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Comparing clinical and radiological findings of patients with the urodynamic study outcome in patients with tuberculous meningitis

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Abstract
Background: Central nervous system (CNS) involvement is one of the most devastating clinical manifestations of tuberculosis (TB), which is noted in 5 to 10% of extrapulmonary TB case. Definitive diagnosis of tuberculous meningitis (TBM) is important to decrease the morbidity and mortality associated with it.
Aims and Objectives: To study and compare clinical and radiological findings with the urodynamic study findings in TBM patients.
Materials and Methods: Fifty one TBM patients were studied in Neurology Department of KGM Medical University, Lucknow. Patients were categorized based on GCS, BMRC staging, Modified Barthal Index, X ray findings and MRI brain imaging and compared with the urodynamic study outcome (normal or abnormal).
Results: A significant association was observed between GCS Score, BMRC Stage III and Baseline Modified Barthal Indexand abnormal Urodynamic study. No statistically significant association was observed between diagnostic category and chest X-ray findings and abnormal Urodynamic study. MRI brain showed significant relationship of meningeal enhancement, hydrocephalus, basal exudates, and infarcts with abnormal urodynamic study.Maximum patients with poor outcome belonged to BMRC III ($p=0.016$) and those having low GCS value (GCS<14) ($p<0.05$).No statistically significant association was observed between diagnostic category of TBM and final outcome ($p=0.205$). Hydrocephalous, basal exudates and tubercular infarct were the CT findings which affected the outcome of patients significantly ($p<0.05$).
Conclusion: GCS Score, BMRC Stage III and Baseline Modified BarthalIndex had significant association with abnormal urodynamic study. Meningeal enhancement, hydrocephalus, basal exudates, and infarcts were significantly associated with abnormal urodynamic study. BMRC stage III and low GSC value were the significant predictors for poor outcome.

Keywords: modified Barthel Index, urodynamic study, X-ray, BMRC Stage

Introduction
Infection of the CNS is one of the most devastating clinical manifestations of tuberculosis [1]. In an American epidemiological study of extrapulmonary tuberculosis, up to 10% of cases showed CNS involvement, while CDC data indicated that 6.3% of extrapulmonary cases (1.3% of total tuberculosis cases) had CNS TB. In a Taiwan study, 1.5% of TB deaths between 1997 and 2001 were attributable to CNS disease, a percentage that had increased from previous years [2]. CNS TB has the highest mortality rate (20% to 50%) among all forms of TB, and it is associated with more serious complications and sequel [3].
The TBM has a strong propensity to affect the basal parts of the brain. The meningitis process may affect the cranial cerebrospinal fluid (CSF) pathway, the spinal subarachnoid pathway, or both. Microscopic pathological feature of tuberculous meningitis is formation of epithelioid cell granulomas with Langhans giant cells, lymphocytic infiltrates and caseous necrosis [4, 5].
Radiological diagnostic methods such as computer tomography and magnetic resonance imaging (MRI) have greatly enhanced the diagnostic accuracy of TB of the CNS, but they are still not pathognomonic for the disease [6]. In TB meningitis CT or MRI of the brain may reveal thickening and intense enhancement of meninges, especially in basilar regions. Multichannel urodynamic evaluation is the mainstay of evaluation in patients with neurogenic LUT dysfunction. The main objective in assessing patients with suspected neurogenic bladder dysfunction is to determine what effect the neurologic disease has on the entire urinary tract so that treatment can be implemented to relieve symptoms and prevent upper and lower urinary tract damage.
Hence in present study we tried to compare clinical and radiological findings with the urodynamic study findings.

Materials and Methods
Fifty one TBM patients were studied who were attending Neurology OPD and indoor patients of GM and associated hospital of KGM Medical University, Lucknow.
All newly diagnosed cases of TBM fulfilling consensus diagnostic criteria of TBM as described by Marais *et al.* 2010 were included.
For defining TBM two criterion were used (A; Clinical entry criteria plus one or more of the following: acid-fast bacilli seen in the CSF; Mycobacterium tuberculosis cultured from the CSF; or a CSF positive commercial nucleic acid amplification test, B; Acid-fast bacilli seen in

the context of histological changes consistent with tuberculosis in the brain or spinal cord with suggestive symptoms or signs and CSF).

Definite tuberculous meningitis is defined as if patients should fulfill criterion A or B. Probable tuberculous meningitis is defined as patients having clinical entry criteria plus a total diagnostic score of 10 or more points (when cerebral imaging is not available) or 12 or more points (when cerebral imaging is available) plus exclusion of alternative diagnoses. At least 2 points should either come from CSF or cerebral imaging criteria. Possible tuberculous meningitis is defined as patients having clinical entry criteria plus a total diagnostic score of 6–9 points (when cerebral imaging is not available) or 6–11 points (when cerebral imaging is available) plus exclusion of alternative diagnoses. Possible tuberculosis cannot be diagnosed or excluded without doing a lumbar puncture or cerebral imaging.

Patients having local causes of bladder dysfunction (e.g. Cystitis, BPH, stress incontinence) and patients having compressive myelopathy due to vertebral tuberculosis (Pott's spine) or PIVD, stuporous and comatose patients (who are not able to follow commands in urodynamic study) and patients with more than 30 days of antituberculous chemotherapy will be excluded from study.

Written informed consent in Hindi/English to participate in the study was taken from the patient or the guardian/ relatives, prior to enrollment. The study was approved by the Institutional Ethics Committee, KGM Medical University. A detailed history taking, general physical and neurological examination was done and recorded on a predesigned proforma.

Patients were classified according to the British Medical Research Council (BMRC) stage criteria, as follows: patients with stage I disease had a Glasgow Coma Scale score of 15 with no focal neurologic signs; patients with stage II had signs of meningeal irritation with slight or no clouding of sensorium and minor neurological deficit (cranial nerve palsies) or no deficit (Glasgow coma scale score 11-14), and patients with stage III had severe clouding of sensorium, convulsions, focal neurological deficit and involuntary movements (Glasgow coma scale score <10).Each patient was evaluated by Modified Barthel Index (MBI) and classified as given in Table 1.

Table 1: Modified Barthel Index parameters and scoring (MBI)

Parameter	Finding	Points
Bowels (preceding week)	continent	2
	Occasional accident (once a week)	1
	incontinent (or needs to be given exams)	0
Bladder (preceding week)	continent	2
	occasional accident (once per 24 hours)	1
	incontinent or catheterized and unable to manage	0
Grooming (preceding 24-48 hours)	independent	1
	needs help	0
Toilet use	independent	2
	needs some help	1
	dependent	0
Feeding	independent	2
	needs help	1
	unable	0
Transfer (from bed to chair and back)	independent	3
	minor help (verbal or physical)	2
	major help (one to two persons physical) can sit	1
	Unable; so sitting balance; need two people to lift	0
Mobility	independent but may make use of a walking aid	3
	walks with the help of one person (verbal or physical)	2
	wheelchair independent	1
	immobile	0
Dressing	independent (including buttons zips, laces etc.)	2
	needs help but can do about half unaided	1
	dependent	0
Stairs	independent up and down; must carry any walking aid used to be independent	2
	needs help (verbal, physical carrying aid)	1
	unable	1
Bathing	independent; must get in and out unsupervised and wash self	1
	dependent	0
Total Score		**/20**

MRI brain with Gadolinium contrast was performed in all patients using 1.5 tesla GE MRI machine at baseline. MRI brain with Gad is looked for the presence of meningeal enhancement, hydrocephalus, tuberculoma, or infarcts.

Uroflowmetry and urodynamic study: Uroflowmetry was done in all patients at department of urology. It was done in standing position when possible, otherwise in sitting position. Maximum and average flow rates are measured. Machine used in uroflowmetry was Medtronic Duet Logic G. Residual volume is measured by catheterization.

On cystometrogram urinary flow rate, abdominal pressure, vesicle pressure graph recorded. And also the derived pressure i.e. detrusor pressure graph is recorded. All volumes and pressures are measured in millilitre and centimetre of water. The normal range of urodynamic studies were residual urinary volume <30 ml; first desire to void (FDV) >100 ml but <300 ml, and maximum desire to void (MDV) >200 ml but <600 ml. Increased FDV, or

MDV, or both indicates disturbed bladder sensation. The methods and definitions used for the urodynamic studies conformed to the standards proposed by the International Continence Society. An abnormal bladder-filling phase was indicated by detrusor (bladder) overactivity (i.e., involuntary phasic bladder contractions) and low compliance detrusor (or involuntary tonic bladder contractions with detrusor contraction / detrusor pressure rise <20 ml/cmH2O). An abnormal bladder-voiding phase was indicated by detrusor acontractility (i.e., the inability to contract the detrusor and produce urinary flow/ low flow) or underactive detrusor. Detrusor underactivity is defined as a detrusor contraction of inadequate magnitude and/or duration to effect complete bladder emptying in the absence of urethral obstruction. Detrusor sphincter dyssynergia is defined as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle. First sensation of filling/ desire to void- It occurs at approximately 50% of cystometric capacity. Normal desire to void- This is defined as the feeling that leads the patient to pass urine at the next convenient moment, but voiding can be delayed if necessary. It is felt at about 75% of cystometric capacity. Strong desire to void- This is defined as a persistent desire to void without the fear of leakage. It is felt at approximately 90% capacity.

All patients were followed for 3 and 6 months for their disability and urinary symptoms. 27 patients had follow up urodynamic study at 6 months.

The statistical analysis was performed with the use of Statistical Package for Social Sciences, Version 20.0 for Windows (SPSS, Chicago, IL, USA) and Microsoft Excel. Predictors were identified using univariate and multivariate analysis. Univariate analysis was performed by Chi-square test for non-parametric data and student's "t" test for independent variables for parametric data and relative risks with 95% confidence interval were ascertained. For multivariate analysis, binary logistic regression was performed to see the significance of results. Kaplan-Meier analysis was performed to estimate the event free survival for the outcome with or without urodynamic abnormality using to Log Rank test. Statistical significance was defined at a p value of < 0.05 and wherever analysis was done it was two-tailed.

Results

Mean age of study cohort was 28.5 ±13.34 years with Male: Female of 29:22. Mean duration of illness (days) was 71.7±52.9. History of Tuberculosis was present in 11 (21.5%) patients out of 51.

Out of 51 patients of tuberculous meningitis, a total of 36 (70.6%) had abnormal urodynamic findings. Thus the prevalence of urodynamic abnormalities among patients of tuberculous meningitis was 70.6%.

Table 2: Comparing different findings with the Urodynamic study

Variable		Urodynamic study		Total (n=51)	χ2, p value	
		Normal (n=15)	Abnormal (n=36)			
Diagnostic Category	Definite	5 (33.4)	21(58.4)	26 (50.9)	5.859;	0.0536
	Probable	4 (26.6)	11 (30.5)	15 (29.5)		
	Possible	6 (40)	4 (11.1)	10 (19.5)		
GCS	≤10	0 (0)	9 (25)	9 (17.6)	22.431;	<0.001
	11-14	2 (13.3)	21 (58.3)	23 (45.1)		
	15	13 (86.7)	6 (16.7)	19 (37.3)		
BMRC Stage	Stage I	9 (60)	8 (22.2)	17 (33.3)	3.953;	0.047
	Stage II	6 (40)	20 (55.6)	16 (56.9)		
	Stage III	0 (0)	8 (22.2)	8 (9.8)		
Modified Barthel Index	Good (>12)	13(86.6)	7(19.4)	20 (39.2)	20.072;	<0.001
	Poor (≤12)	2 (13.3)	29 (80.4)	31 (60.8)		
X-ray Findings	Normal	10 (66.7)	26 (72.2)	36 (70.6)	0.297;	0.586
	Abnormal	4 (26.7)	7 (19.4)	11 (21.6)		
MRI brain findings	Meningeal enhancement	13 (86.7)	36 (100)	49 (96.1)	4.996,	0.025
	Hydrocephalous	6 (42.9)	28 (90.9)	34 (76.6)	6.800,	0.009
	Basal exudates	5 (13.3)	27 (75)	32 (62.7)	7.864,	0.005
	Tuberculoma	2 (14.3)	8 (18.2)	10 (19.6)	0.531,	0.466
	Tubercular Infarct	2 (13.3)	18 (50)	20 (39.2)	5.972,	0.015

Table 3: Comparing different variables with MBI at 6 months

Variables		MBI		Total (n=51)	χ2, p value
		Good (>12)	Poor (≤12)		
Diagnostic Category	Definite	18 (48.6)	8 (57.1)	26 (50.9)	5.114, 0.078
	Probable	9 (24.3)	6 (42.9)	15 (29.5)	
	Possible	10 (27)	0 (0)	10 (19.6)	
GCS	≤10	3 (8.1)	6 (42.9)	9 (17.6)	11.749; 0.003
	11-14	16 (43.2)	7 (50)	23 (45.1)	
	15	18 (48.6)	1 (7.1)	19 (37.3)	
BMRC Stage	Stage I	16 (43.2)	1 (7.1)	17 (33.3)	5.853; 0.016
	Stage II	16 (43.2)	10 (71.4)	26 (51)	
	Stage III	3 (5.4)	5 (21.4)	8 (15.7)	
MRI brain	Meningeal enhancement	35 (94.6)	14 (100)	49 996.1)	0.788, 0.375
	Hydrocephalous	21 (56.8)	13 (92.9)	34 (76.6)	5.957, 0.015
	Basal exudates	19 (51.4)	13 (92.9)	32 (62.7)	7.485, 0.006
	Tuberculoma	8 (21.6)	2 (14.3)	10 (17)	0.347, 0.556
	Tubercular Infarct	8 (21.6)	12 985.7)	20 (3)	17.503, <0.001

Discussion

The age distribution in our study population shows involvement of the young and economically productive member of the family. The mean age of our study population was comparable to 26.6 and 26.7 years reported by other workers from India [7, 8]. However, a recent study involving 160 patients showed a median age of 32.18 years [9].

Male to female ratio in our study was 1.31 (29 vs. 22) which was showing slight male predominance. This was comparable to the data of study conducted in Vietnam with ratio of 3:2 in favour of males [10]. However, female preponderance has been shown in data of Kumarvelu *et al*. [8]

Majority of patients with urodynamic abnormality was in poor BMRC stage II and III. This difference was statistically significant suggesting that higher grade of illness was associated with development of bladder dysfunction as the disease advances.

At the time of discharge or during the follow up, final stratification of the patients was done and patients were classified as having definite TBM in 49%, probable TBM in 29.4% and possible TBM in 21.5%. The incidence of definite TBM in our study population was much higher than that the study by Sinha *et al.* [11] and Anuradha *et al.* [12] as they reported, incidence of definite TBM in 29% of study population. An important point which should be emphasized that adequate collection and early transfer of CSF material to standard laboratories for detection of Mycobacterium tuberculosis may increase the yield.

MRI brain with Gad was done in all patients. 96.1% of them showed meningeal enhancement. Basal exudates were detected in 62.7% of study subjects, 39.2% of patients showed evidence of infarct. Hydrocephalous was seen in 76.6%, tuberculoma in 19.6%. MRI brain revealed significant relationship of meningeal enhancement, hydrocephalus, basal exudates, and infarcts with abnormal urodynamic study suggesting influence of hydrocephalus and meningitis on bladder function. Hydrocephalus probably causes bladder dysfunction by pressure effects from the distended lateral ventricles on the frontal regions [13]. Patients having basal exudates are more likely to develop lumbosacral arachnoiditis due to extension of inflammatory exudates into spinal canal due to effect of gravity [14], which may be the indirectly affecting bladder function in our patients.

Predictors of urodynamic abnormalities, on univariate analysis, were poor baseline modified Barthel index score (p =0.000), low GCS score (p=0.000), poor MRC stage (p=0.047), brain meningeal enhancement (p=0.025), hydrocephalous (p=0.009), basal exudates (p=0.005), tubercular infarct (p=0.015), spinal meningeal enhancement (p=0.000), lumbosacral arachnoiditis (p=0.007).

Follow up urodynamic study was carried out in 38 patients at 6 months. Among the 25 patients with abnormal baseline urodynamics, 72%(n=18) patients had complete resolution of urodynamic abnormalities, 28% (n=7) patients had abnormal urodynamics on follow up at 6 months.

After 6 months, 14 patients (29.8%) either died or survived with severe disability; 37 (72.5%) had good outcome. On univariate analysis, the factors that were associated with death and disability were, BMRC stage III (p=0.025), poor MBI at baseline <12(p<0.001), low baseline GCS score≤10 (p=0.003), hydrocephalous (p=0.015), basal exudates (p=0.006), infarct (p<0.001), spinal meningeal enhancement (<0.001), lumbosacral arachnoiditis (0.046), CSF loculations(0.001). On multivariate logistic regression analysis, none of these factors had any significant association with poor prognosis.

Present study is not devoid of limitations. Small sample size and cross-sectional nature of the study restrict the utilization of findings to whole population, a large randomized clinical trial is needed to strengthen the present study findings.

Conclusion

Significant association between GCS Score, BMRC Stage III and Baseline Modified Barthel Indexand abnormal urodynamic study indicate a significant role in diagnosing TBM patients with abnormal urodynamic study. MRI of brain can also be an important tool in identifying the abnormality as we found a significant relationship of meningeal enhancement, hydrocephalus, basal exudates, and infarcts with abnormal urodynamic study. BMRC stage III and low GSC value were the significant predictors for poor outcome.

References

1. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC, Dye C. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med. 2003; 163:1009-21.
2. Cherian A, Thomas SV. Central nervous system tuberculosis. Afr Health Sci. 2011; 11(1):116-27.
3. Lee J, Lee SY, Choi KJ, Lim JK, Yoo SS, Lee SY, *et al*. Clinical Utility of CT-based bronchial aspirate TB-PCR for the rapid diagnosis of pleural tuberculosis. Tuberc Respir Dis. 2013; 75:150-156.
4. Kennedy DH, Fallon RJ. Tuberculous meningitis. JAMA. 1979; 241:264-8.
5. de Noronha AL, Bafica A, Nogueira L, Barral A, Barral-Netto M. Lung granulomas from *Mycobacterium tuberculosis*/HIV-1 co-infected patients display decreased in situ TNF production. Pathol Res Pract. 2008; 204:155-61.
6. Parimon T, Spitters CE, Muangman N, Euathrongchit J, Oren E, Narita M. Unexpected pulmonary involvement in extrapulmonary tuberculosis patients. Chest. 2008; 134:589-594.
7. Misra UK, Kalita J, Srivastava M. Prognosis of tuberculous meningitis: a multivariate analysis. J Neurol Sci. 1996; 137:57-61.
8. Kumarvelu S, Prasad K, Khosla A, Behari M, Ahuja GK. Randomized controlled trial of dexamethasone in tuberculous meningitis. Tuber Lung Dis. 1994; 75:203-7.
9. Pehlivanoglu F, Yasar KK, Sengoz G. Tuberculous Meningitis in adults: a review of 160 Cases. Scientific World Journal, 2012, 169028.
10. Thwaites GE, Band ND, Dung NH. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med. 2004; 351:1741-51.
11. Sinha MK, Garg RK, Anuradha HK, Agarwal A, Singh MK, Verma R, *et al*. Vision impairment in tuberculous meningitis: Predictors and prognosis. Journal of neurological sciences. 2010; 290(1):27-32.

12. Anuradha HK, Garg RK, Agarwal A, Sinha MK, Verma R, Singh MK, *et al*. Predictors of stroke in patients of tuberculous meningitis and its effect on the outcome. QJM. 2010; 103(9):671-8.
13. Ahlberg J, Norlen L, Blomstrand C. Outcome of shunt operating on urinary incontinence in normal pressure hydrocephalus predicted by lumbar puncture. J Neurol Neurosurg Psychiatry. 1988; 51:105-8.
14. Wadia NH, Dastur DK. Spinal Meningitides with Radiculo-Myelopathy Part 1. Clinical and Radiological Features. J neurol Sci. 1969; 8:239-60.