

## **Prevalence and Determinants of Death from Tuberculosis Meningitis at Ethio-Swedish Children's Hospital**

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**Abstract:** A retrospective Descriptive analysis was made of 92 cases of Tuberculosis meningitis (TBM) admitted to Ethio-Swedish children's hospital in years 1989-1998. Diagnostic criteria included cerebrospinal fluid (CSF) pleocytosis, increases CSF protein, exclusion of other bacterial meningitis by gram stain or culture, suggestive radiographic changes and clinical course and history of exposure to tuberculosis. Thirty five patients were less than 5 yrs old or 5 yrs old. The commonest presenting symptoms were fever, vomiting, and cough, the most frequent physical signs were disturbed consciousness and meningeal signs 51 pt had been exposed to tuberculosis. Forty of the chest radiograms had suggestive of tuberculosis, sixty parents came from low economic status and low educational background. Five patients were taken home against medical advice; 43 died in the hospital, 26 (57%) of the discharged patients had different types of neurological sequelae.

### **INTRODUCTION**

Tuberculosis (Tb) is still one of the main causes of mortality and morbidity in developing countries. The over all incidence of Tb in Ethiopia is estimated to range from 90,000 to 154, 000 cases per year (1). The prevalence is estimated to fall between 180,000 and 308,000 (1, 2). According to the Ministry of health in our country Tb is a leading cause of

out patient morbidity ranking fourth with 3.7%, the third reason for hospital admission constituting 9.4% of all hospital admissions, and the first cause of hospital death being responsible for 27% of all patients who died in hospital (1).

The main source of infection for children are adult patients who are smear positive for acid fast bacillus. This fact has been clearly demonstrated in population where BCG Vaccination have never been implemented (3).

Two factors may increase the impact of Tuberculosis in children in the coming decade: the extension of poverty and global HIV epidemic. (2, 3). The HIV epidemic increases the risk of tuberculosis in the population. The increment in incidence ranges from 20% - 100% in different African countries (3).

The prevalence of Tb in children vary considerably from one country to another and within a given country depending on the socio-economic conditions prevailing in different communities or social groups. When children are exposed to infectious case high proportion of them are infected by the tuberculosis. Of those infected about 10% of them will sooner or later develop signs of the disease in the lungs or other systems. Some of those infected children, especially those under the age of 5 years may die of the most serious complications of primary infections (3,4).

TBM and acute miliary tuberculosis are the two early complications of primary infections which are particularly serious, because they are fatal if they go unrecognized. They are observed at all age groups especially in young children between the ages of 6 months and 4 years. TBM (Tuberculosis meningitis) occurs usually between 2 to 12 months after primary infection, manifested by irregular fever, character disturbance, disinterest towards play becomes irritable and disturbance in sleep pattern (4). The major signs develop within a week consisting of fever, headache vomiting, irritability, neck stiffness and occasional neurological signs such as strabismus, ptosis, and seizure (3, 4, 5).

When the diagnosis of TBM delayed consciousness is gradually impaired to the point of coma. Further delay in diagnosis results in functional sequel of varying severity including paralysis, deafness, and blindness (4, 6, 7). The diagnosis of TBM is difficult even in well equipped centers. In developing countries diagnostic facilities are scarce but high incidence of TBM is likely. In developed countries diagnostic measures are available but the incidence of TBM is falling. TBM

may not be considered early enough or it may be wrongly diagnosed as encephalitis or meningitis of other etiology. In our situation the diagnosis of TBM requires high degree of suspicion on the part of the clinicians. This means that the diagnosis should be based on presenting clinical, radiological, and biological evidences. The timing of treatment is the most crucial factor affecting the ultimate outcome (7,8,9) . Delayed treatment of TBM is associated with a high mortality and serious central nervous system complications.

The prognosis of TBM depends on the clinical stages of illness at the time of initial of therapy. Stage I have excellent outcome whereas most patients in stage 3 even if they survive will have permanent disabilities including blindness, deafness, paraplegia, diabetes insidious and mental retardation (4,7). A number of studies done previously have shown factors related to adverse outcome in TBM. Young age groups have poor outcome. Early diagnosis and prompt treatment will give better prognosis. (6,7,10).

The aim of this study is to determine the prevalence of TBM and to show the outcome and sequelae of the illness and look for determinant of death in children admitted to Ethio-Swedish hospital over 10 years period.

## **PATIENTS AND METHODS**

A retrospective descriptive study was made of the clinical records of patients admitted to the Ethio - Swedish Children Hospital in Addis Ababa with the diagnosis of Tuberculosis meningitis (TBM) over 10 years period (1989 – 1998). During this period a total of 31,767 patients were admitted to the same hospital, of which 164 were diagnosed as Tuberculosis meningitis. It was only possible to retrieve 151 cards.

The diagnosis of TBM was made when the following diagnostic criteria were fulfilled:

Cerebrospinal fluid (CSF) pleocytosis, with or without increased protein concentration. Exclusion of other bacterial meningitis by gram stain or culture.



Presence of evidence for tuberculosis such as: Symptom complex of tuberculosis, contact with known tuberculosis case and chest x- ray evidence of tuberculosis.

Patient who fulfilled the criteria were included in the study. Of the available records 92 fulfilled the above criteria. This study is based on the analysis of those records.

Complete information consisting of identification of the cases, address, complete medical history, social data, physical examination and laboratory data with treatment outcome were collected onto a form prepared for the purpose of the study.

The EPI-Info version 6 statistical programme was used for analysis. Comparison of categorical variables were analyzed using the chi-square test.

## RESULTS

Table 1 shows the age and sex distribution of the cases. The youngest patient was 5 months old. Six patients were younger than 1 year, 29 cases were 1 to 4 years old, 27 were between 5 to 9 years, and 30 were aged 10 to 14 years. Thirty eight percent of the patients were < 5 years of age. There were 60 males and 32 females, giving a male to female ratio of 2:1.

The presenting symptoms are summarized in Table 2. The most common were fever, vomiting, cough, Headache, convulsion and irritability. Many of the patients presented with several symptoms.

Duration of symptoms of less than 2 weeks was observed in 11 patients. Eighty one patients had symptoms for more than 2 weeks. Fifty one(55%) of the patients had history of exposure to tuberculosis cases.

Assessment of the nutritional status showed that 18 patients had satisfactory weight for age ,12 patients were marasmic and 60 were underweight. No information on weight was obtained for 3 children.

The physical findings at admission are summarized in Table 3. Disturbed consciousness and meningeal signs were the most frequent findings.

The leucocyte count in cerebrospinal fluid (CSF) ranged from 10 to 9760cells/ml. In 56 patients the glucose concentration was less 20mg/dl and the protein was greater

than 40mg/dl.

In 40 of the cases the chest x-ray was suggestive of tuberculosis, and it was normal in 20 patients.

PPD was done in 21 cases- it was positive in 9 cases and negative in 12. Thirty five patients were BCG vaccinated.

All patients were treated with antituberculosis drugs. Sixty three patients were treated with streptomycin, Isoniazid, Rifampicin and prednisone. Twenty nine patients received short course chemotherapy with prednisone.

The outcome of the disease in relation to various factors is summarized in Table 4. The outcome is worse in those who were under 5 years old and had symptoms for more than 2 weeks and those who came from low socio- economic status.

Forty (43%) patients died. Five patients were discharged against medical advice, all were critical at discharge. Two were discharged in coma after two months of intensive chemotherapy. Among the 47 patients discharged 26 had one or more neurological sequelae. Twenty one (23%) patients were completely cured.

#### DISCUSSION

In this study the average prevalence of TBM in children aged from 0-14 years admitted to Ethio-Swedish Children's Hospital between 1989-98 was 3.3%, which is a relatively a low figure. The reason for underestimation are several: parental reluctance to seek medical attention early enough, lack of knowledge about the gravity of the disease and distance from the health facility are some of the reasons. Furthermore health workers have difficulty in recognizing TBM in the young because of the non-specific nature of the symptoms.

Before the introduction of effective chemotherapy TBM was invariably fatal.

There is close association between the prognosis and the stage of the disease at which treatment is began (4). A large proportion of patients initiated on treatment after neurological changes developed either die or survive with severe sequelae. Similar findings were seen in our study. Eighty eight percent of the cases were admitted after developing neurological signs like disturbed level of consciousness. Similar complication rates were reported from ESCH), India and South Africa (6,11,12).

In our study only immediate outcome could be reported due to the retrospective nature of the study. In India 119 children who recovered from TBM were followed for 4-8 years and 17 patients died due to severe sequelae; and 47 recovered completely (12).

The outcome of TBM is worse in young children. A report from ESCH and Barcelona Children Hospital showed high rate of mortality and complications in children less than or equal to 3 years (6,8,13). In our study 30% of the cases were less than 3 years. Seventy percent of the cases were malnourished and this may have contributed to the poor outcome.

BCG did not have significant protective effect against TBM(7,11,13). A study in Barcelona reported that BCG vaccination has not changed the risk of developing TBM in children less than 5 years of age. In our study both vaccinated and unvaccinated children were equally affected with TBM.

Sixty five percent of the parents came from low socio-economic group and low parental educational background, both of which are associated tuberculosis and TBM. High

mortality is also directly associated with low parental economic status and low educational background of the parents.

#### Conclusions and Recommendations:

Early diagnosis and treatment of TBM is important for favorable outcome. The findings in the study are comparable with that of other authors. Due to the small number of patients conclusions could not be drawn from this study. A prospective cross sectional study is suggested.



Table 1: Age and Sex distribution of cases of TBM  
ESCH, 1989-1998

Age in years	Male	Female	Total %
< 1	5	1	6 (7)
1-4	19	10	29 (31)
5-9	16	11	27 (29)
10-14	20	10	30 (33)
Total	60	32	92

Table 2: Presenting symptoms among children with TBM  
ESCH, 1989 - 1998.

Symptoms	No. Pts (%)
Fever	91 (98)
Vomiting	51 (55)
Cough	50 (54)
Headache	50 (54)
Convulsion	42 (45)
Irritability	40 (43)
anorexia	47 (52)
Weight loss	45 (48)
Neck stiffness	25 (27)

Table 3: Physical signs among Children with TBM

ESCH, 1989 - 1998

Physical signs	No. Pts (%)
Disturbed consciousness	81 (88)
Meningeal signs	49 (53)
Ophthalmoplegia	8 (10)
Monoplegia	-
Paraplegia	-
Facial Palsy	10 (11)
Rigidity	18 (19)
Hemiplegia	15 (16)
Hydrocephalous	4 (4)

Table 4: Out come of TBM in relation to various factors,



	No. Of Children			
		Alive	Died	p. value
Age	< 5	15	14	<0.12945
	≥ 5	30	26	
Sex	M	27	27	<0.4730
	F	18	13	
Address	A/A	22	22	<0.8766
	out A/A	20	15	
Nutrition	- Marasmic	4	8	<0.081800
	- Under wt.	37	23	
	- Standard	9	9	
BCG Vaccination	yes	23	13	<0.0718
	No	26	20	
	Unknown	5	6	
Parents Income	< 250 birr	29	31	<0.295294
	≥ 250 birr	13	7	
Parents Education	- illiterate	15	21	<0.06003
	- read & write	18	15	
	> 12 grade	7	1	
Duration of Illness	< 2 wks	7	3	<0.5428
	> 2 wks	38	36	
Treatment Started	- at admission	10	20	<0.1706
	- < 72 hrs	11	9	
	- ≥ 72 hrs	18	10	

## REFERENCES

1. Ministry of Health Manual of National Tuberculosis and Leprosy Control Program Ethiopia, 1997.
2. A Clinical Manual WHO: TB/96,200, 55-61.  
Pierre C. et al. Childhood tuberculosis still with us. *Children in the tropics*, 1992(196-197): 42-47
3. Stark JR. Tuberculosis. In: Behrman R E, Kliegman R M , editors. *Nelson textbook of pediatrics*. Philadelphia Saunders 1992: 834-836.
4. Kendig EH, Inselman LS. Tuberculosis in Children. 233-257
5. Getnet Z and Esscher E. Ten years Experience of Tuberculosis Meningitis in Children. *Eth. Med. J.* 1984; 22: 49-54
6. Gebremariam A. Predictors of mortality in Childhood Neurotuberculosis: A retrospective study of 84 cases. *E Afri Med J.*1990;67: 756-760
7. Daniel TM. New approaches to the Rapid Diagnosis of Tuberculosis Meningitis. *J. Infect Dis.* 1987; 155: 599-602
8. Humphries MJ, Jcair TR and Gabriel M. Factors of Prognostic Significance in Chinese Children with Tuberculosis meningitis. *Tubercle* 1990; 71: 161-168
9. Ahuja GR, Mohan KK, Prasad K, Behari M . Diagnostic Criteria for Tuberculous Meningitis and their validation. *Tuberc. Lung Dis.* 1994; 75: 149-152.
10. Berman S, Kibel MA, Fourie PB, Strebel PM. Childhood tuberculosis and tuberculosis meningitis: High incidence rate in Western Cape South Africa. *Tuberc. Lung Dis.*1992; 73: 349-355.
11. Ramachandran P, Durapandian M, Rechtha AM, Mahalaskshni SM and Prabracar R. Long Term Status of Children Treated for Tuberculous Meningitis in South India. *Tubercle* 1989; 70: 235-239.
12. Ayuela PEM. Trends in tuberculosis meningitis in Barcelona in Children aged 0-4 years: Correlation with the annual risk of tuberculosis infection. *Tubercle and Lung Disease.* 1994; 75: 423-428