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BIOLIFE RESEARCH ARTICLE

Prognosis of bacterial meningitis patients according to clinical criteriae and laboratory results on admission

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Aim: The purpose of this study was to detect prognostic factors of acute bacterial meningitis on admission.
Methods: Analysis of clinical and laboratory data of 60 adult acute bacterial meningitis patients admitted at Alexandria fever hospital between July 2014 to February 2015 including: age, sex, vital signs, conscious level, CSF findings, routine lab tests, metabolic acidosis, and causative organism was done initially on admission and then correlated with the patients' outcome on discharge which was either complete recovery (68.3%), recovery with sequelae (13.3%), or death (18.3%).
Results: Factors associated with poor outcome were: Old age (P= 0.019), hypotension (p=0.003), low GCS (P=0.001), uremia (p=0.041), metabolic acidosis (P= 0.016), history of chronic hypertension (P= 0.018), Delayed referral &long duration of symptoms (P= 0.024).
Conclusion: Acute bacterial meningitis patients having any of those poor prognostic criteria should be considered high risk patients and should have the priority for ICU admission and intensive monitoring.

Key words: Acute bacterial meningitis, prognostic factors.

INTRODUCTION

Bacterial meningitis is a medical, neurologic, and sometimes neurosurgical emergency that requires a multidisciplinary approach.

Untreated, bacterial meningitis is almost always fatal. With treatment, mortality from bacterial meningitis depends on various factors such as the age, pathogen, and the severity of the generalized illness, a decreased level of consciousness or an abnormally low count of white blood cells in the CSF. (Van de Beek et al., 2006).

Early risk assessment of acute bacterial meningitis patients on admission is important for physicians for taking decisions about the level of care (ward or high-care facility) especially in resource limited areas with limited number of ICU beds, and is also important for informing the patient and his or her relatives about the prognosis of his current medical disease.

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PATIENTS AND METHODS

Patients:

This study was a prospective study performed on a registry of 60 adult patients admitted at Alexandria fever hospital between July 2014 to February 2015

and proved to have bacterial meningitis by cerebrospinal fluid analysis. Patients below 18 years old and patients proved by CSF analysis to have viral, fungal, or tuberculous meningitis were excluded from the study.

Methods:

All the patients enrolled in the study were evaluated by history taking, clinical examination, including initial vital signs, Glasgow coma score (GCS), clinical signs of meningitis, CSF analysis, CT brain, and routine laboratory tests. Patients' initial clinical data were collected and recorded to be compared with the outcome on discharge. At discharge, all patients underwent a neurological examination, and the Outcome was graded according to the Glasgow Outcome Scale. Accordingly, patients were classified to three groups on discharge. The first are those who died (Glasgow outcome scale 1) , The second are those who recovered with moderate to severe disability (Glasgow outcome scale 2,3,4) and the third group with mild or no disability (Glasgow outcome scale 5).

Statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's exact test or Monte Carlo correction. The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agstino test, if it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used. For normally distributed data, comparison between more than two populations was analyzed F-test (ANOVA) to be used and Post Hoc test (LSD). For abnormally distributed data, Kruskal Wallis test was used to compare between different groups and pair wise comparison was assessed using Mann-Whitney test. Significance of the obtained results was judged at the 5% level.

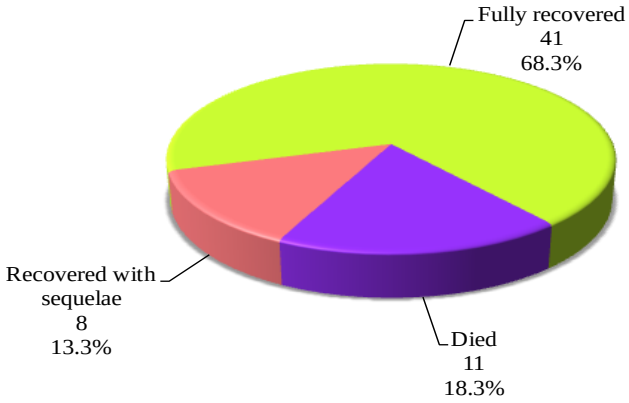
RESULTS

The patients were classified according to their outcome to three main groups:

The first group included the patients who were fully recovered and they were 41 patients (68.3%), and the second group included those who died and they were 11 patients (18.3 %), and the third were the patients who recovered with sequelae, and they were 8 patients (13.3 %). Figure (1)

The sequelae of the 8 patients were hemiparesis in two patients, seventh cranial nerve palsy in another two patients, two patients had aphasia, one patient had hearing loss, and the last had persistent cognitive impairment on discharge.

Figure-1. Classification of the patients according to the outcome.

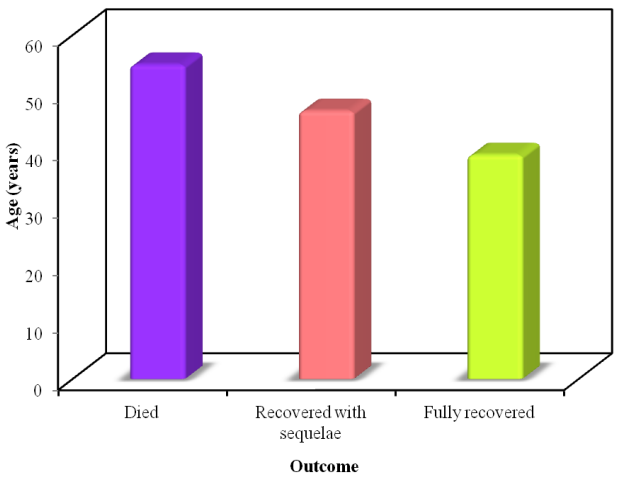


This study described important criteria as poor prognostic factors on admission which is: old age, hypotension, Low Glasgow coma score, long duration of symptoms before starting antibiotics, metabolic acidosis, uremia and history of being hypertensive.

Male to female ratio was 1.5:1 with no significant difference between males and females in their outcome.

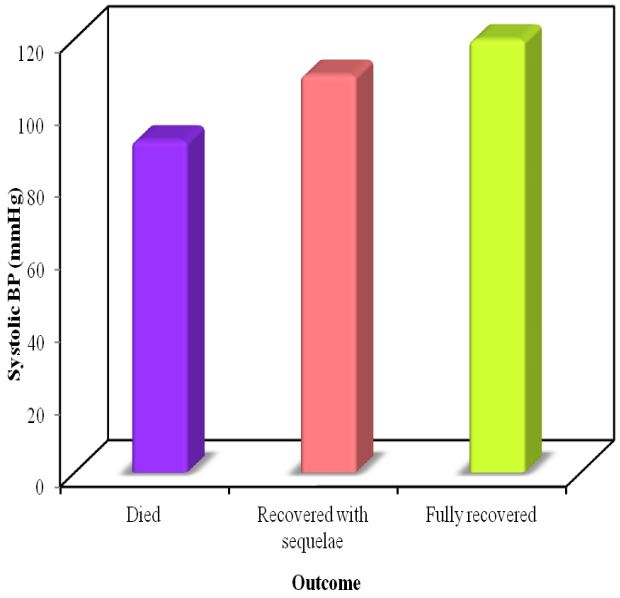
The age of patients ranged from 18 to 82 years. Old age was associated with poor prognosis, the mean age of the patients who died was 54.82±16.85, and in the group who recovered with sequelae was 46.75 ± 19.51 and in the fully recovered group the mean age was 39.07 ± 15.72. Fig (2)

Figure-2. Relation between patients' age and outcome.



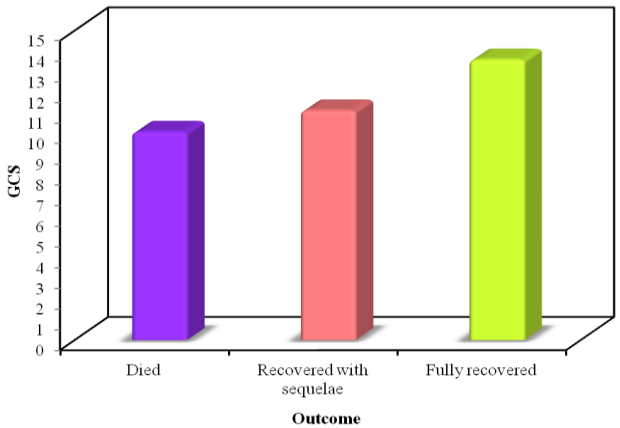
Low systolic blood pressure was associated with higher mortality rate. The mean systolic pressure in patients who died was 91.82± 14.01 mmHg, in those who recovered with sequelae was 110 ± 27.7 mmHg and in the fully recovered patients mean systolic pressure was 119.76 ± 23.93 mmHg. Figure (3)

Figure-3. Relation between outcome and Systolic blood pressure (mmHg)



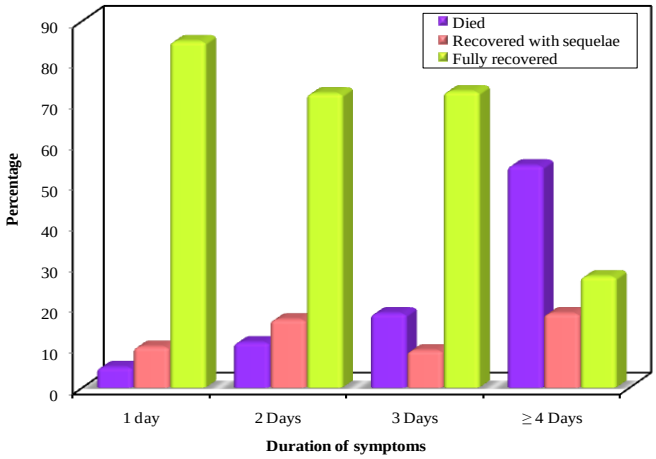
The conscious level, assessed by the Glasgow coma score (GCS) ranged from 5 out of 15 to 15 out of 15 with mean 10.09± 3.39 in the patients who died, 11.13± 2.17 in those who recovered with sequelae, and 13.59± 1.88 in the fully recovered ones. There was statistically significant correlation between low GCS and higher mortality rate. Figure (4).

Figure-4. Relation between outcome and Glasgow coma score (GCS).



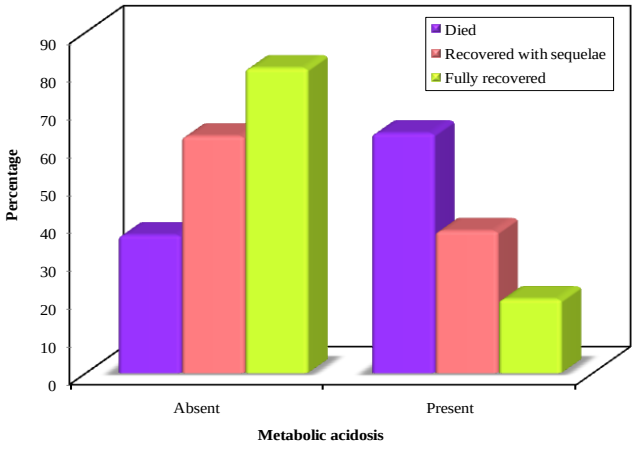
33 % of the patients presented at the first day of the onset of the disease, 30 % on the second day, 18.3 % on the third and 18.3 % after 4 days or more. Among the patients who came on the first day, Full recovery reached 85%, recovery with sequelae was 10% and death was only 5%. On the other side, in patients who were referred to the fever hospital 4 days or more, the mortality rate reached 54.4%, recovery with sequelae was 18.2 %, while complete recovery was only 27.3%. Figure (5).

Figure-5. Relation between outcome and duration of symptoms



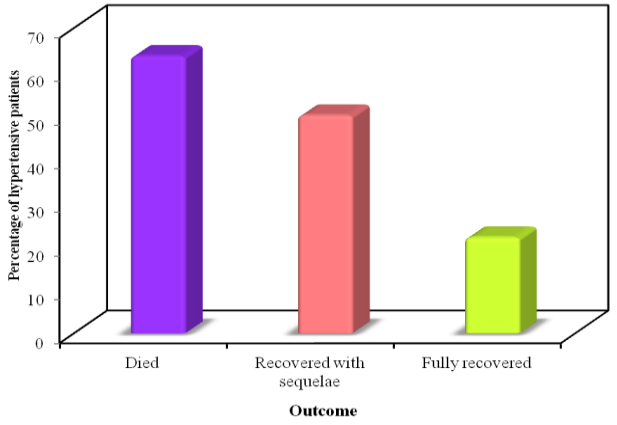
Metabolic acidosis was a poor prognostic factor. In the fully recovered group of patients , metabolic acidosis was present in 19.5 %, in those who recovered with sequelae 37.5 % had metabolic acidosis, while in the third group of the patients who died , 63.3% had metabolic acidosis. Figure (6).

Figure-6. Relation between outcome and metabolic acidosis



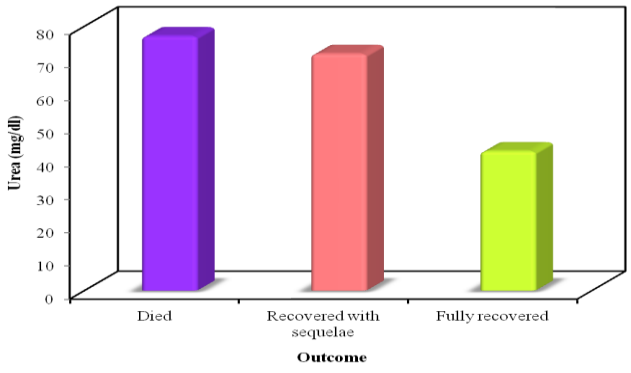
33.3% had history of hypertension, 20 % were diabetic, 11.7 % had renal impairment, 10 % had hepatic insufficiency, and 10 % suffered other diseases such as old cerebrovascular stroke, ischemic heart disease, chronic obstructive pulmonary disease and epilepsy. History of being hypertensive was associated with poor prognosis in which 63.3 % of the patients who died were hypertensive, compared to 50 % of those who recovered with sequelae, and only 22% of the fully recovered patients. While the other co-morbidities didn't affect the prognosis. Figure (7).

Figure-7. Relation between outcome and chronic hypertension



High serum urea levels were associated with poor prognosis. In the group of patients who died, the mean serum urea level was 77± 53.77mg/dl, in the patients who recovered with sequelae it was 71.63 ± 56.31mg/dl and in the fully recovered patients was 42.15 ± 24.65 mg/dl. Figure (8).

Figure-8. Relation between serum urea and outcome.



The following items were assessed and had no prognostic value:

Heart rate, respiratory rate, temperature, Meningeal signs, convulsions, neurological deficits, CSF analysis, the causative organism, liver function tests, serum sodium and potassium, random blood sugar, INR, CRP and D Dimer.

DISCUSSION

Previous studies were conducted aiming at identifying the most accurate prognostic factors for acute bacterial meningitis.

Several factors were selected and assessed as prognostic factors for risk assessment in meningitis, most of which were evaluated in the present study.

This study described three prognostic factors on admission which to our knowledge have not been previously reported which are metabolic acidosis, uremia and history of being hypertensive.

In addition to these newly described factors, the study confirmed the prognostic value of other factors that strongly correlated with adverse outcome in this study in agreement with other similar studies which are: Low Glasgow coma score on admission, old age, long duration of symptoms before starting antibiotics, and hypotension.

On the contrary, some predictive factors of poor outcome in similar studies were not so in this study, such as streptococcus Pneumoniae being the causative organism and association with pneumococcal pneumonia, Tachycardia, low CSF leucocytic count, high CSF protein and low CSF glucose levels, Bacteremia, leucocytosis, thrombocytopenia and coagulopathy, convulsions and need for mechanical ventilation.

Factors significantly affect mortality:

Old age in meningitis patients is a strong predictor of adverse outcome in the present study and most similar studies (Van de Beek et al., 2004; Bohr et al., 1985; Ispahani et al., 1983; Weisfelt et al., 2008; Hoen et al., 1993; and Flores-Cordero et al., 2003).

According to Hoen et al., (1993), age was the second predictor of mortality (The first was low GCS on admission), and risk of death increased seven folds if the age of the patient was above 45 years.

In another study by Ispahani et al., (1983), they mentioned both old age (above 40) and very young age (below 2 months) as predictors of poor outcome.

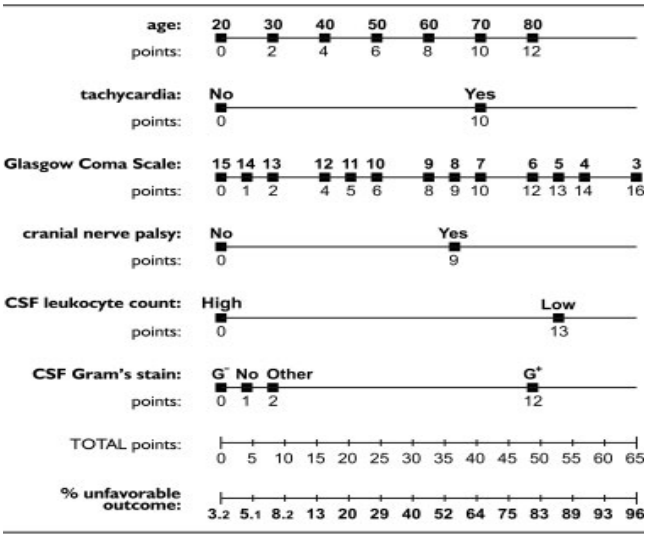
In a study by Weisfelt et al., (2008) as the age increases, the total points in a bedside risk score for adverse outcome increases and consequently, this significantly increases the percent of unfavorable outcome. Figure (9).

Low GCS was repeatedly confirmed as a very strong predictor of adverse outcome.(Van de Beek et al.,(2004) ; Ispahani et al.,(1983) ; Bohr et al., (1985) ; Hoen et al., (1993); Lu et al., (2002) ; Flores-cordero et al., (2003) ; Weisfelt et al., (2008); Auburtin et al., (2002) ; Vibha et al., (2010); Aronin et al., (1998); Kastenbauer et al., (2003)) According to Hoen ., (1993), as previously mentioned, low GCS

was the first predictor of adverse outcome. He also stated that low GCS increases risk of death by ten folds. In another study by Weisfelt et al., (2008) in which the data of the 696 patients of the Dutch meningitis cohort study were analyzed to derive and validate a bedside risk score for adverse outcome within the first hour after admission in adults with acute bacterial meningitis, in this study the criteria included in the final score were given points according to severity. Figure (9)

In addition to other factors, the lower the GCS, the higher the percent of unfavorable outcome. It is noticed that the lowest GCS is given the highest points of the whole score which strongly emphasizes the predictive potential of the initial GCS of the patient on admission.

Figure-9. Weisfelt's Bedside risk score for adverse outcome within the first hour after admission in adults with acute bacterial meningitis.



Early referral to fever hospital correlated with high cure rate while late referral correlated with high mortality rate. Full recovery in patients who came on the first day was 85% compared to 27.3% among the patients who came 4 days or more after the onset of their symptoms.

Duration of symptoms before referral to the fever hospital indicates the time lag or delay before receiving antibiotics and proper supportive care. The main cause of this delay in the present study was mainly low index of suspicion, improper diagnosis by the initially examining physician, and referral from a health care facility to another without receiving empirical antibiotic therapy till admission at the Fever hospital.

Zaky et al., (2014) in a similar prospective study done in Imbaba fever hospital in Egypt stated that mortality was high in patients admitted after 7 days of their symptoms. According to Lu et al., (2002) poor prognosis was associated with delay in antibiotic administration till GCS deteriorated to 10 or less. Also according to Bohr et al., (1985) sequelae persisted when antibiotic therapy was delayed.

Hypotension (defined as systolic blood pressure less than 90 mmHg) is a very sensitive indicator of systemic compromise in any disease.

In bacterial meningitis it indicates severe sepsis, and if not responsive to fluids it indicates septic shock which significantly worsens the prognosis. According to Aronin et al., (1998) three major criteria were described as predictors for adverse outcome. The first was hypotension; the others were disturbed conscious level and convulsions. Also according to Lu et al., (2002) septic shock was associated with poor outcome.

Metabolic acidosis was described as a poor prognostic factor. It may be caused by convulsions and lactic acidosis if present early in the first 24 hours of the disease, while late it may be due to hypotension and septic shock especially in case of delayed referral which indicates systemic compromise and significantly affects prognosis.

In the present study, metabolic acidosis was associated with adverse outcome while in most similar studies metabolic acidosis was not analyzed as a prognostic factor.

On the contrary, in a study by Auburtin et al., (2004), an opposite new finding was described in which metabolic alkalosis with arterial PH > 7.47 surprisingly increased the risk of mortality. They explained this finding possibly because metabolic alkalosis caused by hyperventilation leads to cerebral vasoconstriction which decreases cerebral blood flow resulting in cerebral ischemia.

Uremia according to this study was associated with poor prognosis. A similar finding described by Vibha et al., (2010) stated that elevated serum creatinine was associated with adverse outcome.

Associated Co morbidity has been shown to be associated with an adverse outcome for adults with acute bacterial meningitis. However, the definition of co morbidity is difficult. Some studies have combined e.g. pneumonia, head trauma, ear or sinus infections, malignancy or immune disorders as underlying or predisposing diseases.

In the present study hypertension as a co morbidity was associated with poor prognosis.

This might be explained by the unfavorable cerebro-vascular effect of chronic hypertension on the cerebral circulation leading to multiple lacunar infarcts due to occlusive small vessel disease resulting in sub cortical white matter ischemia, or could be an association between hypertension and old age as most of the old aged patients in the study were hypertensive.

Factors non-significantly affect mortality:

On the contrary, some clearly predictive factors of poor outcome in similar studies were not so in the present study which could be attributed to the relatively smaller number of patients on whom our study was carried, such as pneumococcal meningitis and associated pneumococcal pneumonia, Tachycardia, low CSF leucocytic count or high protein or low glucose level, Bacteremia, leucocytosis, thrombocytopenia and coagulopathy, convulsions and need for mechanical ventilation.

Streptococcus Pneumoniae was the causative organism in 33.3% of the cases of the present study, followed by Hemophilus influenzae in 25 %, and Neisseria meningtidis in 15%, while the causative organism was not detected in 26.6% of the cases.

Streptococcus Pneumoniae was associated with worse prognosis according to Van de Beek et al., (2004) and Kastenbauer et al., (2003).

This was not observed in the present study but this could be due to the presence of unidentified causative organism in 26.6% of the cases which is probably due to the uncontrolled use of antibiotics prior to hospital admission.

Tachycardia (defined as heart rate > 120 beat/ min) was associated with poor outcome (Van de Beek et al., (2004) ; Weisfelt et al., (2008)), but was not described in any other study as a prognostic factor because most of the patients were usually tachycardic due to fever regardless their outcome.

Some studies showed relation between values of CSF analysis and prognosis.

According to Van de Beek et al., (2004) and Kastenbauer et al., (2003) low WBC count in the CSF analysis was associated with poor prognosis. Low WBC count indicates excessive bacterial growth in the cerebrospinal fluid and inadequate patient's immune response.

High CSF protein level in other studies (Kastenbauer et al., (2003) ; Ispahani et al., (1983)) was associated with unfavorable outcome, and low CSF glucose level according to Hoen et al., (1993) was a poor prognostic factor.

Bacteremia -Positive blood culture- was associated with unfavorable outcome in the study by Van de Beek et al., (2004) ; Ispahani et al., (1983) ; and Bohr et al., (1985).

In the present study blood culture was not done routinely to all patients and was not evaluated as a prognostic factor.

Low white blood count < 15,000 was associated with adverse outcome according to Vibha et al., (2010). Similar to low WBC count in CSF, it indicates attenuated immune response.

Low platelet count according to Auburtin et al., (2004) was a poor prognostic factor being a marker of severe sepsis.

In a prospective study by Kowalik et al., (2007) adult patients diagnosed with acute bacterial meningitis were observed for platelet count, D Dimer and INR during the first three days in relation to the severity and outcome of the disease. Unfavorable outcome was associated with platelet count < 170,000, INR > 1.1 and D Dimer > 850 ng/ dl.

The presence of neurological deficit was associated with adverse outcome according to Weisfelt et al., (2008); Flores-Cordero et al., (2003) and Kastenbauer et al., (2003) while in the present study; it had no significant correlation with the patients' outcome.

Need for mechanical ventilation either on admission or within 48 hours was associated with worse prognosis according to Auburtin et al., (2004).

Requirement of mechanical ventilation represent features of severe disease and is usually associated with low GCS as the main reason for intubation and mechanical ventilation which significantly worsens the prognosis. The need for mechanical ventilation was not evaluated as a prognostic factor in this study.

Convulsions occurred in 30 % of patients in the present study and were not associated with poor outcome in contrast to other studies in which convulsions were one of the important prognostic factors. (Aronin et al., (1998) ; Lu et al., (2002) ; Kastenbauer et al., (2003) ; Flores-Cordero et al., (2003)).

CRP was significantly high in most of the patients. Being high in almost all patients, it had no predictive value.CRP value on admission in similar studies was valuable in differentiating bacterial and aseptic meningitis yet it had no prognostic value.

In a study by Singh et al., (1995) 100 children diagnosed with acute bacterial meningitis, Sequential CRP was higher in the patients who developed complications than those who didn't.

Some factors were evaluated and had no prognostic value in the present study and most similar studies such as gender, presence of fever, electrolyte disturbances, random blood sugar, and liver function tests.

The present study has some limitations. First, the number of patients was relatively small. Second, the prognostic factors were evaluated only on admission, and the course of the patients was not reassessed during their hospital stay. And third, the outcome was assessed only on discharge, and thus we have no information on long term morbidity and mortality.

CONCLUSION

- In acute bacterial meningitis patients, Low GCS is a very sensitive sole indicator of poor prognosis.
- Hypotension, metabolic acidosis and uremia are poor prognostic factors that indicate systemic compromise.

- Old age and history of chronic hypertension increase risk of complications and mortality.
- Early referral to fever hospital and avoiding delay of antibiotic administration is improves the patients' prognosis
- Acute bacterial meningitis patients having any of the following red flags: Low GCS, old age, chronic hypertension, uremia, hypotension, or metabolic acidosis, should be considered high risk patients and should have the priority for ICU admission and intensive monitoring.
- Causes of delayed antibiotic administration should be addressed and prevented to improve outcome by increasing physicians' awareness and index of suspicion to signs and symptoms of meningitis and to start empirical antibiotic therapy at the emergency department on minimal suspicion without waiting for CT brain or lumbar puncture or laboratory results or patient referral to the fever hospital.

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