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Original Research Article

Clinical and Radiological Predictors of Outcome in Tuberculous Meningitis

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Abstract

Tuberculosis (TB) is a disease which has been affecting humanity since archaic ages. Robert Koch demonstrated that tuberculosis was caused by Mycobacterium tuberculosis in 1882. Tuberculous meningitis was first described as a distinct pathological entity in 1836.

Materials and Methods: The study was conducted in the Department of Medicine of ESIC Medical College and Hospital & GIMS Medical College, Kalaburagi from May 2022 to February 2023.

Results: One subject was diabetic and two were hypertensive. Two patients had underlying renal disease. None had underlying liver disease. Demographical features like sex of the subjects and age groups was not significantly associated with severe disability (P = 0.278, > 0.05; p = 0.156, > 0.05 respectively).

Conclusions: Even after complete treatment of TBM, morbidity remains high. Fever, headache, vomiting, altered sensorium are most common symptoms. Convulsion is a less common symptom. Abducens nerve is the most commonly involved cranial nerve.

Keywords: Tuberculosis, Radiological, Cranial Nerves.

Introduction

Tuberculosis (TB) is a disease which has been affecting humanity since archaic ages. Robert Koch demonstrated that tuberculosis was caused by Mycobacterium tuberculosis in 1882.[1] Tuberculous meningitis was first described as a distinct pathological entity in 1836.[2] TB is second to HIV as an infectious cause of death globally. In 2009, the global prevalence was 14 million, incidence was 9.4 million and mortality due to TB was 1.7 million.[3] An estimated 2 billion people carry latent infection, which represents a vast reservoir for future active TB cases. Tuberculosis remains a worldwide burden, with a large majority of new active tuberculosis cases occurring in underdeveloped and developing countries.[4-5] In fact, India, China, Indonesia, Nigeria, and South Africa rank first to fifth in the total number of incident cases of tuberculosis.[4-5] In 80% of new tuberculosis cases, social and demographic factors such as poverty, overcrowding, malnutrition, and a compromised immune system play a major role in the worldwide epidemic, while the remaining 20% of tuberculosis cases are associated with HIV in sub-Saharan Africa.[4-5]

The incidence of extrapulmonary TB is directly related to the prevalence of TB infection. CNS TB comprises approximately 10% of all TB cases.[6] Of the extrapulmonary forms of TB, tuberculous meningitis (TBM) is the most severe. It is difficult to diagnose and treat for a number of reasons: the pathology is poorly understood; rapid, sensitive and affordable diagnostics have yet to be developed; drug resistance is crucial to clinical outcome, and the optimal dose, duration and composition of anti-TB treatment regimens have still not been determined.(7) In addition, owing to an increasing number of immunocompromised hosts caused by the prevalence of AIDS, increasing numbers of older people, the wider use of immune -suppressive agents, and other factors, TBM remains a serious clinical and social problem.[5, 8-10] Owing to its relative rarity and the wide spectrum of its neurological symptoms, CNS tuberculosis remains a formidable diagnostic challenge.[5, 8-10]

Materials and Methods

The study was conducted in the Department of Medicine of ESIC Medical college and Hospital & GIMS Medical College, Kalaburagi from May 2022 to February 2023.

Inclusion Criteria: All cases of tuberculous meningitis -definite, probable and possible (as per above mentioned criteria)

Exclusion Criteria:

1. Patients whose CSF is positive for VDRL test/India ink stain/ Cryptococcal antigen/ Gram stain/ Pyogenic bacterial culture/ Fungal culture.
2. Patients who are HIV positive.
3. Patients who are currently on anti-tuberculous treatment.
4. Patients who do not consent for the study.

Statistical Analysis:

The data were analyzed using the Statistical Package for Social Sciences software version 17 for Windows (SPSS, Chicago, IL, USA). A univariate analysis was performed by Pearson chi-square test between various clinical as well as investigational parameters and three outcome groups- good, intermediate and severe disability. For analysis death was also included in severe disability group.

Results

Demography:

In this study, 35 subjects who fulfilled the inclusion criteria were included. Among 35 subjects, 21(60%) subjects were male and 14(40%) were female.

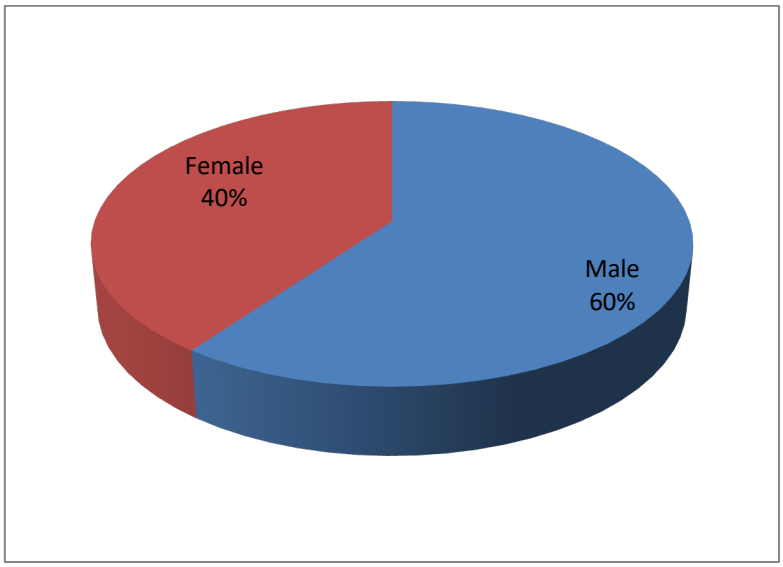

Figure 1: Distribution of subjects according to sex

Age of these subjects varied from 18 years to 72 years. Mean age was 32.8 years (SD 15.5). 22(63%) subjects were <30 years, 7(20%) subjects were between 30- 50 years and 6(17%) subjects were >50 years.

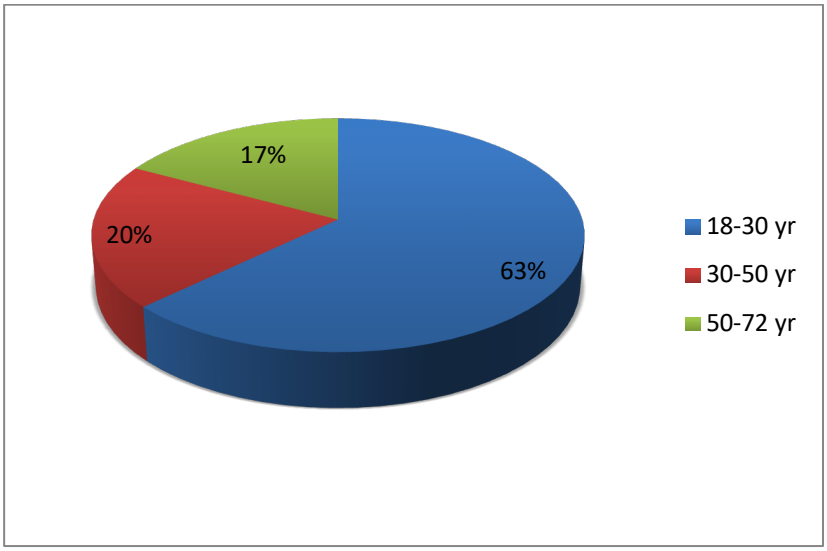

Figure 2: Distribution of subjects according to age groups

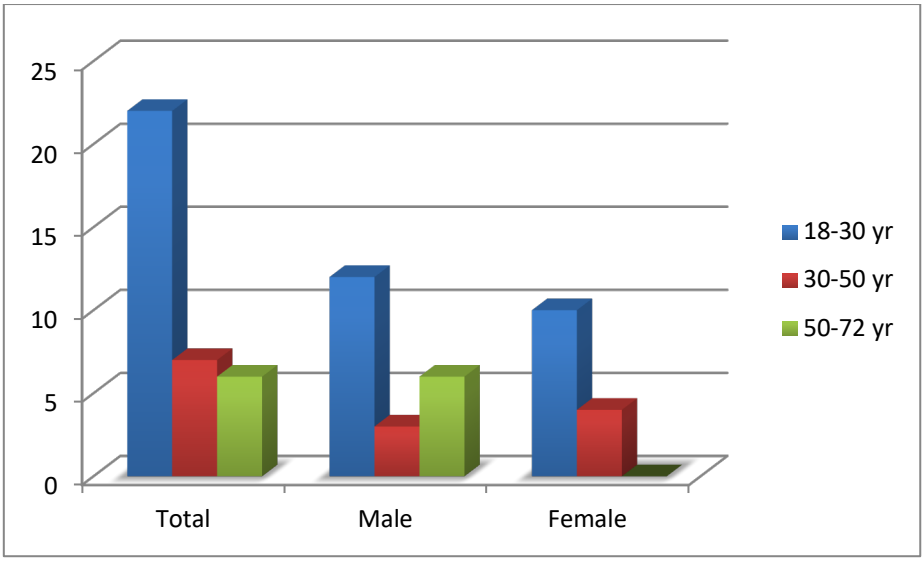

Figure 3: Distribution of male and female subjects according to age groups

Of these 35 subjects, one was "Definite" case of TBM, 12 were "Probable" and 22 were "Possible" cases of TBM.

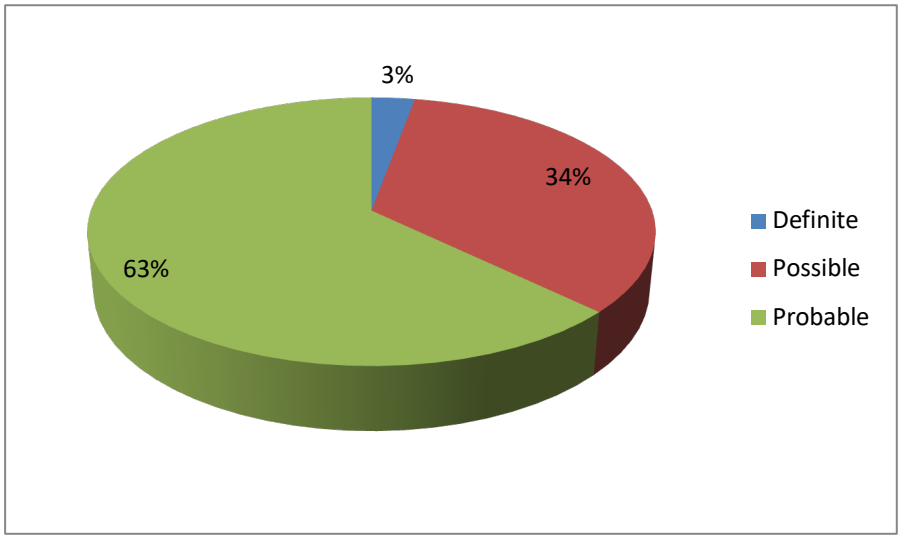

Figure 4: Distribution of subjects according to type of case of TBM

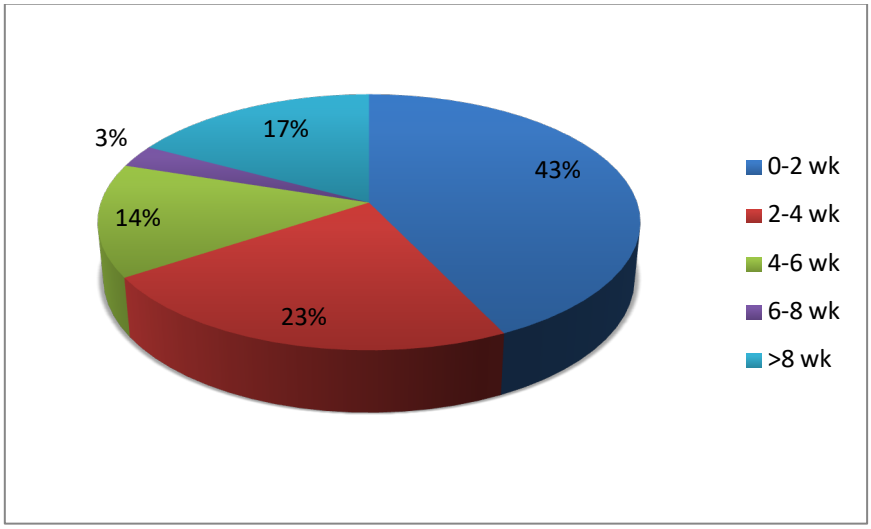

Figure 5: Distribution of subjects according to symptom duration

One subject was diabetic and two were hypertensive. Two patients had underlying renal disease. None had underlying liver disease. Demographical features like sex of the subjects and age groups was not significantly associated with severe disability (P = 0.278, > 0.05; p = 0.156, > 0.05 respectively). Type of case of TBM- Definite/ Possible/ Probable- was not significantly associated with severe disability (p = 0.311, >0.05).

Clinical Features:

a. Duration of symptoms

The duration of symptoms varied from 5 days to 60 days with the mean duration of symptoms being 26.66days (SD 20.04). 15(43%) subjects had symptoms ranging between 0-2 weeks, 8(23%) had symptoms between 2-4 weeks, 5(14%) had symptoms ranging between 4-6 weeks, one(3%) had symptoms between 6-8 weeks and 6(17%) had symptoms for >8 weeks(i.e. 20% subjects had symptoms for >6 weeks). Presence of symptoms for >6 weeks was significantly associated with severe disability (p = 0.021, < 0.05).

b. Symptoms

Fever (91%) and headache (91%) were most common symptoms. Vomiting was seen in 71% subjects. About half of the subjects were in altered sensorium on presentation. Convulsions (11%) and limb weakness (6%) were less common. Two subjects had hemiparesis and one subject had paraparesis. 7(20%) subjects had tuberculosis in past. Presence of fever, headache and presence of limb weakness not significantly associated with severe disability (p = 0.281, > 0.05; p = 0.528, > 0.05; p = 0.085, > 0.05 respectively).

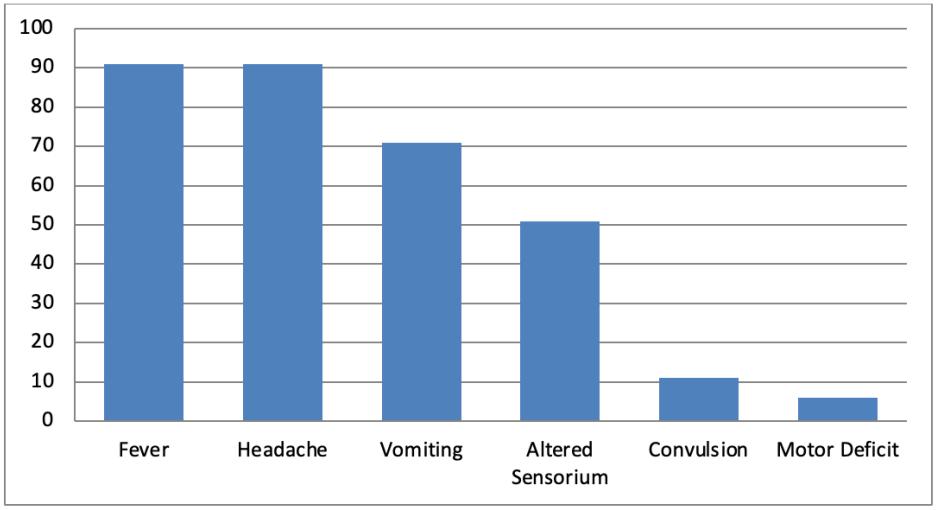

Figure 6: Symptoms (percentage)

16(46%) subjects presented in stage I, 13(37%) in subjects stage II and 6(17%) in stage III of TBM. A significant association was observed between advanced stage of TBM at presentation and severe disability (p = 0.000, < 0.05).

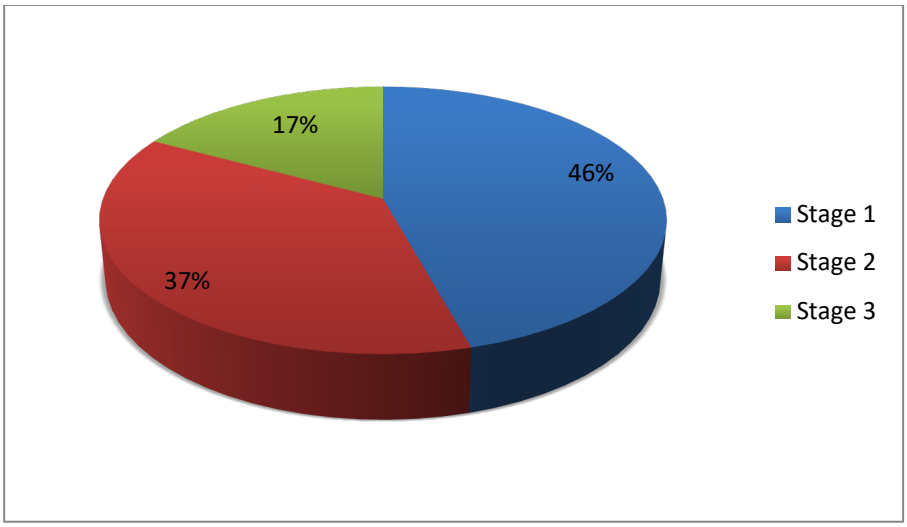

Figure 7: Distribution of subjects according to stage of TBM at presentation

Neck rigidity was present in almost all subjects (97%). Kernig's sign was present in 66% subjects. Presence of kernig's sign was not significantly associated with severe disability (p = 0.22, >0.05).

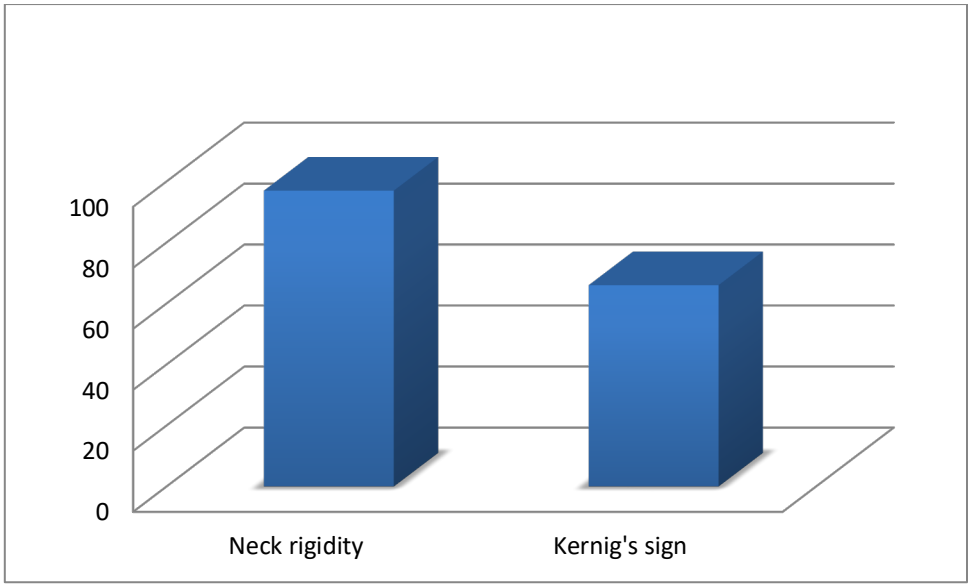

Figure 8: Comparison between Neck rigidity and Kernig's sign (Percentage)

Axillary lymphadenopathy and cervical lymphadenopathy was present in two and one subjects respectively. Presence of axillary and cervical lymphadenopathy was not significantly associated with severe disability (p = 0.128, >0.05; p = 0.767, >0.05 respectively).

c. Cranial nerve involvement

Cranial nerve involvement was seen in 15(42.5%) subjects. Most commonly involved cranial nerve was abducens nerve (28%) followed by oculomotor nerve (11%). Abducens nerve was involved in 10 subjects-on right side in 3 subjects, on left side in 4 subjects and bilateral in 3 subjects. Oculomotor nerve was involved in 4 subjects. Partial oculomotor nerve palsy was seen in 3 subjects and complete oculomotor palsy in one subject. LMN type facial nerve palsy was seen one (3%) subject. Both abducens and oculomotor nerves were involved in one subject. Presence of oculomotor nerve palsy, abducens nerve palsy and facial nerve palsy was not significantly associated with severe disability (p = 0.177, > 0.05; p = 0.611, > 0.05; p = 0.462, > 0.05 respectively). Papilloedema was present in 14(40%) subjects. Presence of papilloedema was significantly associated with severe disability (p = 0.001, < 0.05).

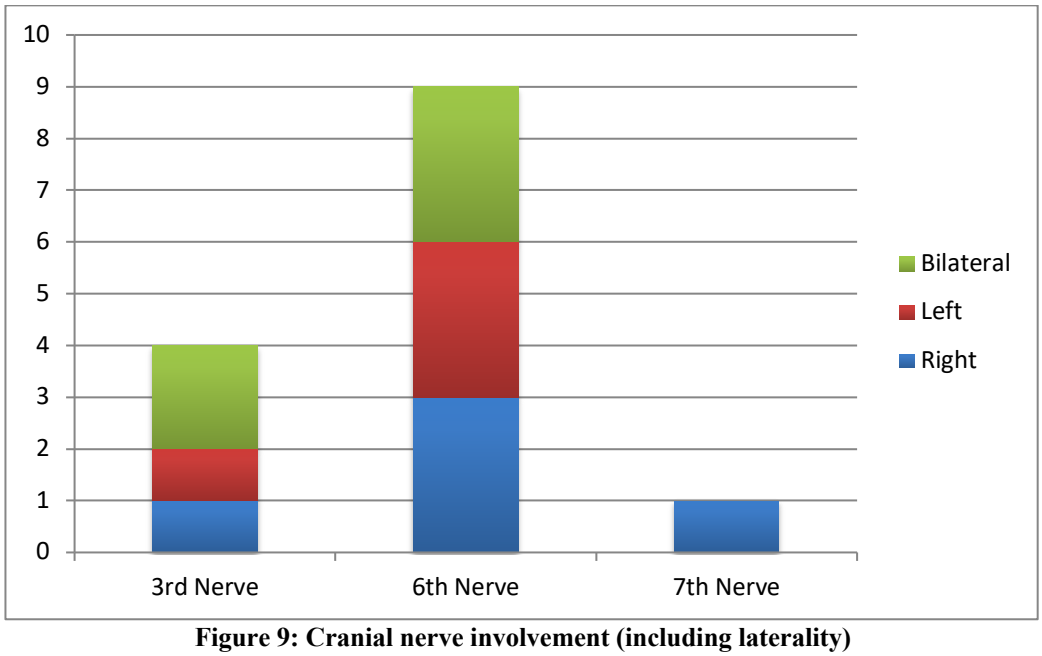

Figure 9: Cranial nerve involvement (including laterality)

Among 4 subjects with oculomotor nerve palsy, partial oculomotor nerve palsy was seen in 3 subjects and complete oculomotor palsy in one subject.

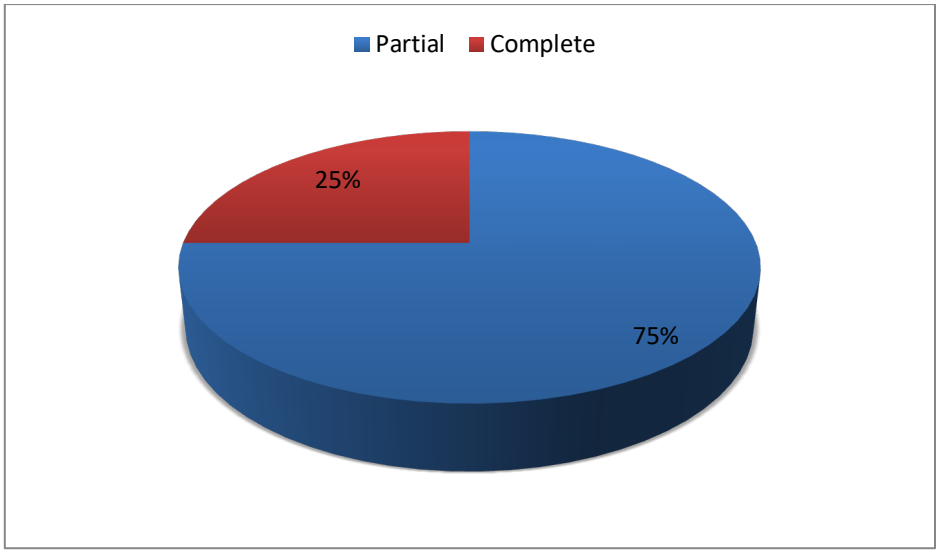

Figure 10: Type of Oculomotor nerve palsy

Mantoux test was positive in 13(37%) subjects. Hyponatremia was seen in 6(17%) subjects. Positive mantoux test and hyponatremia were not significantly associated with severe disability ($p = 0.245, > 0.05$; $p = 0.693, > 0.05$).

Discussion:

Though tuberculous meningitis was described as a separate entity way back in 1836, even today it remains a challenge to diagnose and to treat. Even after complete treatment morbidity and mortality remains high. Approximately half of survivors suffer from long-term neurological sequelae.[10]In this study 35 subjects who fulfilled our inclusion criteria were included. 60% subjects were male and 40% were female. Similar male predominance was also seen by Lu CH et al and UK Mishra et al.[11,12] Age of these subjects varied from 18 years to 72 years. Average age was 32.8 years, which correlates with other studies where in average age ranged between 30 years and 37 years.[13-14] 22(63%) subjects were <30 years, 7(20%) subjects were between 30- 50 years and 6(17%) subjects were >50 years. TBM has a varied presentation. Fever (91%) and headache (91%) were most common symptoms. Even in studies conducted by Fan HW et al[15] and Hosoglu et al[16] fever and headache were present in >90% of subjects. Vomiting was seen in 71% subjects. Convulsions and limb weakness were less common. At presentation about half of the subjects were in altered sensorium. The duration of symptoms ranged from 5 days to 60 days with the mean duration of 28.56days.In a study by Hosoglu P et al, mean duration of symptoms was 12 days.[16]16(46%) subjects presented in stage I, 13(37%) in subjects stage II and 6(17%) stage III of TBM. Similarly in a study by Hosoglu, 60% patients presented in stage II and III[16]. Neck rigidity was present in almost all subjects (97%). Kernig's sign was present in 66% subjects. Cranial nerve involvement is a frequent finding in TBM. It was seen in 15(42.5%) subjects. Whereas in a study by Sharma P et al and Cagatay AA et al, cranial nerve were involved in 38% cases and 30.9% respectively[17,18] Abducens nerve was most commonly involved. Similar finding was observed in other studies also.[18] It was involved in 10(28%) subjects. Oculomotor nerve was involved in 4(11%) subjects. This finding correlates with that of Verma B et al, wherein oculomotor nerve was involved in 12% of cases.[19] Complete oculomotor nerve palsy was seen in one subject. Partial oculomotor nerve palsy was more common than complete oculomotor nerve palsy. This finding correlates with other studies. [17,19]. The third nerve involvement has been explained by basal meningitis, either a direct infiltration of the nerve or by a fibrous band pressing over it. LMN type facial nerve palsy was seen one (3%) subject. It occurs either due to direct infiltration or due to fibrous band pressing over it in basal meningitis. Both abducens and oculomotor nerves were involved in one subject. Papilloedema was present in 14(40%) subjects, whereas in another study papilloedema was seen in 8% subjects.[19]In our study mantoux test was positive in 13(37%) subjects; whereas in a study by Alsoub et al, positivity was 50%.[20] Hyponatremia was seen in 6(17%) subjects. Hyponatremia occurs because of the syndrome of inappropriate ADH secretion (SIADH) and cerebral salt wasting syndrome (CSW). It is critical to manage hyponatremic in patients appropriately, as a hypo-osmolar state will worsen brain edema. Both syndromes require a different approach, but it may be difficult to distinguish between the two.[21] In our study hyponatremia was not significantly

associated with severe disability. However in a study by Gujjar AR, hyponatremia was an independent predictor of death or severe disability.[17] Evidence of extracranial tuberculosis was present in 14 patients (40%) –abdominal tuberculosis and pulmonary tuberculosis were most common. Other types seen were- pott's spine, axillary lymphadenopathy and cervical lymphadenopathy.

Conclusions:

Even after complete treatment of TBM, morbidity remains high. Fever, headache, vomiting, altered sensorium are most common symptoms. Convulsion is a less common symptom. Abducens nerve is the most commonly involved cranial nerve. Presence of tuberculosis outside nervous system should be looked for. Abdomen and pulmonary system are most common site for extra cranial tuberculosis. CSF examination and imaging of head should be done in all suspected cases of TBM.

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