stage II and 1.88% in Stage I and the mortality was 75.47% among them mainly those who presented in Stage III<sup>10</sup>.

#### CONCLUSION:

It is concluded that Polymerase Chain Reaction is the method for Rapid diagnosis of Tuberculous Meningitis. PCR was done on CSF and it was positive in 50.94% compared to Bactec and conventional smear and culture which showed positivity of only 15.09% & 3.77% respectively.

Although many studies have shown higher sensitivity of PCR on sputum but the decrease sensitivity in case of CSF.

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