CNS TUBERCULOSIS AND STROKE, BURDEN, MANAGEMENT CHALLENGES AND FUTURE NEEDS FOR CARE AND RESEARCH

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Abstract:
Introduction: Tuberculosis is an ancient disease that is known to have existed in prehistoric times. Tuberculosis is one of the commonest communicable diseases in a majority of the developing countries. Objectives: The main objective of the study is to analyse the CNS tuberculosis and stroke, burden, management challenges and future needs for care and research. Material and methods: This cross-sectional study was conducted in Civil hospital Karachi during 2019-2020. In this study 55 patients age range 1 to 5 years suspected of having tuberculosis meningitis were included in the study. The 5cc blood was taken for the analysis of further biochemical test. Results: A total 55 patients were included in the study. Out of these 55 patients 32 patients were in highly probable TBM group and 18 cases in group II (Probable TBM) and 5 patients belonged to group III (Possible TBM). Out of these 55 patients 27(50.94%) patients were male and 26 (49.05%) female. This study was conducted in age groups 2 month to 14 years. Table 01 shows the basic biochemical profile of these 55 patients. Conclusion: It is concluded that hematological and biochemistry parameters are important, simple, and cheaper method in analyzing the pattern of health status among TB patients.

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INTRODUCTION:

Tuberculosis is an ancient disease that is known to have existed in prehistoric times. Tuberculosis is one of the commonest communicable diseases in a majority of the developing countries. It is caused by the Mycobacterium tuberculosis, which usually affects the lungs but may cause lesion in any organ or tissue of human body[1]. In more advanced countries the incidence has declined rapidly since the end of Second World War but disease is still present. Decline in the incidence came due to improvement in socioeconomic condition of people, improved sanitation and housing, BCG vaccination, early case detection and treating the affected persons. However, in developing countries tuberculosis is still a major health problem. In recent years there is resurgence of tuberculosis in Western countries due to AIDS, increasing number of immigrants from developing countries and increasing level of social deprivation in some inner-city areas of the developed world[2].

As children are only infected from infective adults, tuberculosis in children is a direct reflection of tuberculosis in adults. Tuberculosis continues to be a constant threat to the child population where-ever there is poverty, overcrowding and malnutrition[3]. In studies of tuberculosis, a differentiation has to be made between tuberculous infection evident by a positive tuberculin test and tuberculous disease in which there is clinical, radiological or bacteriological evidence of infection. The great majority of infected people remain asymptomatic[4].

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[5]. 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 cavitary or non cavitary pulmonary tuberculosis and 0.3% were sputum positive on microscopy and/or culture[6]. 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. 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[7].

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[5]. 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.

Objectives
The main objective of the study is to analyse the CNS tuberculosis and stroke, burden, management challenges and future needs for care and research.

MATERIAL AND METHODS:
This cross-sectional study was conducted in Civil hospital Karachi during 2019-2020. In this study 55 patients age range 1 to 5 years suspected of having tuberculosis meningitis were included in the study. The 5cc blood was taken for the analysis of further biochemical test.

Clinical analysis
1. History of fever, headache and neck stiffness of more than 2 weeks duration.
2. History of contact with active case of tuberculosis.
3. Abnormal neurological symptoms including nuclear rigidity, cranial nerve paresis, positive brudzinski signs, positive kernig sign, posturing, deep tendon reflexes abnormality, clonus. Full anterior fontanella and or signs. Lethargy, irritability, scizures, hemiareses, weakness irregular respiration, hypothermia.
4. Poor response to antibacterial therapy.
5. Clinical improvement after antituberculous therapy.

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.

Statistical analysis
The collected data were analyzed using SPSS software (version 17). The results are presented as a mean with 95% confidence interval limits or standard deviations. The significant value for $P < .05$ was accepted as statistically significant.

RESULTS:

A total 55 patients were included in the study. Out of these 55 patients 32 patients were in highly probable TBM group and 18 cases in group II (Probable TBM) and 5 patients belonged to group III (Possible TBM). Out of these 55 patients 27(50.94%) patients were male and 26 (49.05%) female. This study was conducted in age groups 2 month to 14 years. Table 01 shows the basic biochemical profile of these 55 patients. Thus, extrapulmonary TB was more common in the cirrhotic patients than pulmonary TB ($P < 0.05$). Most common presenting symptom was loss of appetite (82%) and fever (67%), weight loss (34%) and increasing ascites (25%). Maximum number of cases 32(60.37%) were between 1-5 years. Next common age group was 6-10 years, 11(20.75%).

Table 01: Clinical Features of Patients with TB

Clinical symptoms	Number (%)
Fever	45 (67%)
Unexplained weight loss	23 (34%)
Loss of appetite	55 (82%)
Increasing ascites not responding to diuretics	17 (25%)
Cough	8 (12%)
Pain abdomen	14 (21%)
Pulmonary tuberculosis	25 (37%)
Extrapulmonary TB	42 (63%)
Pleural effusion	10 (16%)
Nodal (chest)	3 (4%)
Intestinal	3 (4%)
Peritoneal	19 (29%)
Bone	3 (4%)
Meningeal	1 (1.5%)
Disseminated	2 (3%)
Liver	1 (1.5%)

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 02: 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	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
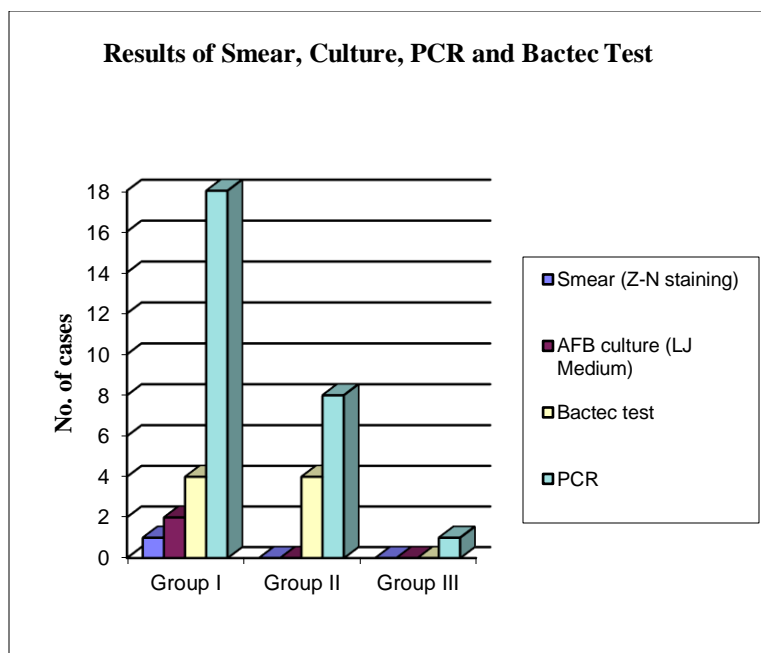**P <0.05 (using Z score for proportion)**

Figure 01: Result of Smear, Culture, PCR and Bectec 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 infections agent. In developing countries like Pakistan tuberculosis continuous to be major health problem[7]. The factors responsible for failure to control tuberculosis in Pakistan are low socioeconomic conditions, lack of health education, non-compliance and drug resistance[8]. 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[9].

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[10].

CONCLUSION:

It is concluded that hematological and biochemistry parameters are important, simple, and cheaper method in analyzing the pattern of health status among TB patients. 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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