In-Hospital Complications of Acute Meningo-Encephalitis among Children Admitted at AL-Sadaqa General Teaching Hospital

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Abstract

Introduction: Acute meningo-encephalitis (ME) is one of the most dreadful infections in children, frequently associated with high rates of complications and potentiality for death. This study aimed to find out the types and frequencies of complications among children with acute viral and bacterial, and the possible factors influencing their occurrence.

Methods: This prospective descriptive study was conducted on children (1 month – 14 years of age) admitted in AL-Sadaqa Teaching Hospital - Aden with acute ME confirmed by cerebrospinal fluid analysis, during the period 1st January- 30th June 2010.

Results: Out of the 60 patients included in this study, 40% had bacterial and 60% were with viral ME. Males predominated in both bacterial (54.2%) and viral (66.7%) ME. In the two types; majority of the patients were < 5 years of age (83.3%, and 86.1% respectively). Complications were observed in 50% of the studied samples, being in higher frequency among patients with bacterial (63.3%) than those with viral (36.7%) infection, p=<0.001. Complications were more frequent in relation to age <5 years (83.3%), male gender (60%), duration of illness before admission 3-7 days (83.4%), and lack of exclusive breast feeding during the first six months (80.6%). Common complications were increased intracranial pressure (53.3%), anemia (50%), and hypoglycemia (43.3%), and all were seen in significant higher proportions of patients in the bacterial group than those in the viral variety: (70.8% vs. 41.7%), (66.7% vs. 38.9%), (66.7% vs. 27.8%), respectively ($p < 0.05$). The case fatality rate was 2.8 % in viral ME, and 12.5 % in the bacterial type.

Conclusion: Acute ME commonly associated with multiple and serious complications and may lead to fatal outcome. Therefore, active measures to promote immunization, and exclusive breast feeding, along with early diagnosis and proper treatment are highly recommended.

Keywords: Bacterial Meningo-Encephalitis, Viral Meningo-Encephalitis, Under 5 years, Lack of exclusive breast feeding, Increased intracranial pressure.

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مضاعفات التهاب السحايا الحاد بين الأطفال المرقدين في مستشفى الصداقة التعليمي العام

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ملخص الدراسة

المقدمة: يعتبر التهاب (خمج) السحايا الحاد **(Acute meningo-encephalitis)** من الأمراض الأكثر ترويعا بين الأطفال، وغالبا ما يرتبط بنسبة عالية من المضاعفات، وربما الموت. هدف الدراسة هو تحديد أهم المضاعفات بين الأطفال المصابين بالتهاب السحايا الفيروسي والالتهاب البكتيري والعوامل المحفزة لحدوثها.

المنهجية: أجريت هذه الدراسة الوصفية المستقبلية على الأطفال (1 شهر - 14 سنة) المرقدين في مستشفى الصداقة التعليمي / عدن والذين تأكدت اصابتهم بالتهاب السحايا الحاد (الفيروسي والبكتيري) عن طريق تحليل السائل النخاعي، خلال الفترة 1 يناير – 30 يونيو 2010.

النتائج: بلغ عدد الاطفال المصابين بالتهاب السحايا الحاد الذين شملتهم هذه الدراسة 60 مريضا. التهاب السحايا الفيروسي تمثل ب60% والالتهاب البكتيري ب40%. غالبية المرضى كانوا من الذكور في النوعين البكتيري (54.2%) والفيروسي (66.7%)، ومعظمهم كانوا دون الخامسة من العمر بنسبة 83.3% و86.1% على التوالي. لوحظت المضاعفات في 50% بين عينة الدراسة، وكانت متعددة في التهاب السحايا البكتيري (63.3%) أكثر من الفيروسي (36.7%). كانت المضاعفات أكثر حدوثاً بين المرضى دون الخامسة من العمر (83.3%)، الذكور (60%) فترة المرض قبل الترقيد 3-7 ايام (83.4%)، المرضى الذين لم يتلقوا الرضاعة الطبيعية الحصرية (المطلقة) خلال الأشهر الستة الأولى من العمر (80.6%). تمثلت أبرز المضاعفات بما يلي: زيادة الضغط داخل الجمجمة (53.3%)، فقر الدم (50%)، ونقص السكر في الدم (43.3%) وكلها أكثر حدوثاً في النوع البكتيري من الفيروسي والفرق ذو دلالة إحصائية (70.8% و 41%.)، (66.7% و 38.9%)، (66.7% و 27.8%) على التوالي. بلغ معدل الوفيات بين مرضى النوع الفيروسي 2.8%، والبكتيري 12.5%.

الاستنتاج: التهاب السحايا الحاد من الأمراض الخطيرة التي غالباً يصاحبها العديد من المضاعفات الخطيرة التي قد تؤدي إلى الوفاة. وعلية، يتوجب تنشيط وتفعيل الأساليب الوقائية بما يشمل التطعيم ضد الأمراض المعدية وتشجيع الرضاعة الطبيعية الحصرية إلى جانب تشخيص و علاج المرضى المصابين بصورة مبكرة و سليمة.

الكلمات المفتاحية: التهاب السحايا البكتيري، التهاب السحايا الفيروسي، دون 5 سنوات، الرضاعة الطبيعية الحصرية، زيادة ضغط الدماغ.

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Introduction

Acute meningo-encephalitis (ME) is one of the most potentially serious infections occurring in infants and children[1,2]. It is commonly associated with a high rate of complications, which may occur early during the course of treatment or as late events that generally result in permanent neurological sequelae [3,4]. The risk is greater in young children, patients with gram negative bacilli, meningococcal, pneumococcal or herpes simplex infections, and among those having late diagnosis and treatment [5-7]. Though many complications are shared by acute viral and bacterial ME, they are more common and often severe in the pyogenic type [8-10]. Increased intracranial pressure (ICP) is the commonest, earliest, and most serious of all acute complications, while epilepsy, hearing loss and other cognitive and motor deficits are the main frequently reported neurological sequalae [4,5,7].

In acute bacterial ME, the mortality rate of untreated patients approaches 100%, and even with optimum treatment it is still in the range of 10 - 40% [11,12]. The mortality rate in acute viral ME is much lower than that of bacterial causes, the highest is seen with herpes simplex infection [2,5,11].

To highlight the complications of acute viral and bacterial ME and their relation to age, sex, exclusive breast feeding and duration of illness before admission among patients admitted in AL-Sadaqa Teaching Hospital- Aden.

Methods

Study design, population and sitting

This prospective descriptive study was conducted on children admitted with acute viral and bacterial ME in AL-Sadaqa Teaching Hospital- Aden during the period January 1st – June 30th 2010.

Inclusion criteria

Children admitted under the diagnosis of acute ME were eligible for inclusion in this study, if they met the following criteria:

- age > 1 month to 14 years
- suggestive clinical features of the disease with at least 3 of the followings: seizures, vomiting, alteration of consciousness, and neck stiffness
- cerebrospinal fluid (CSF) findings indicative of bacterial or viral infection
- agreement of the mother or attending relative to participate in this study.

Exclusion criteria

One or more of the following:

- age <1 month
- patients diagnosed on clinical suspicion without performing lumbar puncture (LP) regardless the reason for that,
- those with traumatic LP, and their CSF could not be analyzed.
- refusal to participate in this study.

Data collection

A well designed open-closed questionnaire was used for data collection, which included: patient age, sex, presenting complaints, symptoms and signs, birth history, family history, developmental history, any history of trauma/wound, drugs, immunization, ear problems, exam findings and duration of illness.

Drugs used before admission, final diagnosis and complications at the time of discharge and final outcome were also recorded.

Each patient was personally evaluated by the authors during hospitalization by performing an interview with the mothers (58 patients) or attending relatives (2 patients). An initial clinical examination, and daily follow up and assessment of the patient's conditions were performed.

Investigations

The following main investigations were performed for the patients:

- LP: all patients were subjected for an immediate LP followed by CSF analysis: WBCs total and differential counts, glucose and protein levels, gram stain and culture in chocolate, Mac Conkey and blood agar.
- Blood for hemoglobin and total white blood cells counts.
- Initial blood glucose assessment (at time of admission).

Other investigations were performed according to the patient's conditions.

Definitions

Types of acute ME: two types were included in this study; acute bacterial and acute viral meningoencephalitis.

- Acute bacterial ME: it was considered according to the following characteristics [3,11,12]:
  - Suggestive clinical features of fever in addition to 3 or more of the following: seizures, repeated vomiting, alteration of consciousness, neck stiffness, and other signs of meningeal irritation.
  - CSF findings: - Leukocytosis ≥ 10 /mm3, neutrophile predominance, Glucose level of < 40 mg/dl, Protein level of > 40 mg/dl. With or without positive gram stain and/or culture.

  Note: in partially treated patients, neutrophile predominance was not considered essential.
- Acute viral ME: it was considered for children with the following characteristics [3,13]:
  - Suggestive clinical features of viral infection (parotitis, exanthems), and at least three of the following: fever, seizures, repeated vomiting, alteration of consciousness, neck stiffness.
  - Suggestive CSF findings: Leukocytosis ≥10 /mm3 with or without lymphocytosis, Glucose level of ≥ 50 mg/dl, except for patients with mumps, protein level of > 40 mg/d with negative gram stain and culture.

Complications

- Increased intracranial pressure: patients who had 3 or more of the following features: refractory seizures, repeated vomiting, headache, bulging fontanel, cranial nerves palsy, or focal neurological signs, decerebrated or decorticated posture, irregular breathing [2].
- Hypoglycemia: random blood glucose of <50 mg/dl [14].
- Seizures: repeated/refractory seizures, which appeared for the first time after 48 hrs of initiating therapy, and/or those re-appeared after initial control [5].
- Anemia: hemoglobin level< 10 g/dl, being severe for a level of < 6 g/dl [15].
- Focal neurological deficits: included motor defects, ataxia, and aphasia [6].

Data processing and statistical analysis

The data were entered into and analyzed by the Statistical Package

for Social Sciences (SPSS) Software, version15; using frequency distribution and percentages. The statistical tests (Chi-square, Fisher exact and Hypothesis tests of difference in percentages). The level of significant for these tests was 5%.

Ethical consideration

The mother or attending relative for each patient was informed about this study and its main aims, and her/his verbal consent was obtained before including the patient in this study. Her/ his refusal to participate or continue in this research was respected.

Results

The study included 60 patients, 60% of them had acute viral ME and 40% were with the bacterial type. There were more males than females; forming a male to female ratio of 1.6:1; in both acute viral (66.7% vs. 33.3%), and bacterial ME (54.2% vs. 45.8%). On the other hand, the two types were presented in higher proportions of patients < 5 years of age than those 5-14years; viral (86.1% vs. 13.9%) and bacterial (83.3% vs. 16.7%) with statistically significant differences ($p < 0.05$) as shown in Table 1

Table 1: Types of Acute Meningo-Encephalitis by Sex and Age Groups of Patients.

Items	Types of meningo-encephalitis				Total	%	#*p*
	Viral		Bacterial				
	No.	%*	No.	%*			
Sex							
Males	24	66.7	13	54.2	37	61.7	<0.001
Females	12	33.3	11	45.8	23	38.3	
Total	36	100	24	100	60	100	
Age (years)							
< 5	31	86.1	20	83.3	51	85	<0.001
5-14	5	13.9	4	16.7	9	15	
Total	36	100	24	100	60	100	----

** Percentages were calculated from the total of each column # Calculated by the Chi-square test.*

Table 2. shows that complications were observed in 50% of patients, being more frequent among those with bacterial (63.3%) than with viral ME (36.7%). The difference was significant ($p<0.001$).

The frequency of complications was significantly higher in relation to age where it was significantly higher among < 5 year compared to those aged ≥ 5 year (83.3% vs.16.7%, $p<0.001$), duration of illness before admission 3-7 days or < 3 days (83.4% vs.16.6%, $p<0.001$), and negative history of exclusive breast feeding than positive (80.6% vs. 19.4%, $p<0.001$). More complications were also observed in males (60%) than females (40%), but with statistically insignificant difference, $p=0.790$.

Table 2: Complications in Relation to Types of Meningo-Encephalitis, Age Groups, Sex, Duration of Illness Before Admission and Exclusive Breast Feeding.

Items	Complications				Total (n=60)		*p*
	Yes (n=30)		No (n=30)				
	No.	%*	No.	%*	No.	%*	
Types of meningoencephalitis							
Viral	11	36.7	25	83.3	36	60.0	<0.001
Bacterial	19	63.3	5	16.7	24	40.0	
Age groups (Years)							
< 5	25	83.3	26	86.7	51	85	<0.001
5– 14	5	16.7	4	13.3	9	15	
Sex							
Male	18	60.0	19	63.3	37	61.7	0.790
Female	12	40.0	11	36.7	23	38.3	
Duration of illness before admission (Days)							
< 3	5	16.6	17	56.7	22	36.7	
3-4	11	36.7	12	40.0	23	38.3	<0.001
5-7	14	46.7	1	3.3	15	25.0	
Exclusive breast feeding in patients < 2 years during the 1st six months of life(n=45)							
Yes	7	19.4	7	77.8	14	31.1	0.001#
No	29	80.6	2	22.2	31	68.9	

**Percentages were calculated from the total of each column.*
#Fisher exact test and others by Chi square test.

In Table 3, the most common complications were increased IC (53.3%), anemia (50%), and hypoglycemia (43.3%). Other relatively common complications were focal neurological deficits (25%), seizures (23.3%), and cranial nerves palsies (18.3%). All identified complications were observed in a significantly higher proportions of patients with bacterial than those with viral ME, $p < 0.05$.

Table 3: Complications among Studied Patients by Types of Meningoencephalitis

Complications	Types of meningo-encephalitis				Total (n=60)		*p*
	Viral (n=36)		Bacterial (n=24)				
	No.	%*	No.	%*	No.	%*	
Increased ICP**	15	41.7	17	70.8	32	53.3	0.030
Anemia	14	38.9	16	66.7	30	50.0	0.040
Hypoglycemia	10	27.8	16	66.7	26	43.3	0.003
Focal neurological deficits	6	16.7	9	37.5	15	25.0	0.030
Seizures	5	13.9	9	37.5	14	23.3	0.030
Cranial nerves palsy	3	8.3	8	33.3	11	18.3	0.014#
Hydrocephalus	0	0	1	4.2	1	1.7	0.217#

Percentages were calculated from total of each type. ***Increased intracranial pressure*
 # Fisher exact test and others by Chi square test.

As shown in Table 4, complications presented in higher proportions of patients < 5 years than those ≥ 5 years of age were anemia (56.9% vs. 11.1%), hypoglycemia (49% vs. 11.1%), and seizures (25.5% vs.

11.1%); the differences for all were statistically significant, $p < 0.05$. On the other hand, increased intracranial pressure, focal neurological deficits and cranial nerves palsies were more frequent in patients ≥ 5years of age, than those < 5 years, with significant difference for only increased intracranial pressure, $p = 0.020$.

Table 4: Complications of Meningoencephalitis by Age Groups of the Patients

Complications	Age groups (Years)				*p*
	< 5 (n=51)		5-14 (n=9)		
	No.	%	No.	%	
Increased ICP	24	47.1	8	88.9	0.020
Anemia	29	56.9	1	11.1	0.010
Hypoglycemia	25	49.0	1	11.1	0.030
Focal neurological deficits	11	21.6	4	44.4	0.140
Seizures	13	25.5	1	11.1	0.030
Cranial nerves palsy	8	15.7	3	33.3	0.210
Hydrocephalus	0	0.0	1	11.1	0.160

**Percentages were calculated from the total of each age group.*

Four of the studied patients, unfortunately, died forming a case fatality rate of 6.7 %. One of the dead patients was from the viral group, with a case fatality rate of 2.8 %. He was male, 2 years old, with dengue hemorrhagic fever, and died within the 1st 24 hours of admission. The other three dead patients were from the bacterial group, forming a case fatality rate of 12.5 %. The three were males, (1,3, and 7 years old), partially treated, referred in complicated bad conditions, with cardiac failure, severe anemia, and evidence of increased intracranial pressure, and all of them died within the 1st 48 hours of admission.

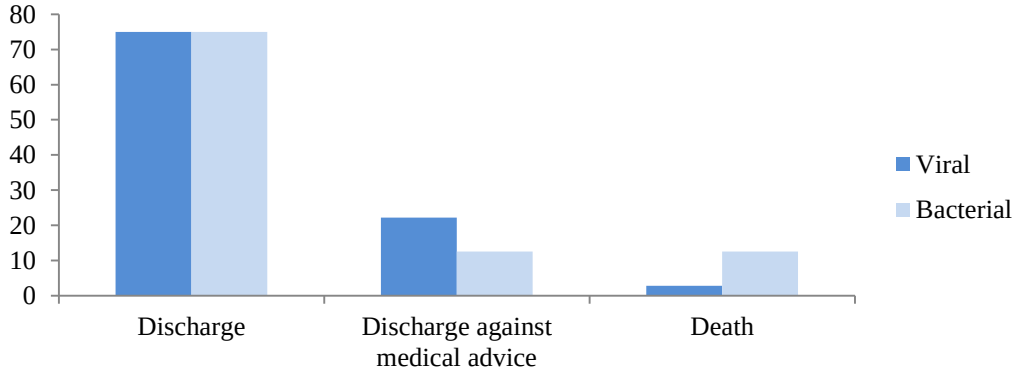

Figure 1: Outcome of The Patients Distributed by Types of Meningoencephalitis

Discussion

Acute ME is a highly complicated dreadful infection, and an important cause of childhood morbidity and mortality in both developed and developing countries [1,2].

In the present study, out of the total 60 patients with ME, 50% developed complications, which is a high figure reflecting seriousness of the disease, and could be contributed by several factors including: the high virulence of organisms, the greatest sensitivity of the involved system, and the CSF inadequate concentrations of complements, and antibodies [2,8]. Higher frequency of complications was found in a significant association with bacterial ME (63.3%), but not with the viral variety (36.7%), which is in accordance with many other reports [9,12,16,17]. This is because, the inflammatory response in the subarachnoid space with bacterial infection is of higher degree than that of the viral one [1,8].

The frequency of complications was significantly higher in patients <5 years as compared to those ≥ 5 years (83.3% vs.16.7%, p=<0.001). This result is supported by some other reports [10,18,19], and mainly attributed to the lower immunity levels in young children.

A significant higher frequency of complications was also observed in relation to duration of illness before admission 3-7 days (83.4%, p=<0.001) and negative history of exclusive breast feeding during the 1st six months of life (80.6%, p=0.001). The result related to duration of illness is expected, and could be explained by increased severity of the disease as treatment is delayed. While that for exclusive breast feeding is consistent with the reports of Gomes *et al* [18] and Salih *et al* [19]. These significant results, however, may suggest that age <5 years, longer duration of illness, and lack of exclusive breast feeding during the 1st six months of life are important risk factors for a higher frequency of complications in acute ME.

This study had shown that the identified complications in the two types of the disease were almost identical, being in significant higher proportions among patients with the bacterial type, $p < 0.05$.

Increased ICP was the commonest of all complications. It was recognized in 70.8% of patients with bacterial ME. This result is coinciding with reports from Kosovo [7] and Qatar [20], where it was the commonest complication of bacterial ME as well, found in 62.3% and 58% of patients, respectively. In viral ME, it was observed in 41.7% of patients, which is near to 15.8% reported by Beig *et al* [16], and 48.1% found in Rorabaugh *et al* [10] study. Increased ICP is the commonest and most serious early complication of acute ME, particularly that caused by bacterial infections. It occurs as a result of the inflammatory process, (cell death and secretions), increased capillary venous permeability, and obstructed reabsorption of the CSF. It may also be contributed by the inappropriate secretion of antiduritic hormone (ISADH) at early stage of the disease [2,8,10].

Anemia was recognized in 38.9% of patients with viral ME, compared to 21% in other study [10], and in 66.7% of patients with bacterial ME, which is resembling figures reported from Angola (66.7%) [21] and Mozambique (70%) [22]. Anemia is frequently seen in children with acute infections, said Kaplan [23] It results from an interaction of several factors, including; decreased intake, decreased absorption, increased

demands for iron and other essential nutrients in febrile patients, along with inadequate erythropoiesis, and hemolysis caused by bacterial toxins [15,24].

Hypoglycemia is a common complication of acute ME, being more common among young patients with pyogenic infection. It is mainly attributed to several factors including: less intake, frequent vomiting, impaired gluconeogenesis in the liver and increased utilization of glucose in the brain [14]. In agreement with that, hypoglycemia was found in a significant proportion of patients with bacterial ME (66.7%, p=0.030), a result being almost similar to 60% reported by Ogunlesi *et al* [25]. It was also identified in 27.8% of patients had the viral variety, which may indicate its importance as a complication of viral ME.

Seizures, which have been mentioned as important complication of acute ME [1,2], were recorded in 37.5% among patients with the bacterial type, similar to those reported by Pelkonen *et al* (34%) [21] and Franco-Paredes *et al* (37%) [4]. In the viral group, they were documented in 13.9% of patients, which corresponds to previously reported data 16.5% [9] and 11.5% [10].

Motor and sensory deficits and cranial nerves palsies are relatively common complications in acute ME, particularly that caused by pyogenic infections. They may result from cerebral hypoxia, bacterial invasion (cerebritis), toxic encephalopathy, elevated intracranial pressure, and damage to the cerebral cortex [1,2,8]. In this study, focal neurological deficits were found in 37.5% of patients with bacterial ME, a finding is not far from those reported by Pelkonen *et al* 23% [21] and Urowayino *et al* 31.3% [26] whereas in the viral group, 16.7% of patients developed neurological deficits. Relevant figures were available in the revised literatures for comparison. However, some authors [9,16] have mentioned that, it is a suspected complication in acute viral ME, especially that caused by herpes and adenoviruses. Cranial nerves palsies were detected in 33.3% of patients with bacterial ME, which is similar to 33.3% reported by Mahmoud *et al* [27]. In the viral type it was present in 8.3% of patients, compared to 4% found in Ahmed *et al* [13] study.

In relation to age, a significant association was found for increased ICP, anemia, hypoglycemia, and seizures, while the remaining complications were distributed in non-significant differences. Increased ICP was seen in higher frequency of patients ≥ 5years of age (88.9 %), as compared to those <5 years (47.1%). It is mentioned as a common complication in children at all ages. However, it may be less recognized in infants due to the greater distensibility of their skulls, which may minimize its manifestations [1,18].

Anemia was more common in patients <5 years (56.9%, p<0.05). This is most probably related to the more severity of the disease in young children, and could also be contributed by the high prevalence of under-nutrition they have

Hypoglycemia and seizures, are mentioned as important complications of acute ME, especially frequent among infants and young children [14,18,25]. In this study, they

were seen in significant higher proportions of patients <5 years than those ≥5 years.

The case fatality rate in viral ME was 2.8%, being not different from those reported in Egypt [28] (3.4%), and India [29] (3.8%). In bacterial ME, the case fatality rate was 12.5%, which is between two previously reported results in Yemen, 10% [12] and 14.3% [30], but lower than other study, 3.3% [31].

Limitations

At the time of study, the rapid diagnostic tests for bacterial agents, polymerase chain reaction (PCR) and serological tests for suspected viruses were not available in Aden Governorate. Viral culture also was not available, but has been mentioned as impractical; it is long time consuming, very expensive, and of relatively low validity. These situations had limited the identification of causative agents, viral in particular and bacterial for patients with negative CSF gram stain and/or culture.

Eleven patients left the hospital early, against medical advice with no further contact with the author. The disease progress in these patients remained unknown, which may affect studied findings. All the discharged patients could not be seen again by the author for assessment of late complications (neurological sequalae). We did not have the opportunities to record hearing impairment in our group of patients

Conclusion

Acute ME is a serious disease associated with a high rate of acute complications which were in a significant association with bacterial ME, age <5 years, late presentation, and lack of exclusive breast feeding.

Acute viral and bacterial ME shared almost the same complications, which were of significant higher proportions in the bacterial type. Increased ICP was the commonest complication in both types, and seen more frequently among patients ≥5 years of age.

Based on the study findings, we recommend:

- Great effort is required to activate the necessary preventive measures against the disease particularly: promotion of immunization, with implementation of mumps vaccine into the national Yemeni program, increasing the people awareness about the disease and its serious outcome, and the importance of exclusive breast feeding during the 1st 6 months of life.
- Improving diagnosis and management of acute ME, by offrring the essential facilities.
- Establishment of a special neurological out patient's clinic for follow up.
- Encouraging further epidemiological community-based study to clarify the non-confirmed aspects in this hospital-based study.

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References

1. Jan MM. Meningitis and encephalitis in infants and children. Saudi Med J 2012; 33(1): 11-6.
2. Mann K, Jackson MA. Meningitis. Pediatr Rev 2008; 29 (12):417-29.
3. Rasul C, Muhammad F, Hossain M, Ahmed K, Rahman M. Acute meningo-encephalitis in hospitalized children of southern Bangladesh. Malays J Med Sci 2012; 19(2): 67-73.
4. Franco-Paredes C, Lammoglia L, Hernandez I, Santos-Preciado J. Epidemiology and outcomes of bacterial meningitis in Mexican children: 10-year experience (1993—2003). Int J Infect Dis 2008; 12(4): 380-6.
5. Vasilopoulou V, Karanika M, Theodoridou K, Katsioulis A, Theodoridou M, Hadjichristodoulou C. Prognostic factors related to sequelae in childhood bacterial meningitis: data from a Greek meningitis registry. BMC Infect Dis 2011; 11: 214.
6. Pelkonen T, Roine I, Monterio L, Correia M, Pitkaranta A, Bernardino L, *et al*. Risk factors for death and severe neurological sequelae in childhood bacterial meningitis in sub-Saharan Africa. Clin Infect Dis 2009; 48(8):1107-10.
7. Namani S, Milenkovi´ Z, Koci B. A prospective study of risk factors for neurological complications in childhood bacterial meningitis. J Pediatr 2013; 89(3): 256 - 62.
8. Koedel U, Klein M, Pfister H. New understandings on the pathophysiology of bacterial meningitis. Curr Opin Infect Dis 2010; 23(3): 217–23.
9. Biaukula V, Tikoduadua L, Azzopardi K, Seduadua A, Temple B, Richmond P, *et al*. Meningitis in children in Fiji: etiology, epidemiology, and neurological sequelae. Int J Infect Dis 2012; 16(4): e289–95.
10. Rorabaugh M, Berlin L, Heldrich F, Roberts K, Rosenberg L, Doran T, *et al*. Aseptic meningitis in infants younger than 2 years of age: acute illness and neurologic complications. Pediatrics 1993; 92(2): 206-11.
11. Dash N, Al Khusaiby S, Behlim T, Mohammadi A, Mohammadi E, Al Awaidy S. Epidemiology of meningitis in Oman, 2000–2005. Eastern Mediterranean Health J 2009; 15(6):1358-64.
12. Al Khorasani A, Banajeh S. Bacterial profile and clinical outcome of childhood meningitis in rural Yemen: A 2-year hospital-based study. J Infection 2006; 53(4): 228-34.
13. Ahmed Z. CSF Analysis in childhood meningitis with special reference to LDH [dissertation]. Bangalore: Rajiv Gandhi University; 2008.
14. Jan I, Tsai T, Chen J, Jerng J, Hsu H, Hung P, *et al*. Hypoglycemia associated with bacteremic pneumococcal infections. Int J Infect Dis 2009; 13(5): 570-6.
15. Sherry B, Smith A, Kronmal R. Anemia during Haemophilus influenza type b meningitis: lack of an effect of chloramphenicol. Dev Pharmacol Ther 1989; 12(4): 188 -99.
16. Beig F, Malik A, Rizvi M, Acharya D, Khare S. Etiology and clinico-epidemiological profile of acute viral encephalitis in children of western Uttar Pradesh, India. Int J Infect Dis 2010; 14(2): e141-6.

17. Alshehari A, Al-Selwi A, Albahloly M. Epidemiology and Outcome of Acute Bacterial MeningitisAmong Children in Saudi Haospital Hajjah, Northwest Territories of Yemen. American J Pediatrics 2018; 4(3): 56-60.
18. Gomes I, Melo A, Lucena R, Cunha-Nascimento M, Ferreira A, Goes J, *et al*. Prognosis of bacterial meningitis in children. Arq Neuropsiquiatria 1996; 54(3): 407-11.
19. Salih K, Saeed N, Karsani M, El Ageb R, Salih A, Ibrahim S. Characteristics of morbidity and mortality in children less than 5 years of age with acute bacterial meningitis in Omdurman, Sudan. J Med Med Sci 2011; 2(6): 920-4.
20. Elsaid M, Flamerzi A, Bessisso M, Elshafie S. Acute bacterial meningitis in Qatar. Saudi Med J 2006; 27(2): 204-10.
21. Pelkonen T. Improving outcome of childhood bacterial meningitis by simplified Treatment-Experience from Angola [dissertation]. Helsinki: University of Helsinki; 2011.
22. Sigauque B, Roca A, Sanz S, Oliveiras I, Martinez M, Mandomando I, *et al*. Acute bacterial meningitis among children, in Manhica, a rural area in southern Mozambique. Acta Trop 2008; 105(1): 21-7.
23. Kaplan K, Oski F. Anemia with Haemophilus influenzae meningitis. Pediatrics 1980; 65(6):1101- 4.
24. Shurin S, Anderson P, Zollinger J, Rathbun K. Pathophysiology of hemolysis in infections with Haemophilus influenza Type B. J Clin Invest 1986; 77(4): 1340-8.
25. Ogunlesi T, Okeniyi J, Oyelami O. Pyogenic meningitis in Ilesa, Nigeria. Indian pediatr 2005; 42(10): 1019-23.
26. Urowayino O, Afolabi L, Chinyere E, Olufunmilayo G. Neurological sequelae in children with pyogenic meningitis in a tertiary center in Lagos (Nigeria). Afr J neurol scien 2004; 23(2): 31-7.
27. Mahmoud R, Mahmoud M, Badrinath P, Sheek-Hussein M, Alwash R, Nicol A. Pattern of meningitis in Al-Ain medical district, United Arab Emirates - a decadal experience (1990-99). J Infect 2002; 44(1): 22-5.
28. Farag H, Abdel-Fattah M, Youssri A. Epidemiological, clinical and prognostic profile of acute bacterial meningitis among children in Alexandria, Egypt. Indian J Med Microbiol 2005; 23(2): 95-101.
29. Joardar S, Joardar G, Mandal P, Mani S. Meningitis in children: a study in Medical College & Hospital, Kolkata. Bangladesh J child Health 2012; 36(1): 126 - 32.
30. Sallam A. Etiology and presentation of acute bacterial meningitis in children at AL-Thawrah Hospital, Sanaa, Yemen. J Ayub Med Coll Abbottabad 2004; 16(4): 40-3.
31. AL-Sonboli N, AL-Harazi A, AL-Zoa A. Determinants of Mortality of Acute Bacterial Meningitis among Yemeni Children in a Tertiary Referral Hospital in Sana'a. Med. J Cairo Univ 2017; 85(4): 1543-9.