PIDSP Journal, 2001 Vol. 5 No. 1

RISK FACTORS FOR COMPLICATIONS IN BACTERIAL MENINGITIS

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Abstract

Objective: **The objective of this study is to determine if the following factors: age at diagnosis, sex, duration of symptoms before treatment, previous antibiotic therapy, signs and symptoms, CSF picture, etiology, peripheral WBC count and blood culture are correlated with the development of complications in bacterial meningitis.**

Methods: **A retrospective study of 90 patients with bacterial meningitis was performed. These patients were divided into group A, uncomplicated bacterial meningitis and group B, complicated bacterial meningitis. In the phase I analysis, both groups were compared as to the different clinical and laboratory features mentioned. In the phase II analysis, the patients in group B were categorized into group B1 (patients with subdural effusion/empyema, brain abscess, cerebral infarction), group B2 (patients with hydrocephalus, group B3 (patients with combination of B1 and B2). These three groups were compared as to the different clinical laboratory features in bacterial meningitis.**

Results: **Patients with bacterial meningitis are likely to develop complications with longer duration of illness before diagnosis, previous antibiotic therapy before admission and bulging fontanelle. It is shown also that in patients with complicated bacterial meningitis, those with seizures and a CSF: serum glucose ratio of less than 0.20 have an increased risk of having hydrocephalus as a complication.**

Recommendations: **Clinicians should anticipate complications in patients with a history of longer duration of illness before diagnosis, previous antibiotic therapy and bulging fontanelle by doing neuroimaging studies on this set of patients. In the absence of neuroimaging studies, one can refer these patients to a tertiary care center for anticipatory care. A prospective study should be done to corroborate the results of this study.**

INTRODUCTION

Bacterial meningitis is one of the most potentially serious infections in infants and older children. Despite extensive knowledge on the diagnosis and management of this disease, this remains a significant problem in health care.

One demanding aspect of this disease is its high risk for acute complications and chronic morbidity. During treatment of bacterial meningitis, a clinician is faced with possible complications, which include development of subdural effusion or empyema, cerebral infarction, brain abscess, ventriculitis and hydrocephalus. Adding to this list, he may encounter systemic complications such as electrolyte and fluid imbalance. He may also be faced with debilitating neurologic sequelae, which include sensorineural hearing loss, motor abnormalities, speech delay and learning difficulties.

In an effort to control these complications, there have been studies that look into the different risk factors that are associated with these complications.

In 1985, Louis Weinstein observed that there are complications found to be frequent in the certain etiologic agents for meningitis. *Streptococcus pneumoniae* meningitis is associated with subdural empyema, hemiplegia, cerebral venous thrombosis, ventriculitis and hydrocephalus. *H. influenzae* meningitis is associated with deafness and coma or seizures early in the course of infection. Sterile subdural effusion, is also a common complication which is relatively not seen in other bacterial infections.

Snedeker, J., et al in 1990 observed that young age, rapid onset of illness, low peripheral white blood cell count, increasing heard circumference and high levels of cerebrospinal protein and bacterial antigen in children aged 1-18 months are associated with subdural effussion. However, it has also been observed that there is no greater incidence of seizures, hearing loss, neurologic deficits and developmental delay on long-term follow-up.

In the study of Letson, GW of Alaska native infants in 1992, *H. influenzae* meningitis results in 7% of patients having hydrocephalus as a complication and 29% having motor abnormalities. This study also revealed a unique set of predictors for sequelae in Alaska native infants. These are seizures at admission, glucose levels in CSF of less than 1.1 mmol/L and male gender with a significant predictive interaction between male gender and age less than 6 months at admission. On further review of literature, Chang in 1997 showed that patients with bacterial meningitis who developed complications requiring neurosurgical intervention (subdural empyema, brain abscess and hydrocephalus) have a history of inadequate treatment and longer duration of illness before diagnosis.

Keywords: *bacterial meningitis, subdural effussion, Hemophilus influenzae, Risk factors, uncomplicated and complicated bacterial meningitis*
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In the local setting, studies that look into clinical and laboratory features of patients that may be risk factors for the development of complications of bacterial meningitis are lacking. The identification of these risk factors may provide vital information in the prevention of debilitating complications and decreasing morbidity and mortality of this disease entity.

OBJECTIVES

General: To identify risk factors for the development of complications in bacterial meningitis

Specific:

1. To determine if the age at diagnosis, sex, duration of symptoms before treatment and previous antibiotic therapy influence the risk for development of complications in bacterial meningitis.
2. To determine the signs and symptoms in bacterial meningitis which are associated with complications of this disease.
3. To determine the CSF picture (WBC count, protein, sugar and CSF: serum glucose ratio) and the specific etiology of bacterial meningitis by culture or phadebact that are likely associated with development of complications.
4. To determine the peripheral WBC count and blood culture that are likely associated with the development of complications.
5. To determine if the mentioned clinical and laboratory data correlate with the development of a specific complication in complicated bacterial meningitis.

Subjects and Methods:

One hundred forty-one (141) records of patients with discharged diagnosis of bacterial meningitis, uncomplicated or complicated, admitted at Philippine Children's Medical Center from January 1994-December 1999 were reviewed.

The diagnosis of bacterial meningitis was based on the following:

1. Positive history and physical examination attributable to bacterial meningitis such as fever, convulsions, poor feeding, increased sleeping time or decreased activity, nuchal rigidity, positive Brudzinski or Kernig sign, focal neurologic signs and evidences of increased intracranial pressure;
2. WBC count of at least 1,000 cells/mm^3 or 1 x 10^6/L with poly morphonuclear and CSF sugar less than 40 mg/dl or less than 2.2 mmol/L and CSF: serum glucose ratio of less than 0.40, protein of more than 50 mg/dl or 0.5 g/L[1] with positive or negative culture or Phadebact.

The following patients were not included in the study:

1. Patients who had no cranial ultrasound
2. Patients with normal CSF results and the diagnosis were only based on cranial ultrasound findings
3. Patients 0-28 days old
4. Patients whose CSF analyses were done after more than three days of antibiotics administered from the time of admission.

Out of 141 patients, only 90 patients were included for analysis. Twenty (20) patients had no cranial ultrasound done. Twenty-three (23) patients had their lumbar puncture done more than three days after intravenous antibiotic treatment from the time of admission. The lumbar puncture results of these patients may be normal or may not anymore be reflective of the values that may be associated with increased risk of development of complications. The choice for the specified period of time of 3 days was based on the study that showed that intravenous antibiotics used for 2 to 3 days prior to lumbar puncture did not either the CSF cell count or protein or glucose concentrations.[1] Furthermore, Conly, JM in 1983 observed that only 50% of patients had elevated WBC count after a standard 7 – to 10-day course of antibiotic therapy.[11] Five (5) of the 141 patients were within the 0-28 days age range. Two (2) of the patients died of Disseminated Intravascular Coagulation secondary to Septic Shock with cranial ultrasound finding or meningitic changes and hydrpcephalus. Because of the patients' instability, lumbar puncture was not done. One (1) patient was diagnosed to have mixed bacterial meningitis (Bacterial and TB meningitis).

The following features in the remaining 90 patients were noted:

1. Sex
2. Age at Diagnosis
3. History
    - Duration of symptoms before diagnosis
    - Fever
    - Poor feeding
    - Irritability
    - Increased sleeping time
    - Decreased activity
    - Seizures
    - Previous antibiotic administration (intravenous or oral)

4. Physical Examination
   - Decreased sensorium
   - Nuchal rigidity
   - Kernig sign
   - Brudzinski sign
   - Bulging fontanelles
   - Widening of sutures
   - Hypertenstion
   - Bradycardia
   - Apnea
   - Focal neurologic defictis
   - Papilledema
5. CSF picture
   - WBC count
   - Sugar
   - CSF: Serum glucose ratio
   - Protein
   - Culture/Phadebact
6. CBC
   - WBC count
7. Blood Culture

The cranial ultrasound result (during the course of acute illness or during confinement) was also noted.

If the patients had cranial ultrasound findings of subdural effusion/empyesema, brain abscess, infarct and communicating hydrocephalus, the patients were classified under group B, complicated meningitis. If the patients had cranial ultrasound findings of meningitic changes , normal or incidental findings which were not related to bacterial meningitis, the patients were classified under group uncomplicated meningitis. In phase 1 analysis, these two groups were compared according to the different clinical and laboratory features and correlation of these features with the development of complications is determined. In phase II analysis, the complications seen in group B had been categorized into group B1 (patients with subdural effusion/empyema, brain abscess and infarct), group B2 (patients with communicating hydrocephalus) and group B3 (patients with any combination of B1 and B2). Clinical and laboratory features of these three groups were compared and correlation of these features and the development of a specific complication (B1, B2, B3) was determined.

Definition of terms:

Complicated Bacterial Meningitis

During the treatment of bacterial meningitis complications may occur and these may be may be due to CNS or systemic effects of infection. For the purpose of this study, the complications of interest were limited to subdural effusion/empyema, infarct, brain abscess and hydrocephalus as seen through cranial ultrasound done during the acute course of illness or during the period of patient's stay in the hospital.

Uncomplicated Bacterial Meningitis

Bacterial meningitis that did not develop complications mentioned above.

Statistical Analyses

Data were analyzed using the Pearson Correlation Test/t-test for independent samples and Chi-square test and Fischer's Exact test for categorical variables. Analysis of variance was used for numerical data. The confidence level was set at 95% with p-value of $p<=0.05$ considered as significant.

RESULTS

Phase 1 Analysis

The demographic characteristics of the 90 cases of bacterial meningitis were summarized in Table 1.1

Table 1.1 **Demographic characteristics of patients with bacterial meningitis who did not develop complications (Group A) and who develop complications (Group B)**

1. Sex	Group A N*=30	Group B N*=60	p-value
Male	17(57%)	40(67%)	0.368(NS)
Female	13(43%)	20(33%)	
2. Age (in months)			
Mean +/- S.D.	7.5+/-7.06	8.9+/-10.72	0.05(NS)

*Numbers represent number of cases unless otherwise labelled

It was observed that there were more males (57% in group A and 67% in group B) than females (43% in group A and 33% in group B) with bacterial meningitis but there was no significant correlation between sex and the development of complications using the chi-square test with level of significance of <0.05.

The mean age in months for the two groups were 7.5+/- 7.06 and 8.9+/-10.72 for group A and group B respectively with the highrest percentage of cases in age group less than 6 months (53% in groups A and B). There was also no significant corelation between the age of patient on admission and development of complications.

Table 1.2 summarized the clinical features of patients in the two groups.

Table 1.2. Features in the history of patients with bacterial meningitis without complications (group A) and with complications (group B)

	Group A N=30	Group B N=60	p-value
Duration of Symptoms before Diagnosis (in days)	6.06+/-4.18	10.18+/-7.34	<0.0055
Fever	25(83%)	53(88%)	0.518 NS
Poor feeding	5(17%)	14(23%)	0.475 NS
Irritability	2(40%)	17(28%)	0.269 NS
Increased sleeping time	8(27%)	11(18%)	0.378 NS
Decreased activity	3(10%)	4(7%)	0.597 NS
Seizures	19(63%)	45(75%)	0.255 NS
Vomiting	11(37%)	8(13%)	0.011 S
With previous antibiotic intake	7(23%)	38(63%)	0.000 S

It was observed that the duration of symptoms before diagnosis (in number of days) was significantly higher in patients of group B with mean of 10.18 number of days compared with the mean of 6.06 days in patients of group A.

In both groups, the common presenting symptoms were fever (83% in group A and 88.5% in group B) and seizures (63% in group A and 75% in group B). It was also observed that vomiting that vomiting occurs frequently in group A than in group B (p value of 0.011).

Table 1.2 also showed that the number of patients who were given antibiotics prior to diagnosis in group B was significantly higher than the number of patients in group A (p-value of 0.00). Most of the patients were given oral antibiotics such as Amoxicillin, Cefalexin and Chloramphenicol, three to five days prior to diagnosis and treatment in this center. Intravenous antibiotics given prior to diagnosis include Ampicillin and Gentamycin and Ceftriaxone in 3 patients.

Table 1.3 summarized the physical examination findings in both groups. The most common presenting sign in both groups was hyperthermia (83% in group A and 88.5% in group B) with a mean temperature of 38°C). Among the physical examination findings noted in these patients, bulging fontanelle was significantly correlated with the development of complications.

Table 1.4 shows the CSF picture of these patients on admission. It was shown that patients in group B had a higher number of CSF WBC with a mean of 2117.55 +/- 6691.88 x 10^6/L compared with 457.13 +/- 868.83 x 10^6/L of patients in group A. However, WBC count on admission had a p-value of of >0.05 and was not significantly correlated with development of complications.

Table 1.3. Physical examination of patients with bacterial meningitis without complications

	Group A (N=30)	Group B (N=60)	p-value
Temperature (°C)	38.09+/-0.651	38.29+/-0.825	0.258 NS
Nuchal Rigidity	9(30%)	17(28%)	0.872 NS
Kernig Sign	1(3%)	5(8%)	
Brudzinski sign	2(7%)	2(3%)	0.469 NS
Bulging Fontanelle	4(13%)	22(36%)	<0.05 S
Widening of Sutures	1(3%)		0.333 NS
Hypertension	-	5(8%)	0.080 NS
Bradycardia	-	-	-
Apnea	2(7%)		0.109 NS
Focal Neurologic Deficits	7(23%)	12(20%)	0.330 NS
Papilledema	-	-	-

Table 1.4. CSF WBC count of patients bacterial meningitis without complications (group A) and with complications (group B)

CSF WBC Count	Group A	Group B	p-value
500x 10^6/L or less	24(80%)	44 (73%)	>0.05 NS
>500 x 10^6/L	6 (20%)	16 (27%)	
Total	30 (100%)	60 (100%)	
Mean +/- S.D.	457.13 +/- 868.83 x 10^6/L	2117.55 +/- 6691.88 x 10^6/L	

Table 1.5 showed that the CSF sugar, protein and CSF: serum sugar ratio on admission in groups A had no statistical significant difference with that of group B.

Table 1.5. CSF Biochemistries in group A and group B

	Group A (N=30)	Group B (N = 60)	P-value
1. Sugar 1mmol//l or less >1mmol/L Mean +/- S.D. 9 (mmol/L)	3 (10%0 27 (90%) 2.017 +/- 1.683	 24 (40%) 36 (60%) 1.831 +/- 0.961	0.505 (NS)
2. Protein 3 g/l or less >3 g/L Mean +/- S.D. (g/L)	25 (83%) 5 (17%) 2.040 +/- 1.119	 48 (80%) 12 (20%) 1.969 +/- 1.131	0.776 (NS)
3. CSF: serum glucose ratio <0.20 0.20-0.40 >0.40 Mean +/- S.D.	8 (27%) 11(37%) 11(37%) 0.343 +/- 0.174	 25 (41%) 19 (31%) 16 (26%) 0.314 +/- 0.245	0.995 (NS)

Table 1.6 showed that different bacteria isolated from CSF culture. In both groups, most did not grow organisms on culture. These were patients who have been diagnosed with bacterial meningitis based on the clinical picture and characteristic CSF cell count and biochemistries. The most common organism that has

been isolated was *H. Influenzae* with 4 cases in each group. Other isolates were *Streptococcus pneumoniae*, *Pseudomonas*, *Salmonella* and *E. coli*. In Table 1.7, using Phadebact, *H. Influenzae* was also the most common organism. However, Phadebact was not done in all patients. It was also observed that the etiologic agent in bacterial meningitis was not correlated with the development of complications.

Table 1.6. Etiologic agents isolated by CSF culture in Group A and Group B

	Group A (N=30)	Group B (N = 60)	P-value
Culture			0.43 (NS)
Negative	24 (80%)	51 (85%)	
Haemophilus influenzae	4(13%)	4 (7%)	
Streptococcus pneumonae	-	4(7%)	
Pseudomonas	-	1(2%)	
Salmonella	1(2%)		
Escherichia coli	1(2%)		

Table 1.7. Etiologic agents isolated by Phadabact in Group A and Group B

	Group A (N=30)	Group B (N = 60)	P-value
Phadebact			
Negative	1 (3%)	4 (5%)	
Haemophilus influenzae	2 (6%)	6 (10%) 4 (7%)	
Streptococcus pneumonae		- 4 (7%)	
Escherichia coli	2 (7%)		
Not Done	25(83%)	46(76%)	

Table 1.8 showed the peripheral WBC count in both groups with a Mean of 16,040+/-8,454 in-group A and 17,302+/-9,998 in-group B. In both groups, segmenters predominated. Table 1.8 also showed that most patients in both groups had a negative result in blood culture. It was observed that a positive blood culture did not mean a positive CSF culture. These tables showed that the peripheral WBC count, and result of blood culture did not correlate with the development of complications.

Table 1.8. Peripheral WBC count and blood culture in Group and Group B

	Group A (N=30)	Group B (N = 60)	P-value
1.WBC Count			>0.05 (NS)
20,000 or below	20 (67%)	45 975%)	
>20,000	10 (33%)	15 (25%)	
Total	30 (100%)	60 (100%)	
Mean +/- S.D.	16,040 +/- 8,454	17,302 +/- 9,988	
2. Blood culture			0.052 (NS)
NEGATIVE	25 (83%)	59 (98%)	
H. Influenzae	1 (3%)	-	
Streptococcus pneumoniae	-	1 (2%)	
Pseudomonas	2 (7%)	-	
Salmonella	1 (3%)	-	
E. Coli	-	-	
Staphylococcus coagulase	1 (3%)		

In group A, the most common ultrasound finding was menigitic changes with 70% and 27% showing normal result. Three percent (3%) showed choroid plexus cyst.

Phase II Analysis

In group B, the most common complication was B3, a combination of group B1 (subdural effusion/empyema, brain abscess and cerebral infarct) and B2 (communicating hydrocephalus) with 29 cases (48%). Group B1 had 20 cases (33%) and group B2 had 11 cases (18%). Using analysis of variance and chi-square test to correlate the same independent variables with the three groups of complications, it was found that there was a significant statistical difference between seizures and CSF: serum glucose ratio of less than 0.20 with the development of hydrocephalus, as shown in the following tables(2.1-2.7).

Table 2.1 Demographic characteristics of patients in Group B

Sex	Male	Female	Total	P-Value
Group B1	6	5	11	0.563 (NS)
Group B2	13	7	20	
Group B3	21	8	29	
Total	40	20	60	

Age (in months)	Group B1 (N*=11)	Group B2 (N=20)	Group B3 (N=29)	Total	P-Value
Means+/- S.D	11.45+/-18.36	8.65=+/-8.28	7.43+/-9.00	8.98+/-10.720	0.701 (NS)

*Numbers represent number of cases unless otherwise labelled

Table 2.2 Clinical features in the history of patients in Group B

	GroupB1 (N=11)	Group B2 (N = 20)	Group B3 (N=60)	Total	P-Value
Duration of symptoms before diagnosis (days)	7.45+/-6.06	11.65+/-7.33	9.41+/-7.75	10.18+/-7.34	0.557 (NS)
Fever	9	18	26	53	0.757 (NS)
Poor feeding	1	5	8	14	0.456 (NS)
Irritability	4	4	9	17	0.556 (NS)
Increased sleeping time	3	5	3	11	0.299 (NS)
Decreased activity	1	2	1	4	0.626 (NS)
Seizures	5(45%)	19(95%)	21(72%)	45	0.009 (S)
Vomiting	2	1	1	8	0.445 (NS)
Previous antibiotics	7	13	13	38	0.978 (NS)

Table 2.3 Physical examination in patients in Group B

Physical Examination	GroupB1	Group B2	Group B3	Total	P-Value
Temperature (°C)	38.11+/-0.64	38.28+/-0.82	38.37+/-0.76	32.29+/-0.82	0.677 (NS)
Decreased sensorium	1	4	2	7	0.357(NS)
Nuchal rigidity	3	7	7	17	0.706 (NS)
Kernig sign	1	-	4	5	0.228 (NS)
Brudzinski sign	1	1	2	4	0.907 (NS)
Bulging fontanelle	6	8	8	22	0.267(NS)
Wideningof sutures	-	1	-	1	0.362 (NS)
Hypertension	2	2	1	5	0.305 (NS)
Bradycardia	-	-	-	-	
Apnea	1	1	-	2	0.316(NS)
Focal neurologic deficitis	1	6	5	12	0.332(NS)
Papilledema	-	-	-	-	

Table 2.4 CSF picture of patients in Group B

	GroupB1 (N=11)	Group B2 (N=20)	Group B3 (N=29)	Total (N=60)	P-Value
1. WBC count					0.335 (NS)
500 x 10⁶/L or less >500 x10⁶/L Mean+/-S.D.	8 3 3951+/-12049 x 10⁶/L	13 7 2961.95+/-6788 x 10⁶/L	23 6 839.62+/-3082 x 10⁶/L	44 16 21117.55+/-6691 x 10⁶/L	
2. Sugar (mmol/L)					0.818 (NS)
1 or less >1 Mean+/-S.D.	4 7 1.99+/-1.41	9 11 2.12+/-1.87	11 18 1.62+/-0.96	24 36 1.831+/-0.96	
3. Procen (g/L)					0.994 (NS)
3 or less >3 Means+/-S.D.	7 4 1.99+/-1.24	15 5 1.96+/-1.14	26 3 1.95+/-0.99	48 12 1.969+/-1.131	
4. CSF: serum glucose ratio					0.009 (S)
<0.20 0.20-0.40 0.40 Mean+/-S.D.	4 3 4 0.302+/-0.236	11 2 7 0.303+/-0.311	10 14 5 0.305+/-0.202	25 19 16 0.304+/-0.245	

Table 2.5 Etiologic agent isolated by culture in patients in group B

	Group B1 (N=11)	Group B2 (N=20)	Group B3 (N=29)	Total (N=60)	P-Value
Culture					0.43(NS)
Negative	9	16	26	51	
H. Influenzae	2	1	1	4	
Streptococcus Pneumonia	-	2	2	4	
Pseudomonas	-	1	-	1	

Table 2.6 Etiologic agent isolated by Phadebact in patients of group B

	Group B1	Group B2	Group B3	Total	P-Value
Phadebact					0.689(NS)
Negative	-	2	2	4	
H. Influenzae	1	3	2	6	
Streptococcus Pneumonia	1	-	3	4	
Not Done	9	15	22	46	

Table 2.7 Peripheral WBC count and blood culture of patients in Group B

	Group B1	Group B2	Group B3	Total	P-Value
1. WBC count					0.258(NS)
20,000 or less >20,000 Mean +/-S.D	6 5 20,480+/-12,600	16 4 17,700+/-8,210	23 6 15,820+/-10.330	45 15 17,302+/-9,988	
2. Blood culture					0.581(NS)
Negative Strep. pneumoniae	11	20	28	59	

DISCUSSION

Despite extensive knowledge on the pathophysiology and treatment of bacterial meningitis, it still ranks high in morbidity and mortality. Because of this, several studies, both abroad and locally, are still being done on different facets of this disease in a continuing effort to decrease its morbidity and mortality.

As mentioned, the complications of interest are subdural effusion/empyema, brain abscess, infarct and hydrocephalus. The reason behind the author's interest is the fact that these complications present with signs and symptoms that are also present in uncomplicated bacterial meningitis and which can only be confirmed by neuroimaging studies such as cranial ultrasonography. Not all centers in the Philippines have a cranial ultrasound machine. Clinicians rely on the clinical acumen and available laboratory examinations in the diagnosis and management of their patients. Identification of the risk factors for the development of complications in bacterial meningitis place clinicians a step ahead in the management of bacterial meningitis, both uncomplicated and complicated.

The general objective of this study has been met in phase 1 analysis, correlating the different clinical and laboratory features of bacterial meningitis with the risk of complications. It is shown that the duration of symptoms, previous antibiotic therapy and a bulging fontanelle correlates with development of complications during the acute stage of this disease.

There have been studies that explore this area of bacterial meningitis using different combinations of clinical and laboratory data and outcome (acute or long-term).[3-8] Kaaresen, et. al. shows that risk factors related to subsequent death or sequelae are symptom duration of more than 48 hours, prehospital seizures, peripheral vasoconstriction, fewer than 1,000 x 10^6/L leukocytes in the CSF and a temperature of 38°C or greater during admission. Prehospital antibiotic treatment given orally or parenterally is unrelated to

outcome.[5] The study of Kaaresen and the current study show that symptom duration is a risk factor for complications. The significant symptom duration in the study of Kaaresen is more than 48 hours and the current study shows symptom duration of 10.18 days.

In another study, it is shown that patients with CSF protein content of more than 5 g/L are more likely to develop communicating hydrocephalus, subdural effusion and brain abscess. CSF protein content indicates the severity of the acute inflammatory response.[1] In the current study, however, most of the patients both with uncomplicated and complicated bacterial meningitis have CSF protein content of 3g/L or less (table 1.5) and it is shown that CSF protein content is not correlated with the development of complications.

Chang in 1997 studied the risk factors of complications requiring neurosurgical intervention in infants with bacterial meningitis. Complications requiring neurosurgery identified were subdural empyema, brain abscess and a combination of both and ventriculitis with severe hydrocephalus. It is observed that history of inadequate treatment, and longer duration of illness before diagnosis is common in the group with complications requiring neurosurgery than in the group with complications requiring no neurosurgical intervention.[8] Although this study of Chang and the current study have comparable results, it is important to note that the groups of Chang that are being compared and the current study differ.

The succeeding studies that will be mentioned are studies that deal with the specific complications separately. Phase II analysis of this study categorizes the different complications into different groups and the different variables are correlated with the complications in each group. It is shown that preadmission seizures and CSF: serum glucose ratio of less than 0.20 correlated with the development of hydrocephalus.

In several studies, subdural effusions remain a common complication of bacterial meningitis, being reported in 20% to 50% of infants and children with this infection.[9] Clinical manifestations include vomiting, enlarging head circumference, focal neurologic deficits and seizures. These clinical findings, however, could not be attributed to subdural effusion per se.[12] Except for the enlarging head circumference, the above symptoms are also seen in patients with uncomplicated bacterial meningitis. In fact, this study shows that vomiting occurs more frequently in-patients with uncomplicated bacterial meningitis. No other studies have been found to corroborate this result. As shown in one study, increased risk for the development of subdural effusion is associated with, young age, rapid onset of illness, low peripheral white blood count, increasing head circumference, and high levels of cerebrospinal fluid protein and bacterial antigen in children aged 1-18 months.[9] In contrast, patients in this study have increased risk of development of complications with longer duration of illness before diagnosis and previous antibiotic intake. This can be explained by reviewing the pathophysiology of subdural effusion. Subdural effusion is due to thrombophlebitis of the veins bridging the subdural space, abnormal vascular permeability at the arachnoid-dura interface or spread of the infection due to arachnoiditis. If infection in the meninges is not controlled immediately, inflammatory reaction is not controlled and thus there will be damage to the meningeal or dural bridging veins or the arachnoid itself. This results in the preferential transudation of low-molecular weight protein into the subarachnoid and subdural spaces.[10] A longer duration of illness prior to diagnosis and subsequent treatment delays the treatment of this infection. In addition, preadmission antibiotic therapy can prolong the duration of illness further by prolonging the time a patient is brought to a physician for appropriate treatment. Antibiotics prior to diagnosis may only partially treat the infection and thus may only partially control the detrimental inflammatory reaction. Subdural effusion then ensues. Age at diagnosis, peripheral white blood cell count, cerebrospinal fluid protein and bacterial antigen is not shown to correlate with the development of complications in this study.

Subdural effusions are more common when meningitis results from *H. influenzae* (45% of all effusions). Less often, pneumococcus (30% of all effusions) and meningococcus (9% of all effusions) are the responsible bacteria.[9] Although it is shown in this study the most common organism isolated in CSF culture and Phadebact is *H. influenzae*, it does not show any correlation with the development of complication.

When a subdural effusion becomes infected, it becomes a subdural empyema.[10] Subdural empyema poses a bigger problem than subdural effusion because empyema does not resolve spontaneously and needs to be drained. Specifically, subdural empyema is not a common complication. Smith and Harding only found 1 case in 34 patients with bacterial meningitis.

Adam and associates found only two cases in their study.[3] This is probably because the arachnoid membrane is acting as an effective barrier to the spread of infection. Generally, only small amounts of fibrinous exudate are found in the microsections of the spinal or cranial dura.[4] In contrast with this study, there are a total of 22 patients (24%) found to have subdural empyema and 17% of these occur with communicating hydrocephalus. One reason that can explain the increased in the frequency of this complication is that patients with complications in this study had longer duration of symptoms before diagnosis and treatment, infection may have not been controlled immediately and thus effusions may become infected resulting in empyema. However, this is just a speculation since the characteristics of patients studied by Adam and associates or Smith and Landing are not known.

Cerebral infarction occurs in 2% to 19% of children with bacterial meningitis and is a major determinant of outcome. This is caused by thrombophlebitis of the cerebral veins which can produce ischemic necrosis of the cortex. Focal areas of wedge-shaped cortical infarction or widespread areas of infarction can be seen in one-third of children with meningitis presenting with seizures, hemiparesis or coma. This necrosis which can be seen by neuroimaging studies (cranial ultrasonography, CT scan or MRI) can occur as early as the second day of illness[10] and is a major determinant of outcome.[4] Although most infarcts are caused by local intravascular pathology, it is observed that acute hydrocephalus can also cause significant increase in intracranial pressure and may precipitate infarction by decreasing cerebral blood flow.[4] In his study, only one patient developed cerebral infarction which occurred with communicating hydrocephalus and subdural empyema, comprising 1% among patients with bacterial meningitis. This small percentage of patients with this complication is probably due to the fact that only cranial ultrasonography was used. In this study; in contrast to other studies which used contrast-enhanced CT scan or MRI, - neuroimaging studies are best visualized cerebral infarcts with the aforementioned technique. This could account for the higher percentage of bacterial meningitis patients detected with cerebral infarction. It is important to note also that symptoms of cerebral infarction such as seizures, focal neurologic deficits and decreased sensorium are not specific for cerebral infarction, and as seen in this study, are not correlated with increased risk of development of complication.

Hydrocephalus is an uncommon complication of meningitis that develops beyond the neonatal period. It can occur early in bacterial meningitis and is most often communicating[1]. It is the result of adhesive thickening of the arachnoid about the cisterns at the base of the brain. Less frequently, hydrocephalus may be non-communicating when the aqueduct of Sylvius or the foramina of Magendie and Luschka are obstructed, by fibrosis and reactive gliosis.[11] Hydrocephalus is seen in 2-20% of patients with bacterial meningitis[1] and is more often seen in pneumococcal meningitis[7]. In this study, 22% of bacterial meningitis patients have hydrocephalus, all communicating. There are 2 cases whose etiology is *Streptococcus pneumoniae*. There is no correlation; however, between the etiologic agent and the risk of developing of hydrocephalus. What is correlated are seizures and CSF: glucose ratio of less than 0.20. In the study of Letson, it is observed that presence of seizures is strongly correlated with major sequelae among which include hydrocephalus, blindness, severe mental retardation, and death.[7] This is consistent with the result of this study. In the study of Letson, it is also shown the CSF glucose of less than 1.1 mmol/L correlates with major sequelae. In the current study, it is the CSF: serum glucose ratio of less than 0.207. These results may be comparable, both indicating that a low CSF glucose is a risk factor for development of hydrocephalus.

Brain abscess consists of localized free or encapsulated pus within the brain substance. This is uncommon in children and is a rare complication of bacterial meningitis.[12] The result of this study is consistent with the previous statement, having only one patient with bacterial meningitis who has developed brain abscess at the left parietotemporooccipital area. This patient also had communicating hydrocephalus and empyema.

LIMITATION OF THE STUDY

Since this is a retrospective study, there has been no control on the timing of the cranial ultrasound. Ideally, the cranial ultrasonography should have been done on admission and monitored thereafter. However, due to financial constraints, some of the cranial ultrasonography of these patients in this study was done days after admission.

CONCLUSION

In this study, patients with bacterial meningitis are likely to develop intracranial complications with longer duration of illness before diagnosis, previous antibiotic therapy before admission and with bulging fontanelles. Furthermore, it is shown that in patients with complicated bacterial meningitis, those with seizures and a CSF: serum glucose ratio of less than 0.20 have an increased risk of having hydrocephalus as a complication.

RECOMMENDATIONS

With the result of this study, the following recommendations are made:

1. Clinicians should anticipate complications in patients presenting with a history of longer duration of illness before diagnosis and previous antibiotic therapy and in patients with bulging fontanelles. The most cost-effective neuroimaging studies should be done on these patients. In the absence of neuroimaging studies, one can refer them to a tertiary care center for anticipatory care.
2. A prospective study should be done to corroborate the results of this study and to control the timing of cranial ultrasonography.

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