Two Clusters of Meningococcal Meningitis in Bunyangabu District, Uganda: October, 2017

Doreen Birungi[1,&], Miriam Nakanwagi[1], Bernard Wandera[2], Steven Ndugwa Kabwama[1,3], Alex Riolexus Ario[1]

[1]Uganda Public Health Fellowship Program, Kampala, Uganda, [2]Ministry of Health, Kampala, Uganda, [3]Makerere University School of Public Health, Kampala, Uganda

KEYWORDS: *Neisseria meningitides*, meningitis, outbreak, Uganda

ABSTRACT

Introduction: On 13 November 2017, the Uganda Ministry of Health through the Public Health Emergency Operations Centre was notified of an unknown illness that caused sudden deaths of 3 children in Bunyangabu District. The case-patients presented with fever, convulsions, loss of consciousness and neck stiffness. We investigated to establish the cause, scope of outbreak and recommend preventive measures. **Methods:** We defined a suspected case as onset of fever, neck stiffness and any of the following: convulsions, loss of consciousness, headache, vomiting, nausea in a resident of Kabonero or Kateebwa sub-counties, Bunyangabu District from 1 September to 30 November 2017. We reviewed medical records and conducted active case finding in affected communities. We analyzed case data by person, place and time and assessed vaccination status of the case-patients. A cerebro spinal fluid (CSF) sample from one case-patient for laboratory analysis was collected and tested using standard gram staining procedure. **Results:** Between 1 September and 30 October 2017, 5 cases with 3 deaths (case fatality rate = 60%) occurred in Bunyangabu District. The mean age of case-patients was 4 years. Two sub-counties of Kabonero and Kateebwa were affected. Of the 5 case-patients, one (20%) had laboratory confirmation of meningococcal meningitis. One (20%) had proof of full vaccination with Pneumococcal Conjugate Vaccine, one (20%) was partially vaccinated and three (60%) had not received any vaccination. **Conclusion:** These were two unrelated clusters of meningococcal meningitis outbreak caused by *Neisseria meningitides*. We recommended that the Ministry of Health extends vaccination to susceptible sub-populations in districts outside the meningitis belt.

[&]CORRESPONDING AUTHOR
Birungi Doreen, Uganda Public Health Fellowship Program, Lourdel towers 4th Floor, Plot 1, Lourdel road, Nakasero, Kampala, Uganda
dbirungi@musph.ac.ug

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Introduction

Meningitis refers to acute inflammation of the meninges of the brain. Persons with acute meningitis present with a sudden onset of severe headache, fever, nausea, vomiting, nuchal rigidity and photophobia. Although it is caused by a number of infectious agents such as bacteria, fungi, viruses, parasites, and rickettsiae, bacteria are the commonest cause [1]. Most cases of post-neonatal meningitis are caused by three types of bacteria: *Streptococcus pneumoniae (S. pneumoniae), Neisseria meningitidis (N. meningitidis)*, and *Haemophilus influenza* type b. Of these types, *N. meningitides* and *S. pneumonia* are known to cause meningitis outbreaks. The mode of spread of the two organisms is by droplet infection from person to person and incubation period varies from 2 to 10 days [2].

Meningitis outbreaks periodically occur in the African meningitis belt causing thousands of deaths The meningitis belt of Sub-saharan Africa covers areas from the Sahel region and Northern Africa (Egypt, Morocco, Tunisia), Eastern Africa (The Democratic Republic of Congo, Kenya, Uganda and Tanzania) and Southern Africa (Angola, Malawi, Mozambique, Namibia, South Africa) [3] These regions are characterized by dusty winds and cold nights between December and June which facilitate the transmission of the disease. They thus experience high incidence and recurrence of meningitis outbreaks [4].

The greater northern part of Uganda lies in the meningitis belt of Sub-saharan Africa [5]. The most susceptible regions include West Nile, Acholi, Teso and Karamoja. As such, Uganda has had a number of meningococcal meningitis outbreaks previously documented. One of the largest outbreaks occurred in a refugee camp in the northern part of the country with more than 96,000 cases over 1 year and a case fatality rate of 13.3% [6,7]. Elsewhere in the meningitis belt in Africa, similar outbreaks have been recorded. For example, a large meningococcal outbreak occurred in West Africa in 2017 registering over 336 deaths [8].

On 13 November 2017, the Uganda Ministry of Health was notified of an unknown illness with sudden deaths of 3 children in Bunyangabu District, western Uganda. The case-patients presented with fever, convulsions, loss of consciousness, neck stiffness and headache. Following this alert, we set out to conduct an investigation to establish the cause and scope of the outbreak and to recommend evidence based preventive measures.

Methods

Setting

Bunyangabu District is located in Toro sub-region in Western Uganda **Figure 1**. It is bordered by Kabarole District to the North, Kamwenge District to the East, Kasese District to the South and Bundibugyo District to the West. Bunyangabu District was curved out of Kabarole district on 1st July, 2017 therefore, by the time of this investigation it was 3 months old. Bunyangabu District does not lie in the meningitis belt of Uganda. It has a total population of 170,247 [9].

Case-Definition and Case- Finding

We defined a suspected case as onset of fever, neck stiffness and any of the following: convulsions, loss of consciousness, headache, vomiting, nausea in a resident of Kabonero or Kateebwa sub-counties, Bunyangabu District from 1 September to 30 November, 2017.

We defined a confirmed case as a suspected case with laboratory confirmation of meningitis.

We conducted active community case finding with the assistance of the District Surveillance Focal Person and community health workers.

We carried out active case-finding in three villages of Kinyampanika A, Kinyampanika B and Kiganga. We reviewed health records in Rwagiba H/C III, Kateebwa H/C II, Godwin clinic, drug shops located in Kamutundu and Kitumba trading centres, Maranatha Children´s clinic, Virika Hospital and Fort Portal Regional Referral Hospital, where case-patients had reportedly attended. We conducted an environmental assessment in the schools and churches that the case patients attended. We visited two primary schools where the deceased children went to school in search of additional cases. We also assessed for proof of vaccination status for each of the case-patients using child health cards.

Descriptive epidemiology

We described case-patients by person, place, time, and clinical presentation, and calculated attack rates (AR) using populations of <15years in the affected villages based on the 2014 Uganda Population and Housing Census data.

We constructed case-cluster maps depicting the case-patients´ village centers using the village coordinates. We used an epidemic curve to describe the course of the outbreak. We constructed the start date by counting back the minimum incubation period (from the date of illness onset of the first case). To construct the end date, we counted back the maximum incubation period (from the date of illness onset of the last case-patient).

Laboratory investigation

At Virika hospital where one of the case-patients had been admitted, a sample of cerebrospinal fluid (CSF) was taken off by a medical officer using a lumbar puncture under aseptic conditions.

The CSF sample was centrifuged for 10 minutes. Using well mixed CSF sediment, a slide smear was prepared and the suspension was left to dry. The smear was fixed by flooding the slide with 95% methanol for 2 minutes and after rinsed with distilled water. The slide was flooded with gram´s iodine for 1 minute and using distilled water it was rinsed. It was then decolorized using 95% ethanol and rinsed with distilled water. Using carbol-fuchsin it was counterstained for 10 seconds and left to dry. The stained smear was then examined under a microscope.

Ethics approval and consent to participate

This investigation was in response to a public health emergency and was therefore determined to be non-research. The MoH gave the directive and approval to investigate this outbreak. The Office of the Associate Director for Science, Center for Global Health, CDC/Atlanta, also determined that this activity was not human subject research, and its primary intent was public health practice or a disease control activity (specifically, epidemic or endemic disease control activity). We sought permission to conduct the investigation from Bunyangabu District Health Office. Also, permission was sought from the health facility administrators to access data about the patients that had sought medical care from these facilities. We sought verbal informed consent in the local language from respondents (survivors, close relatives of the deceased, and local leaders). They were informed that their participation was voluntary and their refusal would not result in any negative consequences.

Availability of data and materials

Primary data was used to support the findings in this investigation. The dataset used during this investigation is available from the corresponding author on reasonable request.

Results

Descriptive epidemiology: A total of 5 case-patients with a mean age of 4 years (±2.5) were identified. Of these, two case patients were identified from active case search while three were identified from health records review. Three children died which translates into a case fatality rate (CFR) of 60%. Case-patients mainly presented with neck stiffness and fever **Figure 2**. Of the five cases recorded in this investigation, one was fully vaccinated with Pneumococcal Conjugate Vaccine, one was partially vaccinated and three had not received any vaccination. From environmental assessment, the outbreak occurred during the dry season of the year.

There were two clusters of cases in two sub-counties, one cluster with 3 cases from Kabonero sub-county and the other with 2 cases from Kateebwa sub-county **Figure 3**. Cases from each of the cluster were closely related. All the 3 cases from Kabonero Sub-county that died were first cousins **Table 1**. The two cases from Kateebwa Sub-county survived and were siblings. Of the three villages affected, Kinyampanika A village had the highest attack rate of 8.1 per 1000 population **Table 2**.

The first case was on 30-Sept-2017, and the next case was on 18-Oct-2017. Cases peaked on 28-Oct-17 and declined to zero thereafter **Figure 4**. The average time from development of symptoms to death was 2 days.

Laboratory findings: From laboratory investigations, gram negative diplococci were detected on gram staining of the CSF.

Discussion

These were two clusters of meningococcal meningitis that occurred in a district that is outside the known meningitis belt of Uganda. The CFR of this outbreak was higher compared to the previous outbreak that occurred in the meningitis belt of Uganda in 1994 [6]. This could be because there was a delay in providing appropriate management to case-patients considering that the average time from development of symptoms to seeking appropriate medical care was 2 days. If bacterial meningitis progresses rapidly, in 24 hours or less, death may occur in half of those that develop it. According to a study conducted among patients with community acquired meningitis showed that the mortality rate among patients that received inadequate antibiotic therapy within the first 24 hours from onset of symptoms was higher than among patients that received adequate treatment [10]. The highest level of a health facility in Bunyangabu is a health centre IV and was not admitting pediatric patients due to lack of a general ward. This led to a possible delay in managing case-patients as they had to seek medical care from a neighboring district. Meningococcal disease as was observed in this outbreak is potentially fatal and needs to be treated as a medical emergency.

In this outbreak, we identified two clusters of case-patients. However, there was no epidemiological link established between the clusters. The case-patients had not attended the same school, health facility or church or social gathering. It is documented that transmission of infection from person to person occurs through inhalation of droplets from the nasopharyngeal secretions by direct or indirect oral contact [11]. It is high likely that these case-patients being at a high risk could have acquired the infection from carriers within their surroundings. Up to 5%-10% of people may be asymptomatic carriers with nasopharyngeal colonization by *N. meningitides* [12]. The case - patients were children less than 5 years of age and not fully vaccinated. Only one case-patient had been fully immunized with three doses of Pneumococcal conjugate vaccine (PCV) which protects against *S. pneumonia* also known to cause meningitis outbreaks. Three of the case-patients had not been vaccinated while one case-patient had received one dose of PCV. A lack of vaccination could have led to the susceptibility of case-patients. It has been shown that persons at risk of meningitis include the unvaccinated and the immune compromised, malnourished, people of low socioeconomic status particularly those that live in overcrowded and poorly ventilated areas [13]. It mainly affects young people between ages 1-30 years, occurring sporadically and in small outbreaks worldwide.

Efforts have been put in place to control the disease through use of meningococcal and pneumococcal conjugate vaccine in the African Meningitis belt [14]. However, Uganda has not yet introduced meningococcal vaccine in the routine schedule. Massive vaccination in Uganda with Men A (MenAfriVac) conjugate vaccine was conducted in 2016 and was prioritized for some areas in the meningitis belt, that is Northern Uganda. Bunyangabu District was not considered to be among the high-risk districts and therefore there was no vaccination conducted. However, there is a high possibility that the meningitis belt could have extended to the South Western parts of Uganda due to various reasons. Areas that experience prolonged dry seasons and low humidity are at a great risk of epidemics[5]. Bunyangabu District lies in the great lakes region and is near Bundibugyo District and Eastern part of the Democratic Republic of Congo which are known to experience outbreaks. Mass vaccination helps in control of epidemics. For example, in Nigeria where there was mass vaccination, there has been a reduction in the number of reported cases [15].

Countries that are within the meningitis belt should conduct continuous surveillance for meningitis outbreaks and extend meningitis vaccination activities in areas outside the belt especially in the susceptible sub-population groups such as children less than five years.

Limitations

A limitation of the investigation is that only one CSF sample was collected from one case-patient and tested. We were unable to collect CSF samples for confirmation from the other case-patients because two of them were in critical condition and so a

lumbar puncture was contraindicated, while the other two had started antibiotic treatment and had considerably recovered. This limitation notwithstanding, efforts were made to conduct thorough case-finding with the help of district community health workers for additional cases in the district.

Conclusion

This was an outbreak of meningococcal meningitis caused by *Neisseria meningitides* with two unrelated clusters of meningitis cases. Most of the affected children were not vaccinated against meningitis. We recommended immunization of the children and young adults for *Neisseria meningitides*. Persons who had been in close contact with the patients were started on prophylaxis treatment to eradicate meningococcal carriage.

Enhanced surveillance following meningitis outbreaks and timely management of meningitis decreases the magnitude of the outbreak. We recommended strengthening of health systems in newly created districts to be able to handle emergencies for all age groups.

What is known about this topic

- Meningitis outbreaks periodically occur in the African meningitis belt causing thousands of deaths.
- Up to 5%-10% of people may be asymptomatic carriers with nasopharyngeal colonization by N. meningitidis.

What this study adds

- Meningococcal meningitis occurred in a district that is outside the known meningitis belt of Uganda.
- There should be a consideration of vaccination of susceptible sub-population in areas outside the known meningitis belt.

Competing interests

The authors declare no competing interests.

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Authors' contributions

All authors contributed substantially to the write-up and review of the manuscript. DB wrote the drafts of the manuscript and revised the paper for substantial intellectual content. MN participated in the outbreak investigation and reviewed the paper for substantial intellectual content. BW participated in the outbreak investigation and revised the paper for substantial intellectual content. SNK participated in supervision of the outbreak investigation and reviewed the draft manuscript for substantial intellectual content. ARA was involved in the review of the paper for substantial intellectual content. All the authors read and approved the final version of the manuscript.

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Tables and figures

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Figure 4: Epi-curve showing the case-patients of meningitis in Bunyangabu District, September-October, 2017

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Table 1: Case Fatality Rate of Meningitis per village in Bunyangabu District, September-October, 2017

Sub-county	Village	No. of cases	No. of deaths	CFR
Kabonero	Kinyampanika A	2	2	100
	Kinyampanika B	1	1	100
Kateebwa	Kiganga	2	0	0

Table 2: Attack Rate by village among meningitis case-patients in Bunyangabu District, September-October, 2017

Village	No. of cases	Population (< 15years)	AR/1000
Kinyampanika A	2	247	8.1
Kinyampanika B	1	190	5.3
Kiganga	2	390	5.2

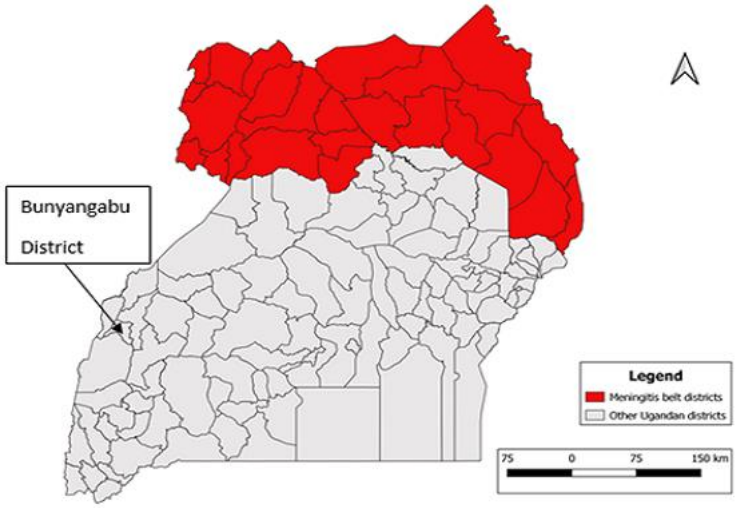

Figure 1: Map showing the location of Bunyangabu District and the Meningitis belt of Uganda

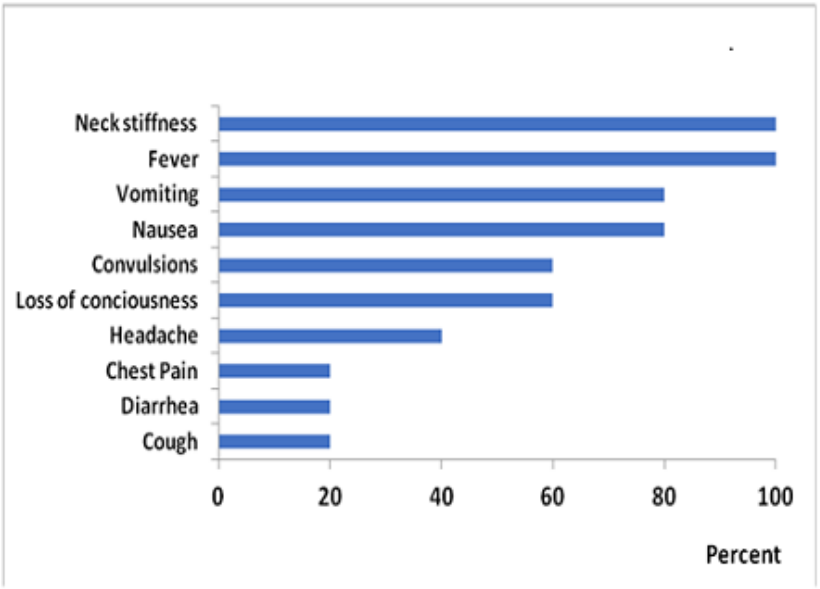

Figure 2: Distribution of symptoms among meningitis case-patients in Bunyangabu District, September-October, 2017

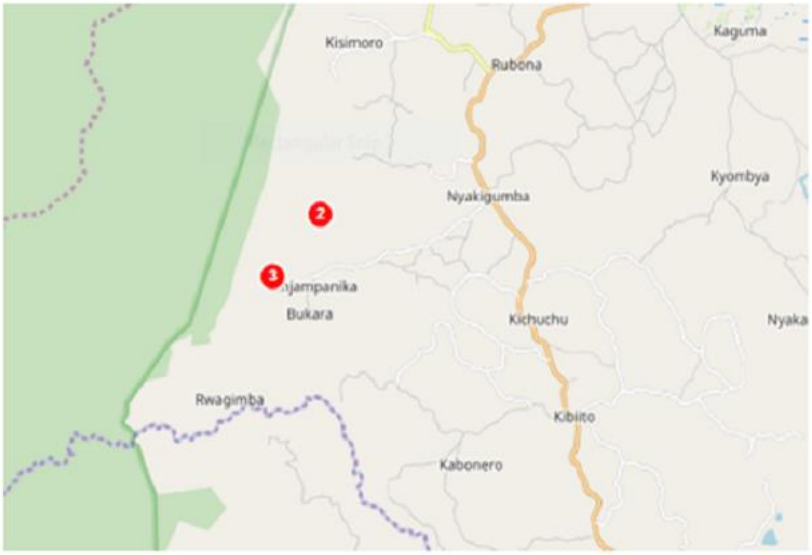

Figure 3: A case cluster-map showing distribution of meningitis case-patients in Bunyangabu District, September-October, 2017

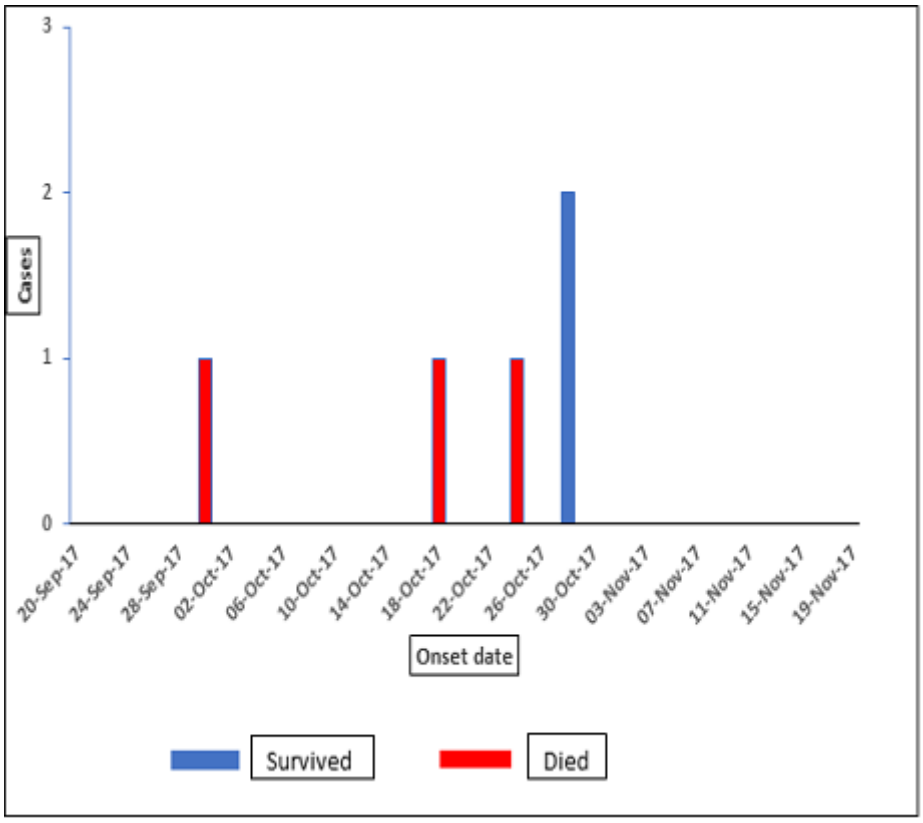

Figure 4: Epi-curve showing the case-patients of meningitis in Bunyangabu District, September-October, 2017