Original Article

Demographic and Clinical Evaluation of Patients with Meningitis in a Hospital of Bangladesh

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Abstract:

Background: Meningitis is an inflammatory disease of the leptomeninges, the tissues surrounding the brain and spinal cord. It is a life threatening central nervous system infection that is prevalent worldwide. The lack of rapid and sensitive tests remains a key issue in diagnosing meningitis and affordability impedes accessing molecular techniques in diagnosing. The challenge of this disease is the emergency identification and prompt treatment required to enable survival, reduce mortality, and prevent long-term sequelae. **Objectives:** The aim of this study was to evaluate the demographic and clinical profile of meningitis in a tertiary care hospital in Bangladesh. **Methods:** This was a cross-sectional observational study conducted in the Department of Neurology at Comilla Medical College Hospital, Cumilla, Bangladesh, during the period from July 2018 to June 2019. A total of 159 patients were enrolled in this study. All cases were diagnosed based on clinical or laboratory criteria. Detailed demographic data were collected and recorded in a structured case report form. **Results:** Among the159 patient,69 were male and 90 were female. The mean ages are 31±20.03 years. The highest number of patients were presented with fever (100%), headache (90%), vomiting (47%) and altered mental status (37%). Among all 159 case of meningitis 62(39%) were bacterial meningitis, 55 (35%) were viral meningitis and 42 (26%) were tubercular meningitis. Diagnosis was made on the besis of clinical findings and radiological, biochemical and CSF study.Regarding seasonal variations, there are 2 peaks : summer and winter, which are responsible for viral and bacterial meningitis, respectively. **Conclusion:** Meningitis is a deadly infection that can spread rapidly if not taken early management. So, proper and rapid detection and other investigational facilities reduce the disability.

Keyword: Meningitis, Epidemiological Profile, CSF Study.

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Introduction:

Meningitis is an inflammatory disease of the leptomeninges, the tissue surrounding the brain and spinal cord, and is characterized by an abnormal number of white blood cells (WBCs) in the cerebrospinal fluid (CSF) in the majority of pateints.[1] Meningitis is a potentially fatal condition because the inflammation is proximity to brain and spinal cord. The classic symptoms of meningitis consist of fever, headache, neck stiffness and altered mental status.[2] Meningitis is caused by infections, Autoimmune disease, neoplasia and medication. The infectious causes of meningitis include bacteria, virus, fungi and parasites.[3] Meningitis can occur in any age group with the extremes of age being the most severely affected. The immune compromised states also has high mortality and morbidity. The overall case fatality rate of bacterial meningitis in adult patients is around 30%.[4-6] Rates of bacterial meningitis very form region to region .[7] Although meningitis is a notifiable disease in many countries,the exact incidence rate is unknown; however in decade from 1990 to 2010 , an estimated global figure of approximately 420000 deaths were associated with meningitis .[8] The burden of disease

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from bacterial meningitis is higher in low resources setting with poor health infrastructure because of higher rate of malnutrition , generally poor living condition and inadequate excess to preventive and curative services, Which may predispose individual to infection and limit opportunities for optimal treatments .[9-11] Bacterial meningitis occurs in about 3 people per 100000 annually in Western countries. Population – wide studies have shown that viral meningitis is more common, at 10.9 per 100000, and occurs more often in the summer. In Brazil, the rate at 45.8 per 100000 annually. Epidemics typically occur in the dry season (December to June), and an epidemic wave can last two or three years, dying out during the intervening rainy season. These cases are predominantly caused by Meningococci.[12] Sub-Saharan Africa has experienced large epidemics of meningococcal meningitis, earning it the label of the 'meningitis belt.[13] In Bangladesh, the major etiological factors show that 18% are meningococcal, 3% pneumococcal, and 3% Hib infections. Bacterial meningitis from vaccine-preventable pathogens causes significant morbidity in Bangladesh among adults and children.[14]

In resource-poor settings with scarce or unreliable diagnostic facilities, patients presenting with meningo-encephalitis are often treated empirically. Local data on the causes of meningo-encephalitis can assist clinicians in determining empirical treatment guidelines and help policymakers and public health officials prioritize health spending, particularly if vaccine-preventable etiologies are identified.[15]

Anectodal evidence suggested that meningo-encephalitis was a common cause of hospitalization in Bangladesh; patients in Bangladesh rarely receive a laboratory diagnosis, and clinical assessment of patients presenting with febrile neurologic disease is tipically insufficient to determine whether patients suffer from encephalitis or meningitis. Two outbreaks of Nipah virus encephalitis , in 2001 and 2003, emphasized the need for a better understanding of the etiology of disease in patients who presented with fever and signs of neurologic disease.[16]

Serious long-term consequences of meningitis include deafness, epilepsy, hydrocephalus, and cognitive deficits, especially if not promptly treated. Certain forms of meningitis can be prevented through immunization against pathogens such as meningococci, Haemophilus influenzae type B, pneumococci, or mumps virus.[17] Early diagnosis and timely treatment are crucial aspects of meningitis management. Identifying the causative agent through laboratory diagnosis remains the gold standard. Unfortunately, the positivity rate of gram staining and culture is low, ranging between 25-40%, particularly in the developing world. Technical difficulties in obtaining enough cerebrospinal fluid (CSF) or delays in receiving CSF culture reports often hinder appropriate antibiotic therapy decisions.[18-19]

The management of bacterial meningitis involves several important questions regarding the optimal timing of therapy. Early antibiotic administration before lumbar puncture (LP) can affect culture results and compromise targeted therapy. Diagnostic testing such as computed tomography (CT) and LP may cause significant delays in antibiotic therapy. Delayed therapy can lead to worse clinical outcomes. Studies have shown that early antibiotics can reduce culture yields, with parenteral antibiotics achieving sterilization of meningococcus in the CSF within 2 hours and pneumococcus within 4 hours. However, if a head CT is required before LP, an average of 6 hours can elapse between presentation and parenteral antibiotics.[20]

Several studies from India report a low cerebrospinal fluid (CSF) culture positivity rate in cases of meningitis. A positive CSF culture has been found to range from 6-50% in cases discovered to be suffering from meningitis. There is a need to distinguish between the types of meningitis based on clinical features and CSF biochemistry, as there are varying grades of urgency as well as different treatment strategies involved in the management of each type of meningitis.[21]

Therefore, we conducted this study with the main objective of examining the demographic and clinical characteristics of meningitis patients at Comilla Medical College Hospital in Bangladesh. This understanding can help with the proper planning of public health resources for prevention, early diagnosis, and treatment.

Methods:

A cross-sectional observational study was conducted in the Department of Neurology and Medicine, Comilla Medical College and Hospital, during the period of July 2018 to June 2019. A total of 159 patients with meningitis, diagnosed based on clinical, biochemical, and other investigational backgrounds, and meeting the inclusion and exclusion criteria, studied.

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The study population consisted of patients aged above twelve years of both genders admitted to the medicine and neurology wards with symptoms such as fever, headache, vomiting, meningeal irritation (e.g., neck rigidity), positive Kernig's sign, and/or positive Brudzinski's sign. Patients who refused lumbar puncture or died before undergoing lumbar puncture, patients with encephalopathy due to metabolic and endocrine causes, patients with recent head trauma, immune compromised patients, patients with known malignant lesions or central nervous system neoplasms, critically ill patients, or patients who refused to give consent or were unable to undergo a CT scan were excluded from the study. Informed written consent was obtained from the patients or their attendants before recruitment into the study. Detailed demographic data were collected from the informants and recorded in a structured case report form. Clinical examinations and relevant investigations, including CSF study (cytology, bacteriology, biochemistry, ADA), and other relevant investigations were performed. Routine follow-up of the patients was conducted. The data were analyzed using SPSS version 22.0 software.

Results:

Table-I: Age distribution of the studied patients according to types of meningitis (n=159).

Age	Viral Meningitis		Bacterial Meningitis		Tubercular Meningitis		Total	Mean± SD
	n	%	n	%	n	%		
≤ 20	13	8.18	14	8.81	11	6.92	38	31±20.03
21-30	9	5.66	16	10.06	17	10.69	42	
31-40	6	3.77	8	5.03	4	2.52	18	
41-50	6	3.77	8	5.03	2	1.26	16	
≥50	21	13.21	16	10.06	8	5.03	45	
Total	55	34.59	62	38.99	42	26.42	159	

Total 159 patients were included in the study. Among 159 patients, 38 cases <20 yrs, 42 cases 21-30 yrs, 18 cases 31-40 yrs, 16 cases 41-50 yrs and 45 cases >50 yrs. Viral Meningitis 55(34.59%), Bacterial Meningitis 62(38.99) and Tubercular Meningitis 42(26.42%).

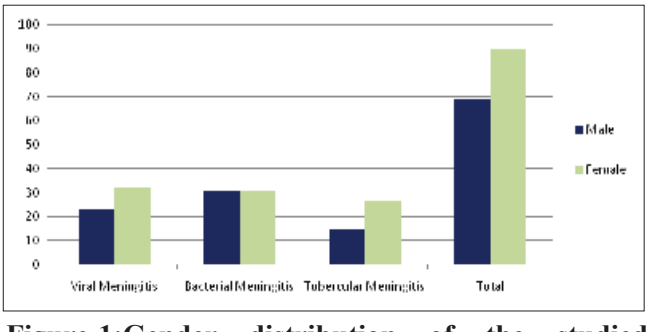

Figure-1:Gender distribution of the studied patients according to types of meningitis (n=159) ,shows that the male patients 69(43.40%) and female were 90 (56.60%).

Table-II: Comorbid condition of cases in different categories of meningitis (n=159).

Risk factor	Viral meningitis		Bacterial meningitis		Tubercular meningitis		Total	%
	n	%	n	%	n	%		
CSOM	2	1.26	3	1.89	1	0.63	6	3.77
Sinusitis (DNS, HIT)	1	0.63	2	1.26	2	1.26	5	3.14
DM (>11 mmol/l)	3	1.89	4	2.52	2	1.26	9	5.66
HTN (140/90 mmHg)	7	4.40	5	3.14	4	2.52	16	10.06

Table-II show that 16 (10.06%) had HTN, 9(5.66%) had DM, 6(3.77%) had CSOM and 5 (3.14%) had Sinusitis.

Table-III: Distribution of the studied patients according to symptoms of meningitis (n=159).

Symptoms	Viral		Bacterial		Tubercular		Total	
	n	%	n	%	n	%	n	%
Headache	48	30.19	54	33.96	40	25.16	142	89.31
Fever	55	34.59	62	38.99	42	26.42	159	100
Vomiting	20	12.58	31	19.50	24	15.09	75	47.17
Altered Mental Status	18	11.32	21	13.21	20	12.58	59	37.10
Photo Phobia	24	15.09	24	15.09	21	13.21	69	43.40
Convulsion	3	1.89	4	2.52	6	3.77	13	8.18

Among the 159 cases, Fever (100%), Headache (89.31%), Altered Mental Status (37.10%), Photophobia (43.40%), Convulsion (8.18%), Vomiting (47.17%).

Table-IV: Fever duration

Fever Duration	Viral Meningitis	Bacterial Meningitis	Tubercular Meningitis
Average (Days)	4.12	4.57	14.62
Range	2-7 days	3-8 days	7-60 days

Average Fever duration was 4.12 days in Viral Meningitis , 4.57 days in Bacterial Meningitis and 14.62 days in Tubercular Meningitis.

Table-V: Distribution of patient according to signs of meningitis (n=159).

Signs	Viral		Bacterial		Tubercular		Total		p-value
	Meningitis		Meningitis		Meningitis				
	n	%	n	%	n	%	n	%	
M Irritation	29	18.24	37	23.27	24	15.09	90	56.60	0.042
Papilledema	4	2.52	3	1.89	16	10.06	23	14.46	0.001
Cranial nerve palsy	2	1.26	0	0.00	8	5.03	10	6.28	0.001
Planter extensor	6	3.77	12	7.55	11	6.92	29	18.23	0.001

Among the 159 cases of meningitis 90(56.60%) cases had signs of Meningeal Irritation. Out of 90, 29 were in Viral meningitia, 37 were in Bacterial meningitis and 24 were in Tubercular Meningitis. Papilledema 23(14.46%) and Cranial Nerve Palsy 10(6.28%).

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Table-VI: Distribution of the patients based on Glasgow Coma Score (GCS) (n=159)

GCS	Viral Meningitis		Bacterial Meningitis		Tubercular Meningitis		Total		P-value
	n	%	n	%	n	%	n	%	
Severe (4-7)	3	1.89	0	0.00	2	1.26	5	3.14	0.032
Moderate (8-10)	5	3.14	5	3.14	8	5.03	18	11.32	0.012
Mild (11-14)	18	11.32	21	13.21	15	9.43	54	33.96	0.015
Normal (15)	25	15.72	31	19.50	17	10.69	73	45.91	0.001

Table-VI show that the GCS scores severe (4-7) were 5(3.14%) , moderate (8-10) were 18(11.32%), mild (11-14) were 54 (33.96%) and normal (15) were 73 (45.91%).

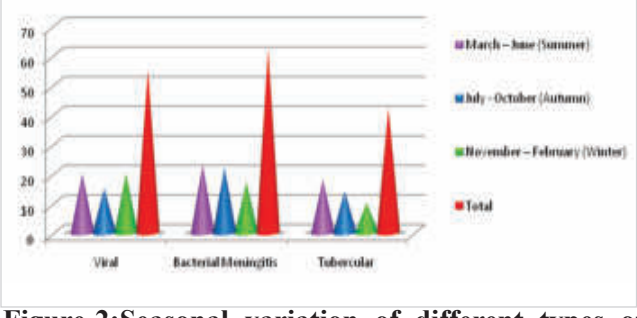

Figure-2:Seasonal variation of different types of meningitis (n=159).

Figure-2 shows that majority of the meningitis case 61 (38.36%) had occurred during the Summer period, followed by 51 (32.08%) had occurred during Autumn , and the remaining 47 (29.56%) had occurred during Winter.

Table-VII: Comparison of laboratory characteristics in different types of meningitis (n=159).

Characteristic		Viral	Bacterial	Tubercular	Total		P value
Anaemia	Male	20	23	12	55	79.71%	
	Female	26	27	17	70	77.77%	
Blood (WBC/cmm)		11041.43±4713.23	11803.18±2905.55	10302.44±2323.30	-		0.001
ESR (mm/1st hr)		33.84±23.94	33.86±20.64	39.78±19.99	-		0.001
CRP (mg/dl)		14.35±16.11	21.23±16.20	19.50±21.24	-		0.001
RBS (mmole/l)		7.03±2.19	6.83±2.48	6.89±1.58	-		0.021
Blood Na+(mmol/lit)		134.05±4.06	137±5.42	136.9±8.32	-		0.031
S creatinine (mg/dl)		1.07±0.37	1.14±0.60	0.98±0.24	-		0.001

(Anaemia → Hb% <12 for Female andHb%<13 for Male)

Table-VII shows that 55(79.71%) males were anaemic and 70 (77.77%) females were anaemic. Mean WBC count highest in Bacterial Meningitis (11803.18±2905.55) and ESR in Tubercular Meningitis (39.78±19.99) and CRP in bacterial Meningitis (21.23±16.20).

Table-VIII: Laboratory Characteristics of CSF (n=159)

CSF		Viral Meningitis	Bacterial Meningitis	Tubercular Meningitis
Sugar (mg/dl)		68.67±24.95	39.12±16.17	62.66±16.10
Protein		71.52±19.03	95.67±27.39	110.52±32.80
Total cells	Total cells/cmm	25.18±10.59	250.48±50.82	100.40±40.33
	Polymorph (%)	5.08±2.78	160.11±25.02	9.51±4.93
	Lymphocyte (%)	20.10±12.19	90.76±26.35	90.31±12.00
ADA (Unit/L)		4.83±3.40	6.72±6.72	14.18±10.60

Table-VIII shows CSF Sugar is highest in Viral Meningitis with a value of 68.67±24.95 and lowest in Bacterial Meningitis with a value of 39.12±16.17. Protein is highest in Tubercular Meningitis with a value of 110.52±32.80 and lowest in Viral Meningitis with a value of 71.52±19.03. Mean polymorph and lymphocyte counts are highest in Bacterial Meningitis with values of 160.11±25.02 and 90.76±26.35, respectively, and lowest in Viral Meningitis with values of 5.08±2.78 and 20.10±12.19, respectively. ADA is highest in Tubercular Meningitis with a value of 14.18±10.60 and lowest in Bacterial Meningitis with a value of 4.83±3.40.

Table-IX: Distribution of imaging results of study population (n=159).

Imaging	Viral Meningitis		Bacterial Meningitis		Tubercular Meningitis		Total	
	n	%	n	%	n	%	n	%
Normal	35	63.6	38	61.3	15	35.7	88	55.34%
ICH/Haemarrhage/ Atrophy/Ischemic/ Infarction	15	27.3	20	32.3	10	23.8	45	28.30%
Enhancing Lesion	3	5.5	3	4.8	9	21.4	15	9.43%
Tuberculoma	2	3.6	1	1.6	8	19.0	11	6.91%
Total	55	100	62	100	42	100	159	100%

Majority of the participants from all three groups (Viral Meningitis = 63.6%, Bacterial Meningitis = 61.3%, Tubercular Meningitis = 35.7%) had normal imaging results. Bacterial meningitis group had the highest prevalence of ICH/Atrophy/Infarction at 32.3% , compared to other two groups. Enhancing lesion and tuberculoma had much higher prevalence among the tubercular group compared to other two groups.

Discussion:

The observational study describes the demographic and clinical profile of patients diagnosed and admitted with meningitis during the period of July 2018 to June 2019 in Comilla Medical College and Hospital. Study design raises a number of important methodological issues-including patients selection sample size, clinical and pathological evaluation all of which exerts a powerfull influence on the results. Using our study results and previous studies we shall address these issues in turn. Most of the published studies on

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meningitis have focused on problems in isolation such as causes or clinically manifestation or features of meningeal irritation. This studies have used a range of different design further more methods of patients selection, diagnostic criteria, timing and duration of follow up vary considerably between studies and therefore it is surprising that reported frequencies of variables in these studies also varied.In this present study, the highest prevalence of meningitis cases was observed in patients over the age of 50 years, but a second peak was also observed among patients aged between 21-30 years. Especially among the tuberculosis meningitis group, the highest number of patients belonged to the age group of 21-30 years, instead of >50 years. This was similar to the findings of many global studies that found TB meningitis to be most common during the early age of life.[22,23] The mean age of all the meningitis patients was 31 years ± 20.03 SD. Overall, female prevalence was observed among participants of all three groups. This was contradictory to the findings of some other studies, where male prevalence was observed among participants.[21,24] We had a higher proportion of female patients (Female = 57%, Male = 43%) in our study, which is contradictory with other studies like Bhat et al.[25], where patients of children were studied. In another Bangladeshi studies of meningitis which consist of 50 patients found male 62% and female 38%,[26] which is disimillar with our study might be due to the fact that less number of patients were included in their study. The Classical triad of meningitis or even the presence of two of the four common symptoms were observed to a lesser extent in our study when compared to the study conducted by Van de Beek et al [27].

Diabetes Mellitus is a major risk factor for the development of various infections, including meningitis. A fair number of our study population had diabetes mellitus. Several aspects of immunity are altered in patients with diabetes. Joshi et al. reported that the functions of polymorphonuclear leukocytes are suppressed in the presence of diabetes mellitus, particularly when acidosis is also present. Moreover, leukocytic adherence, chemotaxis, and phagocytosis are also affected. Antioxidant systems involved in bactericidal activity may also be impaired in patients with diabetes mellitus.[28]

More than two third of all patients in our study were anaemic. Previous authors have demonstrated anemia as a risk for the development of bacterial meningitis.[29] In addition, through not assessed in the present study, crowed houses and smoking also encourage the development of meningitis. Smoking diminishes the protective capacity of epithelial cells covering the respiratory tract.

Patients with bacterial meningitis are usually quite ill and often present soon after symptom onset. For instance, in a series of 301 adults, the median duration of symptoms before admission was only 24 hours (range one hour to 14 days).[30] In our study fever duration for Viral Meningitis was 4.12 days, Bacterial Meningitis 4.57 days and Tubercular Meningitis 14.62 days. The Duration of fever ranges from 2-7 days in viral meningitis, 3-8 days in bacterial meningitis and 7-60 days in tubercular meningitis. The classic triad of acute bacterial meningitis consists of fever, nuchal rigidity, and a change in mental status, usually of sudden onset.[27,31] Older patients (age > 60 years) more commonly present with the triad than younger patients (58 versus 36%).[32]

The most common clinical features include a severe headache (84%) , fever > 38ºC (74%) , stiff neck (74%) , a Glasgow Coma Scale <14 (71%) and nausea (62%).[27,31,33] In a 2004 prospective study of 696 cases of community acquired bacterial meningitis , almost all patients (95%) presented with at least two of four symptoms (ie. Headache, fever, stiff neck, and altered mental status).[27] The absence of all of these findings essentially excludes the presence of bacterial meningitis.[12] Although an appreciable number of patients do not have all three features of meningitis which was also the case in our study it is 44%. Other presenting manifestations in our study are near similar with other studies mention above.

Seasonal variation was observed among the different types of meningitis. The viral meningitis had the highest prevalence during summer and winter period, at 36.36% of prevalence (n=55) each. Bacterial meningitis cases were most common during the summer at 37.10%, followed by 35.48% during autumn and 27.42% during winter. Similarly, tubercular meningitis also had the highest prevalence during summer, autumn and winter in order. But the prevalence of tubercular meningitis was much higher during summer and much lower during winter compared to the other groups. A study was conducted in Kolkata, India that observed two peaks of bacterial meningitis in June and in September. Multiple peaks were found regarding tubercular meningitis and the peak of viral meningitis was less eminent.[34]

Every patients with suspected meningitis should have CSF obtained unless lumbar puncture (LP) is contraindicated. Examination of the CSFis crucial forestablishing the diagnosis of bacterial meningitis, identifying the causative organism and performing in vitro susceptibility testing.[35] In our study different laboratory findings showed that viral meningitis and bacterial meningitis patients had higher mean white blood cells counts compared to TB meningitis patients. Conversely ESR level was highest among the TB meningitis patients. CRP and electrolyte disturbance were higher among bacterial meningitis cases compared to viral and TB meningitis cases. CRP levels were the lowest among the viral meningitis cases. CSF Testing showed that mean values of sugar (mg/dl) was highest among viral meningitis cases, and lowest among bacterial meningitis cases. Bacterial meningitis patients had higher mean protein, total cell count, polymorph and lymphocyte percentage compared to viral and TB meningitis patients. ADA (Unit/L) were the highest among the TB meningitis cases,which was normal as higher ADA levels are observed among TB patients. ADA is present mainly in T lymphocytes and is therefore considered to indicate the cell-mediated immunity. ADA plays an important role in lymphocytic proliferation and a cell-mediated immune response, like in tubercular meningitis, tends to result in elevation of as the cell mediated immune response is seen in TBM, ADA levels are also elevated.Neuro imaging among the present study participants, majority had normal imaging findings, while ICH,atrophy, infarction cases were observed in 20.75% of the cases. Enhancing lesions and tuberculoma were also observed in smaller frequency among the participants, which had higher prevalence among TB meningitis patients compared to viral or bacterial meningitis case.

Conclusion:

In the present study majority of patients are suffering from bacterial meningitis and also the study underscores the fact that absence of fever and neck stiffness does not exclude the possibility of infectious meningoencephalitis. The main focus in all cases should be on early diagnosis & appropriate treatment. Though the design study has few shortcomings, it provides valuable information about clinical & pathological characteristics of meningitis , which can be used in treatment decision thus in improve patients outcomes.

Limitation in this study:

First, this is a cross sectional study of only those cases which were notified and diagnosed as meningitis; thus the true burden of disease in the community may have been under-reported. Secondly, presumed case of viral meningitis could have represented cases of partially treated bacterial meningitis, thus affecting the results. Finally, our study did not follow up on the patients and recognized the complications , including neurological outcomes and survival rates.

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