

Epidemiology and aetiology of the 2023 meningitis outbreak among children in Iraq

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Abstract

Background: Meningitis is still a major public health challenge globally. Both the viral and bacterial forms of the disease have been reported worldwide. In 2023, around 200 children with suspected meningitis were admitted to hospital in Halabja Governorate, Iraq. No outbreak of meningitis had been reported previously in that region.

Aims: To investigate the aetiology and epidemiology of meningitis among children in Halabja Governorate, Iraq, and expedite clinical management and prevention.

Methodology: Blood and cerebrospinal fluid specimens were collected from 197 children admitted to Halabja Paediatric and Maternity Teaching Hospital from 1 March to 1 July 2023 and analysed. The sample *t*-test was used to compare the haematological, serological and biochemical characteristics of the samples.

Results: The majority (76.6%) of the children were aged 2–9 years and 54% were males. The clinical manifestations of the disease were fever (100.0%), headache (89.0%), vomiting (85.7%), and photophobia (72.4%); none of the children had convulsions. The mean values for both neutrophil count and C-reactive protein were statistically significantly raised ($P < 0.05$) and the red blood cells, white blood cells and neutrophil counts, and lactate dehydrogenase values were statistically significantly raised ($P < 0.05$). The causative organism was enterovirus (98.5%), with sporadic cases of streptococcal meningitis (1.5%). All the patients recovered fully.

Conclusion: The rapid diagnosis of the disease was crucial to the therapeutic and prevention control measures for the outbreak. Although it is still unclear how and where this outbreak started, contaminated drinking water and transmission among children in nurseries and schools are suspected. Further investigations are recommended to determine the source of the enterovirus and identify the virus species and serotypes.

Keywords: meningitis, outbreak, epidemiology, enterovirus, children, Halabja Governorate, Iraq

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Introduction

Meningitis is an inflammation of the meninges, a 3-layered membrane that surrounds the brain and spinal cord (1). The incidence of meningitis is annually estimated at 20 cases per 100 000 people, and it can lead to hundreds of thousands of deaths worldwide (2,3). The causative agents include viruses, bacteria, parasites and fungi (3). The most frequently isolated bacteria are *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Listeria monocytogenes* (4,5). Viral meningitis can be caused by cytomegalovirus, enterovirus, herpes simplex virus, influenza virus, parechovirus, mumps virus, measles virus, coronavirus, adenovirus, varicella zoster virus and human immunodeficiency virus (HIV) (6).

Meningitis is considered a serious health issue that requires effective therapeutic, management and prevention plans, particularly in endemic countries (7). Epidemic meningitis has been reported in many countries across the sub-Saharan region of Africa for more than a century (8). Bacterial meningitis is annually

reported at various incidence rates in the countries of Europe, Africa, East Asia, South-East Asia, the Middle East, South America and North America (9). In previous studies, the incidence of bacterial meningitis has been reported as 2.6, 3.7, 4.3 and 3.2 per 100 000 population in the Netherlands, Italy, Kosovo and Iceland respectively (10–13). Research in neighbouring countries in the Middle East has found incidence rates of 3.6, 3.0, 1.0 and 0.9 per 100 000 population in Egypt, Oman, the United Arab Emirates and the Islamic Republic of Iran respectively (14–17). A 2021 study reported the annual incidence rate of bacterial meningitis in Iraq as 1.47 per 100 000 population (18).

Nearly 200 children with suspected meningitis were admitted to a paediatric and maternity teaching hospital in Halabja Governorate, Kurdistan Region, Iraq, in the period March–July 2023. The disease may be endemic in the region; however, to the best of our knowledge, no meningitis outbreak has been reported in the area to date. Thus, this study was conducted to investigate the aetiology and epidemiology of the disease in the

governorate because identification of the causative agent and understanding the epidemiology of the outbreak are of paramount importance for clinical management and rapid planning for prevention of transmission.

Methods

Study type and geographical location

This was a descriptive, observational study on a series of cases carried out in Halabja Governorate, which is situated in the north-east of Iraq, bordering the Islamic Republic of Iran (45° 58' 59" E; 35° 10' 59" N). Halabja is a small, newly established governorate that was separated from Sulaimaniyah Governorate in 2014. The governorate consists of the capital city, Halabja, and the districts of Sirwan, Xurmal, Biyare and Bemo. It has a total area of 889 km² and an estimated population of 140 000. The inhabitants of the governorate are Kurdish, speaking the Sorani and Hawrami dialects.

Demographic data

Demographic data were collected for 197 children who were admitted to Halabja Paediatric and Maternity Teaching Hospital during the period 1 March 2023 to 1 July 2023. Halabja is the least populated governorate in Iraq and the hospital is the sole specialized paediatric hospital providing standard health care services to the entire governorate. Initially, the children were taken by their parents to local public hospitals and private clinics for treatment. Depending on the clinical manifestations of the cases (fever, headache, vomiting, photophobia), meningitis was suspected and the patients were referred to the paediatric and maternity teaching hospital for admission and medical intervention. We obtained parental consent to collect demographic and medical data on the patients (name, address, sex, age, signs and symptoms, source of drinking water and family members with the same health issue) via a questionnaire administered by the researchers.

The patients were identified as positive cases of meningitis based on the laboratory findings and molecular detection of the causative agents.

Clinical specimen collection and analysis

Blood and cerebrospinal fluid (CSF) specimens were collected from the patients who had been admitted with suspected meningitis. We used haematological, biochemical, microscopic and microbiological examinations to analyse the specimens. Complete blood counts were conducted on the blood samples using a haematology analyser (Medonic CBC, Sweden). The erythrocyte sedimentation rate and C-reactive protein (CRP) were determined. The CSF samples were divided into 3 × 1 mL aliquots. The first portion was examined for the cellular components such as total RBC and WBC counts using a manual haemocytometer method. The CSF glucose, lactate dehydrogenase, total protein, and lactate biomarkers were measured (Accent 200, spectrophotometer, Cormay, USA; and Cobas C11

analyser, Roche Diagnostics, USA) in the second portion. The third portion of the CSF sample was analysed for microorganisms using microscopic examination (Gram staining technique), conventional microbiological tests (culturing and susceptibility) and meningitis/encephalitis panel (laboratory incubator, J.P SELECTA, Spain), according to the manufacturers' instructions.

Ethical considerations

Ethical approval (No. 324A, 30 April 2023) for this study was given by a joint committee from Halabja General Health Directorate and Charmo Center for Research, Training, and Consultancy at Charmo University. Consent was given by the parents of the patients and the hospital authorities on the assurance that the data collected would be kept confidential and only used for research.

Statistical analysis

A one sample *t*-test (2-tailed) was used to compare the haematological, serological and biochemical test results with the normal range values for each using Microsoft *Excel*.

Results

Patients and disease characteristics

During the period of the study, 197 children were admitted to Halabja Paediatric and Maternity Teaching Hospital. Just over half of them were males (54.8%, *n* = 108). The majority, 76.6% (*n* = 151), were aged 2–9 years, followed by 16.7% (*n* = 33) aged 10–17 years and 6.6% (*n* = 13) aged 1–23 months. No cases were recorded among children under one month old.

Fever (100.0%, *n* = 197) and headache (89.0%, *n* = 177) were the main clinical manifestations of the disease identified in our patients. Vomiting (85.7%, *n* = 162) and photophobia (72.4%, *n* = 137) were also recorded. Convulsions were not observed in any of the patients admitted to the hospital.

To understand the transmissibility of the disease, the parents were asked whether any other members of the family had had the same health issue. Out of 184 families, only 25% (*n* = 46) stated that they had other children with similar signs and symptoms.

Routine laboratory findings

A number of haematological, biochemical and serological analyses were conducted on blood and CSF specimen collected from the patients (Table 1). From the blood testing, mean values for both neutrophil count and C-reactive protein value were statistically significantly raised (*P* < 0.05). Total white blood cell count was raised in patients aged 2–9 years, but this was not statistically significant (*P* = 2.120). The erythrocyte sedimentation rate was also raised in comparison with the normal range, but again this was not statistically significant (*P* = 0.070). The lymphocyte count was the only blood parameter which fell within the normal range (Table 1).

Table 1 Distribution of mean values for the clinical blood tests and the CSF specimens of children diagnosed with meningitis (n = 197) admitted to hospital, Halabja, 2023

Sample	Test	Age	Normal range ^a	Mean	SD	P-value
Blood	WBC (× 10 ⁹ /L)	0–30 days	9.1–34.0	–	–	–
		1–23 months	6.0–14.0	13.42	5.86	0.244
		2–9 years	4.0–12.0	26.49	10.3	2.120
		10–17 years	4.0–10.5	10.31	0.85	0.825
	Neutrophils (%)		54.0–62.0	65.9 ^b	16.5	0.045
	Lymphocytes (%)		25.0–33.0	23.4	15.4	0.430
	ESR (mm/hr)		< 20.0	29.6	20.7	0.070
CSF	CRP (mg/L)		< 5.0	19.2 ^b	20.0	0.0048
	WBC (cells/μL)	Neonate	< 20.0	–	–	–
		≥ 1 month	< 5.0	661	960	6.00E-11
	RBC (cells/μL)		0	102.5 ^b	229.0	0.000004
	Neutrophils (% cells)		< 25.0	57.8 ^b	30.7	0.012638
	Lymphocytes (% cells)		< 75.0	25.6	20.6	0.91
	Glucose (mg/dL)		> 50.0L	57.8	13.1	–
	LDH U/L		< 40.0	55.0 ^b	33.4	0.00003
	Lactate (mg/dL)		10.0–22.0	23.2	23.8	0.71
Total protein (mg/dL)		20.0–45.0	43.4	17.8	0.34	

SD = standard deviation; WBC = white blood cells; CSF = cerebrospinal fluid; ESR = erythrocyte sedimentation rate; CRP C = reactive protein; RBC = red blood cells; LDH = lactate dehydrogenase. P < 0.05 was considered statistically significant.

^aValues given for normal ranges were defined according to the instruments, commercial kits and methods of analysis usually used in the laboratories. ^bSignificantly different in comparison to the normal range value.

In the CSF testing, red blood cells, white blood cells and neutrophil counts, and lactate dehydrogenase value were statistically significantly raised (P < 0.05) (Table 1).

Causative agents

Meningitis can be caused by viruses, bacteria, fungi and parasites (19). The routine haematological, biochemical and serological tests are not adequate to identify the causative organism, therefore, microbiological identification techniques such as conventional bacteriological examinations and FilmArray meningitis/encephalitis panel (BioFire Diagnostics, bioMérieux, Salt Lake City, USA) were used. The FilmArray panel is a rapid and reliable method for simultaneously testing a specimen for a wide range of microbes that commonly cause meningitis (Table 2). Enterovirus was the only virus detected (98.5% of the cases tested). *Streptococcus pneumoniae* was the only bacterium isolated in our testing (1.5% of the cases tested). No other microorganisms were detected (Table 2).

Discussion

In this paediatric outbreak of 197 patients aged ≤ 17 years in Halabja Governorate, Iraq, the majority (76.7%) were aged 2–9 years. Microbiological examination confirmed enterovirus as the causative agent. Almost all the cases showed the classic signs and symptoms of meningitis. The clinical manifestations were fever (100.0%), headache (89.0%), vomiting (85.7%) and photophobia (72.4%). No convulsion and no fatalities were recorded. Water

contamination and transmission via school nurseries were suspected.

The occurrence of the disease among young patients (<18 years) suggests that the spread of the infection may have been facilitated by crowding in nurseries and schools. The most common age group of the infected

Table 2 Distribution of microbial aetiology of the cases of suspected meningitis (n = 197), Halabja, 2023

Microorganism	%
Bacteria	
<i>Escherichia coli</i> K1	0.0
<i>Streptococcus pneumoniae</i>	1.5
<i>Streptococcus agalactiae</i>	0.0
<i>Neisseria meningitidis</i>	0.0
<i>Haemophilus influenzae</i>	0.0
<i>Listeria monocytogenes</i>	0.0
Viruses	
Cytomegalovirus	0.0
Enterovirus	98.5
Herpes simplex virus 1	0.0
Herpes simplex virus 2	0.0
Human herpesvirus 6	0.0
Human parechovirus	0.0
Varicella zoster virus	0.0
Yeasts	
<i>Cryptococcus neoformans/gattii</i>	0.0

children was 2–9 years, this is consistent with the findings of a study in Egypt (20) but contrasts with the findings of other research in the Islamic Republic of Iran and South Korea (21,22).

We observed that only a quarter of the infected children had siblings with a similar condition. This indicates that the disease was not easily transmissible between family members and the respiratory system was not the main route of transmission. This is supported by the fact that enteroviruses are transmitted through the faecal–oral route or through direct contact with body fluids and secretions (23,24). The main observed signs and symptoms of the disease among the children in our study were fever, vomiting, headache and photophobia, and this is consistent with the findings of other studies (21,22). Importantly, convulsions were not recorded in any of our patients; this contrasts with the findings of some previous studies where 20–50% of the patients developed convulsions (20, 21).

This outbreak of meningitis in Halabja was caused by enterovirus (98,5%). Enteroviruses are common aetiological agents of viral meningitis in many countries, with annual incidence rates of 12–19 per 100 000 population in some high-income countries (25). In 2023, cases of enterovirus/echovirus infection were reported in Croatia, Italy, Spain, Sweden, and the United Kingdom and Northern Ireland (26). However, no outbreak of enterovirus cases was reported in the countries neighbouring Iraq in 2023. The reduction in meningitis attributable to *Streptococcus pneumoniae* to only a sporadic number of cases may be a consequence of the routine childhood immunization programmes in Iraq (27, 28).

The epidemiology of this outbreak was primarily investigated in terms of host-related variables and agent identification, however, the inability to determine the incidence and prevalence rates were limitations of our study: the disease only occurred among children aged up to 17 years, who represent a fraction of the population in the governorate. In addition, the species and serotypes of the enteroviruses were not identified due to the lack of genome sequencing facilities.

The epidemiological data from this study can provide insights for the health authorities to further investigate and determine the risk factors for outbreaks of meningitis in the governorate. This may be useful in developing strategic plans for the prevention of similar outbreaks in the future. For this purpose, raising public health awareness of the environmental sources of the causative agent, its mode of transmission, and the socioeconomic factors involved could be useful for the prevention and management of outbreaks.

Conclusion

This study is the first report of an enteroviral meningitis outbreak among children who required medical attention in Halabja Governorate, Iraq. Although it is still unclear how and where this outbreak started, contamination of the drinking water supply is suspected. Further investigations are recommended to determine the environmental source of the enterovirus and to identify the virus species and serotypes using genomic sequencing.

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Competing interests: None declared.

Épidémiologie et étiologie de la flambée de méningite survenue en 2023 chez les enfants en Iraq

Résumé

Contexte : La méningite reste un problème de santé publique majeur dans le monde. Les deux formes de la maladie, virale et bactérienne, ont été signalées dans le monde entier. En 2023, environ 200 enfants atteints de méningite présumée ont été hospitalisés dans le gouvernorat de Halabja (Iraq). Aucune flambée de méningite n'avait été enregistrée auparavant dans cette région.

Objectifs : Étudier l'étiologie et l'épidémiologie de la méningite chez les enfants du gouvernorat de Halabja, en Iraq, et accélérer la prise en charge clinique et la prévention.

Méthodes : Des échantillons de sang et de liquide céphalo-rachidien ont été prélevés auprès de 197 enfants admis à l'hôpital universitaire pédiatrique et maternel de Halabja entre le 1^{er} mars et le 1^{er} juillet 2023 et ont été analysés. L'échantillon *t* test a été utilisé pour comparer les caractéristiques hématologiques, sérologiques et biochimiques des échantillons.

Résultats : La majorité des enfants (76,6 %) étaient âgés de deux à neuf ans et 54 % étaient des garçons. Les manifestations cliniques de la maladie étaient la fièvre (100,0 %), les céphalées (89,0 %), les vomissements (85,7 %) et la photophobie (72,4 %). Aucun des enfants n'a eu de convulsions. Les valeurs moyennes du compte des neutrophiles et de la protéine C réactive augmentaient de manière statistiquement significative ($p < 0,05$) et les valeurs des globules rouges, des globules blancs et des neutrophiles, et celles de la lactate déshydrogénase s'élevaient de même de manière statistiquement significative ($p < 0,05$). L'agent étiologique était un entérovirus (98,5 %), avec des cas sporadiques de méningite à streptocoque (1,5 %). Tous les patients se sont complètement rétablis.

Conclusion : Le diagnostic rapide de la maladie a été crucial pour les mesures thérapeutiques et préventives visant à contrôler cette flambée. Bien qu'on ne sache toujours pas comment et où cette flambée a débuté, on suspecte

une contamination de l'eau de boisson et une transmission chez les enfants dans les crèches et les écoles. Des investigations plus poussées sont recommandées pour déterminer la source de l'entérovirus et identifier les espèces virales et les sérotypes.

الخصائص الوبائية لفاشية التهاب السحايا في عام 2023 بين الأطفال في العراق وأسباب تلك الفاشية

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الخلاصة

الخلفية: لا يزال التهاب السحايا يمثل تحديًا كبيرًا للصحة العامة على الصعيد العالمي. وقد رُصد الشكلاان الفيروسي والبكتيري لهذا المرض في جميع أنحاء العالم. وفي عام 2023، أُدخلت المستشفيات نحو 200 طفل يُشتبه في إصابتهم بالتهاب السحايا في محافظة حلبجة في العراق. ولم تُرصد سابقًا أي فاشية لالتهاب السحايا في تلك المنطقة.

الأهداف: هدفت هذه الدراسة إلى استقصاء أسباب التهاب السحايا وخصائصه الوبائية لدى الأطفال في محافظة حلبجة بالعراق، وتسريع وتيرة العلاج السريري والوقاية.

طرق البحث: أُخذت عينات من الدم والسائل النخاعي من 197 طفلًا أُدخلوا إلى مستشفى حلبجة التعليمي لطب الأطفال والأُمومة في الفترة من 1 مارس / آذار إلى 1 يوليو / تموز 2023، وخضعت العينات للتحليل. واستُخدم اختبار «تي» للعينة (*t-test*) لمقارنة الخصائص الدموية والمصلية والكيميائية الحيوية للعينات.

النتائج: تراوحت أعمار غالبية الأطفال (76.6%) بين عامين و9 أعوام، وكان 54% منهم ذكورًا. وكانت المظاهر السريرية للمرض: الحمى (100.0%)، والصداع (89.0%)، والقيء (85.7%)، ورهاب الضوء (72.4%)، ولم يُصَب أي من الأطفال بتشنجات. كما أن القيم الوسطية لكل من عدد العدلات والبروتين المتفاعل سبي شهدت زيادة ذات دلالة إحصائية (القيمة الاحتمالية: $P > 0.05$)، وكذلك فإن أعداد كريات الدم الحمراء وأعداد كريات الدم البيضاء وأعداد العدلات وقيم نازعة هيدروجين اللاكتات شهدت زيادة ذات دلالة إحصائية (القيمة الاحتمالية: $P > 0.05$). وكان الكائن المسبب للمرض هو الفيروس المعوي (98.5%)، مع حالات متفرقة من التهاب السحايا الناجم عن العقديات (1.5%). وقد تعافى جميع المرضى تعافياً تاماً.

الاستنتاجات: كان لسرعة تشخيص المرض دور حاسم في تدابير المكافحة العلاجية والوقائية للفاشية. وعلى الرغم من أن كيفية بدء هذه الفاشية ومكان بدئها لا يزالان غير واضحين، إلا أنه يُشتبه في مياه الشرب الملوثة وفي سريان المرض بين الأطفال في دور الحضانه والمدارس. ويُوصى بإجراء مزيد من التقيُّص لتحديد مصدر الفيروس المعوي والتعرف على أنواع الفيروس وأنماطه المصلية.

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