Clinicopathological Evaluation of the Patients with Febrile Illness and Altered Consciousness Admitted in a Tertiary Level Hospital

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This is important to note that altered mental status is not a disease in itself, but rather a symptom with a wide range of potential diagnoses. But a structured approach to assessing the patients with this symptom frequently leads to helpful information and can rule out worst-case scenarios. In cases where fever is followed by changes in consciousness, quick assessment of the patient's level of consciousness and potential causes is decisive. A focused history and physical assessment can help differentiate between structural or medical causes. Asymmetrical neurological findings, such as a dilated and fixed pupil, dysconjugated extraocular movements and asymmetrical motor findings, suggest brainstem dysfunction due to a structural lesion, while symmetrical neurological findings usually indicate a medical disorder. A recent study aimed to identify features of different etiologies, demographic patterns, and common causes of both acute and prolonged febrile illness in patients. This cross-sectional type of observational study was conducted in the Department of Medicine, Mymensingh Medical College Hospital, Bangladesh from April 2014 to October 2015. Over the study period patients admitted with satisfying the inclusion and exclusion criteria of study and purposively selected (non-probability) from the hospitalized patients. Total 100 cases with febrile illness and altered consciousness meeting the exclusion and inclusion criteria were examined and investigated to find out the actual etiology. Out of 100 patients, it was observed that 26(26.0%) of patients were suffering from pneumonia, 22(22.0%) urinary tract infection, 18(18.0%) meningitis, 14(14.0%) typhoid fever, 8(8.0%) meningo-encephalitis, 6(6.0%) cerebral malaria, 4(4.0%) tuberculosis and 2(2.0%) from tuberculoma. The result revealed that large number of patients with febrile illness and altered consciousness were suffering from pneumonia and urinary tract infection.

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Key words: Clinicopathological evaluation, Febrile illness, Consciousness, Altered consciousness

Introduction

Fever is a condition where the body temperature increases beyond the normal daily variation and is accompanied by a rise in the hypothalamic set point[1]. It is a common symptom of various systemic disorders with different fundamental causes. Consciousness is the state of awareness of oneself and the environment when stimuli are provided[2]. Delirium is a transient condition but it can be associated with a high morbidity and mortality rate and is considered a sign of a serious fundamental illness. Altered consciousness can range from a confused state to coma. Fever accompanied by altered consciousness is a serious disorder that can affect anyone regardless of age or gender. Patients with a short history of fever and altered consciousness are often diagnosed with meningitis, encephalitis, cerebral malaria, etc. Meningitis is a common emergency that carries poor neurological outcomes when it is accompanied by coma during the crisis of the disease[3]. Bacterial meningitis has caused serious outbreaks in at least 30 countries in recent years and is a major international health concern[3,4,5]. In Minnesota, a study reported an incidence of acute encephalitis of 3.5-7.5 cases per 100000 patients per year, while in the United States, 20000 cases of encephalitis are reported each year[6,7].

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The incidence of cerebral malaria is higher in developing countries. Coma can occur within hours and unrecognized P. falciparum infections result in a 30.0% mortality rate[3]. Few studies on comatose patients showed central nervous system diseases as the main cause, with 3.2% having meningitis and 3.0% having encephalitis[8,9]. Approximately one-third to one-half of bacterial meningitis survivors experience permanent neurological damage[10]. Chronic meningitis be capable of cause severe neurological disability and may be fatal if left untreated, particularly in the case of tubercular meningitis[11]. After observing several studies, it was considered necessary to evaluate patients who had suffered from fever followed by altered consciousness and was attending a medical college like Mymensingh Medical College Hospital. With this in mind, I conducted a study to determine the underlying causes of this disorder. I believe that the findings of this study will assist medical professionals in understanding and managing patients with similar issues.

Methods

This was a cross-sectional type of observational study and was conducted in the Department of Medicine, Mymensingh Medical College Hospital (MMCH), Bangladesh from April 2014 to October 2015. After obtaining the all official formalities from the Institutional Review Board (IRB) of MMCH this research work was started. All patients admitted into the Mymensingh Medical College Hospital, Mymensingh with febrile illness and altered consciousness admitted in the medicine department of Mymensingh Medical College Hospital, Mymensingh during the study period who satisfied the inclusion and exclusion criteria of the study. The sample size was determined using the following formula: "$N=Z^2pq/d^2$". According to this formula sample size was calculated, sample is 384.16 ~ 384. But due to lack of time and resources 100 patients were included in this study. During the study period, convenience sampling was conducted on patients with febrile illness and altered consciousness that met the inclusion and exclusion criteria and were admitted to the Department of Medicine, MMCH.

Inclusion criteria: i) Patients with altered consciousness i.e. The Glasgow Coma Scale (GCS) ≤14 and ii) Patients with fever >100ºF during the 1st 24 hours of hospitalization.

Exclusion criteria: i) Patient's eligible attendants who were unwilling to give informed written consent, ii) Patient died or left hospital within 24 hours of hospitalization and iii) Patient diagnosed as stroke.

Operational definition

i) Febrile illness: Oral temperature of more than 38ºC is called febrile illness, ii) Altered consciousness: Consciousness is called altered when GCS ≤14, iii) Pneumonia: Pneumonia is characterized by fever, pleuritic chest pain, cough with expectoration and evidence of consolidation on chest X-ray, iv) Urinary tract infection: Urinary tract infection is characterized by burning sensation during micturition, frequency of micturition, lower abdominal or loin pain and presence of pus cells ($\geq 10^5$/ml in case of females and $\geq 10^3$/ml in case of males from mid-stream morning urine sample) in urine for routine microscopic examination with or without fever and pyuria, v) Meningitis: Meningitis is characterized by fever, headache, vomiting, photophobia, neck rigidity on neurological examination and suggestive CSF findings, vi) Typhoid fever: Typhoid fever is characterized by stepladder pattern of fever for 4-5 days with malaise, increasing headache, drowsiness, aching in the limbs, constipation and presence of *Salmonella typhi* organism on blood culture, urine culture or stool culture with or without splenomegaly, vi) Meningo-encephalitis: Meningo-encephalitis is characterized by fever, headache, vomiting, photophobia, neck rigidity and extensor planter responses on neurological examination and suggestive CSF findings, vii) Cerebral malaria: Cerebral malaria is characterized by high fever with chills and rigor which subsides by sweating, seizures and coma with history of hailing from or traveling to a malaria prone area with or without extensor planter responses on neurological examination and positive blood film or serological examination for malarial parasite. viii) Central nervous system tuberculosis (CNS-TB): CNS-TB is characterized by symptoms and signs of CNS infection with radiographical, microbiological or histopathological evidence of tuberculous infection. It encompasses tubercular meningitis (mainly), tuberculoma and tubercular brain abscess, ix) Dengue: Dengue is a viral infection

caused by mosquito bite and characterized by exposure in an endemic area with fever, body ache, rash and conjunctival hemorrhage with thrombocytopenia and positive tourniquet test and the diagnosis is confirmed by seroconversion of IgM or a fourfold rise in IgG antibody titres, x) Sepsis: Patients with suspected infection who have 2 or more of hypotension- systolic blood pressure <100 mm of Hg, altered mental status - GCS scare ≤14, tachypnoea-respiratory rate ≥22 breaths/ minute, xi) Encephalopathy: Encephalopathy is a term that means brain disease, damage or malfunction. It can present a very broad spectrum of symptoms that range from mild, such as some memory loss, altered mental state or subtle personality changes to severe, such as dementia, seizures, coma or death and xii) Socioeconomic status (SES): Socioeconomic status is a widely used concept in medical sociology. It is a measure of the social standing of an individual or a family in the society. The collected data were checked, verified, edited and coded. Data were processed and analyzed using computer software Statistical Package for Social Sciences (SPSS) version 15.0. The test statistics used for analysis of data are Student's t-test (for comparison of data presented in quantitative scale), Chi-square Test or Fisher's Exact Probability Test (for comparison of data presented in categorical scale). For any analytical test the level of significance was set at 0.05 and p-value <0.05 was considered significant.

Results

In this study, the results of obtaining samples with febrile illness and altered consciousness, the frequencies are as follows:

Table I: Frequency of symptoms (n=100)

Symptoms	Number of patients (n)	Percentage (%)
Fever	100	100.0
Headache	62	62.0
Cough	38	38.0
Chest pain	28	28.0
Weight loss	15	15.0
Burning sensation during maturation	14	14.0
Respiratory distress	12	12.0
Myalgia	08	08.0
Haemoptysis	06	06.0
Seizure	04	04.0
Urinary incontinence	48	48.0
Constipation	02	02.0

Table I shows that apart from fever, the most frequent symptoms were headache 62.0%, urinary incontinence 48.0%, cough 38.0% and chest pain 28.0%.

Table II: Frequency of physical signs (n=100)

Signs	Number of patients (n)	Percentage (%)
Elevated body temperature (>100ºF)	100	100.0
Altered higher psychic function	100	100.0
Restricted chest movement	42	42.0
Impaired/dull percussion note on the chest	30	30.0
Bronchial breath sound	26	26.0
Increased vocal resonance	30	30.0
Renal angles tenderness	02	02.0
Crepitation	46	46.0
Flapping tremor	20	20.0
Signs of meningeal irritation	18	18.0
Papilloedema	04	04.0

Table II shows that the elevated body temperature and altered higher psychic function, the most frequent physical signs were relating to the respiratory system such as crepitation (46.0%), restricted chest movement (42.0%), impaired/ dull percussion note on the chest (30.0%), increased vocal resonance (30.0%) and bronchial breath sound (26.0%) probably reflecting the complication as aspiration pneumonia in case of altered conscious patients along with pneumonia.

Table III: Frequency of CBC with ESR findings (n=100)

Findings of CBC with ESR	Number of patients (n)	Percentage (%)
Raised ESR	96	96.0
Neutrophilic leucocytosis	65	65.0
Lymphocytic leucocytosis	10	10.0
Leucocyte count within normal range	06	06.0
Normal ESR	04	04.0

Table III shows that the majority of study patients had raised ESR and neutrophilic leucocytosis and only 10.0% had lymphocytic leucocytosis.

Table IV: Frequency of urine RME findings (n=90)

Findings of urine RME	Number of patients (n)	Percentage (%)
Pus cell	64	71.11
RBC	28	31.11
Albumin	16	17.78
Normal	36	40.00

Table IV shows that about three fourths of the urine RME findings had pus cells in urine probably reflecting the increased rate of indwelling catheterization and urinary tract infection of the patients with altered consciousness.

Table V: Frequency of chest X-ray P/A view findings (n=69)

Chest X-ray findings	Number of patients (N)	Percentage (%)
Normal	39	56.52
Abnormal	30	43.48

Table V shows that chest X-ray had done for 69 patients and in this series only 43.48% patients had abnormal findings or pathology such as consolidation, fibrosis, scarring, calcification, pleural effusion etc which are probably due to pneumonia, old healed tuberculosis etc.

Table VI: Frequency of findings of ICT for malaria (n=40)

Findings of ICT for malaria	Number of patients (n)	Percentage (%)
Negative	34	85.0
Positive	06	15.0

Table VI shows that ICT for malaria was done for only 40 patients. It was observed that only 15.0% of them had positive ICT for malaria.

Table VII: Frequency of CSF study findings (n=35)

Findings of CSF study	Number of patients (n)	Percentage (n)
Normal study	17	48.57
Polymorphic leucocytosis	12	34.29
Lymphocytic pleocytosis	06	17.14
Reduced glucose concentration	15	42.86

Table VII shows that, CSF study was done for only 35 study patients and within 48 hours of hospitalization. It was observed that about half (42.86%) of them had reduced glucose concentration reflecting bacterial infection and about one third (34.29%) had polymorphic leucocytosis and only minority (17.14%) had lymphocytic pleocytosis reflecting bacterial and viral or partially treated bacterial infection respectively. CSF study was normal in case of half of the study patients.

Pie chart shows that diagnosis could not be confirmed in case of more than one fourth (26.0%) of the patients but most frequent diagnosis were sepsis, encephalopathy due to acute infection, meningitis, CNS-TB etc (Figure 1).

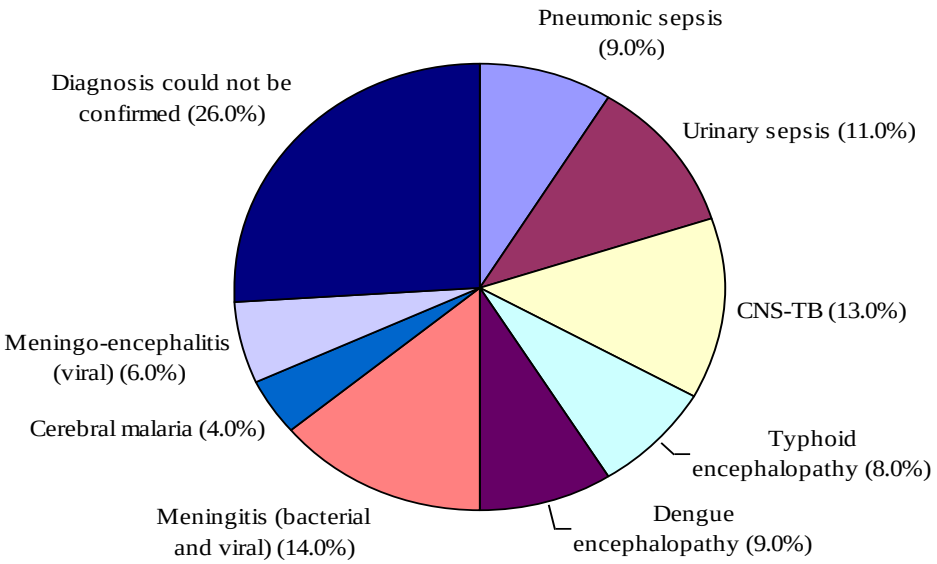

Figure 1: Frequency of diagnosis (n=100)

Discussion

In this study the total (100) cases presented with fever and altered consciousness was studied to correlate the clinical and lab findings with etiology of the subjects. The difficulties in studying such patients were that the patients were unable to participate in face to face interaction with us, lack of culture methods etc. In this study, it was observed that headache was the predominant (62.0%) symptom along with fever. Other common symptoms were cough (38.0%), chest pain (28.0%), weight loss (26.0%) and burning sensation during micturition (20.0%). It was known that headache was a common feature of meningitis, meningo-encephalitis, typhoid fever etc and respiratory features are common presentation in pneumonic sepsis and common complication in all cases of altered consciousness which correlates with the study of Hans-Walter Pfister et al.[12]. Regarding signs, the common signs along with elevated body temperature and altered higher psychic functions were restricted chest movement (42.0%), impaired/ dull percussion note on the chest (30.0%), bronchial breath sound (26.0%), increased vocal resonance (30.0%), crepitation (46.0%) and flapping tremor (20.0%)

but less common signs were papilloedema and renal angle tenderness each were 4.0% and 2.0% respectively. Respiratory signs were common findings in pneumonic sepsis and in aspiration pneumonia which was a common complication in all cases of altered consciousness which correlates with the study of Hans-Walter Pfister et al.[12]. In this study, observation on the findings of complete blood count and erythrocytic sedimentation rate (ESR) was that almost all (96.0%) patients had raised ESR, about three fourths (65.0%) of them had neutrophilic leucocytosis and only 2.0% patients had lymphocytic leucocytosis. Normal leucocytes count and ESR was found in 6.0% and 4.0% of patients respectively. It is known that bacterial infection was the main cause of neutrophilic leucocytosis which was a common observation in pneumonia, urinary tract infection, pyogenic meningitis etc[13]. In this study, urine RME was done for 90 patients and the observations are that about three fourths (71.11%) of patients had pus cells, about one third (31.11%) of patients had RBC and only 17.78% had albumin in urine but about half (40.0%) of them had normal urine. It was known that bacterial infection is the main cause of urinary tract infection and indwelling catheterization, which was common for patients with altered consciousness, was an important risk factor of urinary tract infection[14]. On observation on the findings of chest X-ray postero-anterior view which was done for 69 patients, more than half (56.52%) of the patients had normal finding and only 43.48% of them had abnormal findings, such as consolidation, fibrosis, scarring, calcification, pleural effusion etc. Consolidation with or without pleural effusion is a common X-ray findings in pneumonia (in both community acquired pneumonia and aspiration pneumonia)[15]. The fibrotic lesion, scarring and calcification indicate probable lesions of old healed tuberculosis which was consistent with the study of Jordi Solsona Peiro et al.[16]. In another observation on the findings of ICT for malaria, which was done for 40 patients, test result was negative in case of more than three fourths (85.0%) of patients and was positive for only 15.0% of patients. It was a common finding that ICT was extremely sensitive and specific for *falciparum* malaria[17]. In this study, we had done CSF study only for 35 patients and the observation is that about half (42.86%) of them had reduced glucose concentration which correlates with the study of Tucker C[18], more than one third (34.29%) of them had polymorphic leucocytosis which is a common finding in bacterial meningitis and only 17.14% patients had lymphocytic pleocytosis which is consistent with partially treated bacterial meningitis, viral meningitis, tubercular meningitis, fungal meningitis etc. About half (48.57%) of those patients had normal CSF study. Another observation was ended for the frequency of age among the study population. It had revealed that the most common (26.0%) age group was 51-60 year followed by the age group >60 year (24.0%) reflecting that elderly patients were suffering more from fever with altered consciousness which is consistent with the study of Jin H Han et al.[19]. The least common (6.0%) age group is ≤20 year probably reflecting less admission of this age group into adult medicine department. The mean±standard deviation (Mean±SD) age of patients was (48.7±17.9) year and the range of ages (min-max) is from 18 year to 95 year. This study observation regarding the frequency of diagnosis was that more than one fourth (26.0%) of patients were remained undiagnosed with our limited resources. The most common (20.0%) diagnosis was sepsis followed by infectious encephalopathy (17.0%), meningitis (14.0%), CNS-TB (13.0%), meningo-encephalitis (6.0%) and cerebral malaria (4.0%).

Conclusion

From observation and results of this study we can conclude that the subjects suffering from fever with altered consciousness in medicine indoor ward were also commonly suffering from headache and cough. Most of them were male, came from the rural areas and from lower socioeconomic status. Common age groups suffering from fever and altered consciousness are over 50 year. Suggestive CSF findings were there in particular with meningitis and meningo-encephalitis. Overall, we have failed to reach into a diagnosis in 26.0% cases and most frequent diagnosis were sepsis followed by encephalopathy due to acute infection, meningitis, CNS-TB, meningo-encephalitis and cerebral malaria respectively.

Limitations

This study has many limitations. Due to the altered consciousness of the study patients,

histories taken from their attendance may not be the most appropriate, given the small sample size and short study period. The study's cross-sectional design limits its ability to conduct blood culture or any other culture study. Some critical variables corrected with differential diagnoses were not measured.

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