



# Complications of Acute Meningoencephalitis among Children Admitted to Al-Wahda Teaching Hospital in Aden, Yemen

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## ABSTRACT

**Objective:** To determine the types and frequencies of complications associated with acute meningoencephalitis (ME) among children admitted to hospitals in Aden, Yemen.

**Methods:** This descriptive cross-sectional study was conducted among 60 children (1 month – 14 years of age) admitted to AL-Wahda Teaching Hospital in Aden with acute ME (viral or bacterial) over the period from January to June 2010. Data were collected using a pre-designed questionnaire, and data were presented as frequencies and percentages and analyzed using appropriate statistical tests. Differences or associations between categorical variables were considered statistically significant at  $P$  values  $<0.05$ .

**Results:** ME complications were significantly higher among children aged less than one year compared to those aged one year or older (58.8% vs. 38.5%, respectively) and among those with bacterial ME compared to those with viral ME (79.2% vs. 30.6%, respectively). The complications were also significantly higher among children with history of illness for three or more days before their admission compared to those having been ill for less than three days (65.8 vs. 22.7%, respectively). In addition, children aged less than two years not exclusively breastfed were more prone to ME complications compared to those exclusively breastfed (93.5% vs. 50.0%, respectively). Increased intracranial pressure (ICP), anemia and hypoglycemia were the three most frequent ME complications among children admitted to Al-Wahda Teaching Hospital, being observed in 53.3%, 50.0% and 43.3% of patients, respectively. Increased ICP was significantly higher among children aged five years or older compared to those aged less than five years (88.9% vs. 47.1%, respectively). In contrast, anemia and hyperglycemia were significantly higher among children aged less than five years (56.9% and 49.0%, respectively) compared to those aged five years or older (11.1% each).

**Conclusions:** ME complications are significantly higher among children aged less than one year, infected with bacterial ME, with history of illness for three or more days before their admission and not exclusively breastfed. Increased ICP, anemia and hypoglycemia are the three most frequent ME complications, particularly among children with bacterial ME in Aden, followed by focal neurological deficits seizures and cranial nerve palsy. Although increased ICP is significantly higher among children aged five years or older, anemia and hyperglycemia are significantly higher among children aged less than five years. Active measures to promote immunization and exclusive breastfeeding along with early diagnosis and proper treatment are highly recommended. Further large-scale studies are required to study the pattern of complications following acute ME among Yemeni children.

**Keywords:** Meningoencephalitis, Complication, Intracranial pressure, Seizure, Focal neurological sign, Cranial nerve palsy, Yemen

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## 1. Introduction

Meningoencephalitis (ME) is an inflammatory condition of the leptomeninges and the subarachnoid space. Despite intensive care and therapeutic developments, it is still one of the most potentially serious and life-threatening infections of infants and children.<sup>(1, 2)</sup> It often results in disability or death of 170,000 patients in the world annually, with two-thirds of pediatric deaths occur in low-income countries and approximately half of survivors experience some neurological sequelae.<sup>(3, 4)</sup>

ME is associated with high risk for complications, which are more common and often severe in the pyogenic type.<sup>(5, 6)</sup> Common neurological complications in children include sensorineural deafness, seizure disorders and motor deficits. Approximately 16.0% of pediatric patients in developed countries experience neurological complications compared to 26.0% in developing countries.<sup>(7, 8)</sup> Different types of complications may occur, either as an early acute and often reversible phenomenon or as late events that generally result in permanent sequelae.<sup>(9)</sup>

Increased intracranial pressure (ICP) is the commonest, earliest and most serious complication, presented in most of the patients.<sup>(10)</sup> Repeated seizures usually appear after 48 hours of commencing treatment, and those refractory to treatment are the most common acute complications reported in 30–40% of patients, most frequently among young children.<sup>(6, 8)</sup> There are few studies conducted in Yemen or in countries with similar conditions regarding morbidity and mortality of ME. Therefore, the present study aimed to determine the types and frequencies of complications associated with different types of ME among pediatric patients admitted to hospitals in Aden city, Yemen.

## 2. Methods

### 2.1. Study design, setting and population

This descriptive cross-sectional study was conducted among children admitted with acute ME (viral and bacterial) to Al-Wahda Teaching Hospital in Aden over the period from January to June 2010. Children were included if they met the following criteria:<sup>(11, 12)</sup> aged between 1 month and 14 years, with at least three suggestive clinical features of acute ME of the following manifestations: fever, seizures, vomiting, alteration of consciousness and neck stiffness, with cerebrospinal fluid (CSF) findings indicative of bacterial or viral infection and whose mothers/guardians agreed to give informed consent to participate voluntarily in the study. On the other hand, children were excluded if they were diagnosed on clinical suspicion without performing a lumbar puncture (LP), they had a traumatic LP or left the hospital before data collection, or their CSF was not analyzed. A total of 60 pediatric patients (comprising 2.6 % of the total pediatric admissions over the study period) were enrolled in the present study.

### 2.2. Data collection

A pre-designed open-closed questionnaire was used for collecting data on patient's age, sex, presenting complaints, symptoms and signs, birth history, family history, developmental history, any history of trauma/wound, drugs, immunization and ear problems, exam findings and duration of illness. Data on drugs used before admission, final diagnosis and complications at the time of discharge and the final outcome were also recorded.

Each patient was evaluated during hospitalization by interviewing his/her mother (58 patients) or attending relatives (2 patients), an initial clinical examination (general, respiratory, cardiovascular, abdominal and neurological), daily follow-up and assessment of neurological examination and head circumference and discussion with the treating specialist.



### 2.3. Data analysis

Data were analyzed using the Statistical Packages for Social Sciences (SPSS), version 15.0 (SPSS Inc., Chicago, IL, USA). Chi-square or Fisher's exact tests were used to test differences between categorical variables with the help of a biostatistician. Differences and association were considered statistically significant at  $P$  values  $< 0.05$ .

## 3. Results

### 3.1. Association of ME complications among pediatric patients in Aden with certain characteristics

Table (1) shows that age, type of ME, duration of illness before admission and status of breastfeeding were the characteristics significantly associated with the complications of ME among children admitted to Al-Wahda Teaching Hospital in Aden., while sex was not significantly associated with ME complication ( $P = 0.790$ ). The ME complications were significantly higher among children aged less than one year compared to those aged one year or older (58.8% vs. 38.5%, respectively) and among those with bacterial ME compared to those with viral ME (79.2% vs. 30.6%, respectively). On the other hand, the complications were significantly higher among children with history of illness for three or more days before their admission compared to those having been ill for less than three days (65.8 vs. 22.7%, respectively). In addition, children aged less than two years not exclusively breastfed were more prone to ME complications compared to those exclusively breastfed (86.4% vs. 26.1%, respectively).

### 3.2. Distribution of ME complications according to the cause of ME among pediatric patients

Increased ICP, anemia and hypoglycemia were the three most frequent ME complications among children admitted to Al-Wahda Teaching Hospital, being observed in 53.3%, 50.0% and 43.3% of patients, respectively. Increased ICP was significant-

ly higher among children with bacterial ME than those with viral ME (70.8% vs. 41.7%, respectively) followed by 66.7% for each of anemia and hypoglycemia among children with bacterial ME compared to 38.9% for anemia and 27.8% for hypoglycemia among those with viral ME (Table 2).

**Table 1.** Distribution of ME complications among pediatric patients admitted to Al-Wahda Teaching Hospital, Aden (2010)

Variable	N	Children with complications		P value
		n	(%)	
<b>Sex</b>				
Male	37	18	(48.6)	0.790
Female	23	12	(52.2)	
<b>Age (years)</b>				
< 1	34	20	(58.8)	< 0.001
≥ 1	26	10	(38.5)	
<b>Types of ME</b>				
Viral	36	11	(30.6)	<0.001
Bacterial	24	19	(79.2)	
<b>Duration of illness before admission (days)</b>				
< 3	22	5	(22.7)	<0.001
≥ 3	38	25	(65.8)	
<b>Exclusive breastfeeding*</b>				
Yes	23	6	(26.1)	< 0.001
No	22	19	(86.4)	

N, number of patients with ME; n, number of ME patients with complications; ME, meningoen- cephalitis; \*, calculated for 45 children aged less than two years during the first six months of life.

Table (2) also shows that local neurological deficits were observed in 25% of children with ME, being significantly higher among those with bacterial ME (37.5%) than those with viral ME (16.7%). On the other hand, seizures and cranial nerve palsy were observed among 23.3% and 18.3% of children with ME, respectively, where these were significantly higher among children with bacterial meningitis (37.5% and 33.3%, respectively) compared to those with viral meningitis (13.9% and 8.3%, respectively). Nevertheless, hydrocephalus was the least frequent ME complication, being detected in a child with bacterial ME.

**Table 2.** Distribution of complications according to the cause of ME among pediatric patients admitted to Al-Wahda Teaching Hospital, Aden (2010)

Complication type	Cause of ME			P value
	Viral	Bacterial	Total	
	(N = 36)	(N = 24)	(N = 60)	
	n (%)	n (%)	n (%)	
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 (0.0)	1 (4.2)	1 (1.7)	0.217

ME, meningoen- cephalitis; ICP, intracranial pressure.



### 3.3. Age-specific distribution of ME complications among pediatric patients

Table (3) shows that increased ICP was significantly higher among children aged five years or older compared to those aged less than five years (88.9% vs. 47.1%, respectively). In contrast, anemia and hyperglycemia were significantly higher among children aged less than five years (56.9% and 49.0%, respectively) compared to those aged five years or older (11.1% each). On the other hand, no statistically significant age-specific differences in the distribution of the complications of focal neurological deficits, seizures, cranial nerve palsy or hydrocephalus.

**Table 3.** Age-specific distribution of ME complications among pediatric patients admitted to Al-Wahda Teaching Hospital, Aden (2010)

Complication type	Age (years)				P value
	< 5 (N = 51)		≥ 5 (N = 9)		
	n	(%)	n	(%)	
Increased ICP	24	(47.1)	8	(88.9)	0.022
Anemia	29	(56.9)	1	(11.1)	0.013
Hypoglycemia	25	(49.0)	1	(11.1)	0.028
Focal neurological deficits	11	(21.6)	4	(44.4)	0.148
Seizures	13	(25.5)	1	(11.1)	0.322
Cranial nerves palsy	8	(15.7)	3	(33.3)	0.206
Hydrocephalus	0	(0.0)	1	(11.1)	0.150

ICP, intracranial pressure.

## 4. Discussion

Acute ME is one of the most potentially serious infections and is an important cause of childhood morbidity and mortality in developed and developing countries.<sup>(13, 14)</sup> In the present study, ME complications were frequent, indicating the seriousness of the disease among Yemeni children. Such complications could be attributed to several factors, including the high virulence of the causative agents, the greatest sensitivity of the involved system and the inadequate concentrations of complement and antibodies in the CSF.<sup>(15, 16)</sup> The frequency of complications was significantly higher among children with bacterial ME compared to those with viral variety of the disease, which is in accordance with several published reports.<sup>(17–22)</sup> This could be partially explained by the fact that the inflammatory response in the subarachnoid

space as a result of bacterial infection is more severe than that due to viral infections.<sup>(23)</sup>

The significantly higher frequency of ME complications among children less than one year of age is consistent with that reported by Gomes et al.,<sup>(24)</sup> who reported that complications were more predominant among Brazilian children aged less than one year of age (71%). On the other hand, the significantly higher frequency of ME complications among exclusively breastfed children in their first six months of life in the present study is in agreement with the finding reported among Sudanese children by Salih et al.,<sup>(25)</sup> who found a relation between the lack of exclusive breastfeeding and high frequency of complications following bacterial ME.

The present study revealed that increased ICP was the most frequent ME complication (79.2%) among children from Aden. This finding is consistent with reports from Kosovo and Qatar,<sup>(26, 27)</sup> where it was the most common complication of bacterial ME observed in 62.3% and 58.0% of patients, respectively. Furthermore, anemia was the second most common complication and is consistent with reports elsewhere.<sup>(28–30)</sup> It is noteworthy that anemia is a common complication of acute infections in children, both viral and bacterial, and is attributed to several factors such as decreased intake, decreased absorption and increased demands for iron and other essential nutrients in febrile patients, inadequate erythropoiesis, and hemolysis caused by bacterial toxins.<sup>(28, 31, 32)</sup>

Third to anemia is the complication of hypoglycemia among children with ME in the present study. Hypoglycemia is a common complication of acute ME, being more common among young patients with pyogenic infections. Several factors contribute to hypoglycemia such as less intake, frequent vomiting, impaired gluconeogenesis in the liver and increased utilization of glucose in the brain.<sup>(33, 34)</sup> The present study revealed that hypoglycemia should also be considered as a recognized complication of acute viral ME despite being



related to bacterial ME but not for the viral variety.<sup>(33, 35)</sup>

Refractory seizures were observed in a considerable proportion (37.5 %) of children with bacterial ME in the present study. This finding is in agreement with that (34%) reported from Angola.<sup>(29)</sup> In children with viral ME, seizures were less frequent (13.9%), which is in agreement with those reported elsewhere.<sup>(21, 23)</sup> Refractory seizures mainly result from damage to the cerebral cortex (hypoxia, infarctions, necrosis), and may also be exacerbated by other neurological (e.g. increased ICP, subdural effusion) or metabolic (e.g. hypoglycemia, hyponatremia) complications.<sup>(7, 8)</sup> On the other hand, motor and sensory deficits and cranial nerve 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 ICP and damage to the cerebral cortex.<sup>(15, 16)</sup> In the present study, focal neurological deficits were found in about a third of patients with bacterial ME, which is a little bit higher than those reported from Angola (23%) and Nigeria (31.3%).<sup>(29, 36)</sup> Among children with viral ME, neurological deficits were recognized in 16.7%, but no relevant findings were available in the published literature for comparison. However, it has been mentioned as a suspected complication in acute viral ME, especially that caused by herpes simplex viruses and adenoviruses.<sup>(17, 21)</sup>

Cranial nerve palsies were detected in about a third of patients with bacterial ME in the present study, which is similar to that reported among children from the United Arab Emirates.<sup>(37)</sup> On the contrary, their low proportion among children with viral ME is in line with the low proportion (4.0%) among Indian children.<sup>(38)</sup> On the other hand, hydrocephalus was rare among children with ME in the present study, being diagnosed in only one patient with bacterial ME, which agrees with that reported among Brazilian children,<sup>(24)</sup> where only 2.5% of patients developed hydro-

cephalus before their discharge. Hydrocephalus can occur as an acute/early complication of bacterial ME but is more frequently observed after a few weeks of an apparent recovery.<sup>(14,15)</sup>

Increased ICP was significantly higher among children aged five years or older in the present study. Although it has been described as a common complication in children of all ages, it may be less recognized in infants due to the greater distensibility of their skulls, which may minimize its manifestations.<sup>(24)</sup> On the contrary, hypoglycemia and seizures were significantly higher among children less than five years in the present study. It is to be noted that these complications have been described as frequent complications of acute ME among infants and young children.<sup>(24, 39)</sup>

## 5. Conclusions

The complications of acute ME are significantly higher among children aged less than one year, infected with bacterial ME, with history of illness for three or more days before their admission and not exclusively breastfed in the first six months of their life. Increased ICP, anemia and hypoglycemia are the three most frequent ME complications, particularly among children with bacterial ME, followed by focal neurological deficits seizures and cranial nerve palsy. Nevertheless, hydrocephalus is a rare complication of bacterial ME. Increased ICP is significantly higher among children aged five years or older, but anemia and hyperglycemia are significantly higher among children aged less than five years. However, no statistically significant age-specific differences in the distribution of the complications of focal neurological deficits, seizures, cranial nerve palsy or hydrocephalus. Active measures to promote immunization and exclusive breastfeeding along with early diagnosis and proper treatment are highly recommended, and further large-scale studies are required to study the pattern of complications following acute ME among Yemeni children.



## Ethical considerations

Ethical approval was obtained from the Post-graduate Committee of the Department, and the Ethics Committee of the Faculty of Medicine and Health Sciences, Aden University. Verbal informed consent was obtained from the mothers/guardians of children after explaining them the aim of the study. Participation was on a voluntary basis.

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## Competing interests

The author declares that she has no competing interests associated with this article.

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