On 6th July 2015, the Zambian Ministry of Health received reports of cases of meningococcal meningitis (MM) at a boarding school in Kabompo District. MM is caused by Neisseria meningitidis. We investigated the outbreak to describe epidemiological characteristics, confirmed aetiology, and determined potential risk factors. We reviewed medical records for six reported suspected cases of MM. Cerebrospinal fluid from patients was analysed for presence of N. meningitidis. We interviewed patients, and compared occupancy level against available bed space. A suspected case was a student with fever ≥38°C and headache, neck stiffness, or altered consciousness from 20th June – 17th July. A probable case was a suspected case who was a close contact of a confirmed case. A confirmed case was a suspected or probable case with N. meningitidis detected in CSF. All six case-patients were boarders aged 14-21 years. Three case-patients died. Overall school attack rate was 0.9% (6/683); 1.4% (6/443) among boarders. Clinical characteristics included: headache, fever, neck stiffness, vomiting, coma, and confusion. N. meningitidis serogroup W135 was detected in two cases. Two dormitories had >100% occupancy.

Continued surveillance, health education, and potential vaccination of boarding students should be considered. Crowding may have contributed to the outbreak.

Introduction

Meningococcal meningitis (MM) is a bacterial infection of the meninges caused by Neisseria meningitidis, and transmitted from person to person. Meningococci are classified according to serologic typing based on the biochemical composition of the capsular polysaccharide. There are six serogroups (A, B, C, W-135, X, and Y) that are known to cause almost all worldwide life-threatening disease. Patients often present with fever, rash, meningeal signs (headache, stiff neck) and, altered mental status.
MM is fatal in approximately 50% of cases if appropriate treatment is delayed [1 -3]. The Zambian Ministry of Health has prioritized MM as a notifiable disease reported in the Integrated Disease Surveillance and Response (IDSR) [4]. The literature reveals two documented community-based MM outbreaks among children in Zambia: one in 1974-75 in Kitwe, and another in 1992 in Lusaka [5]. In both outbreaks, children and young adults <30 years old were the most affected. Another commonality in both outbreaks was overcrowding. The Kitwe outbreak was attributed to overcrowding, and similarly almost 90% of cases presenting at University Teaching Hospital (UTH) came from highly populated areas of Lusaka [5]. Although no prior literature was found on MM cases at colleges or boarding schools in Zambia, students at educational facilities are known to be at increased risk for meningitis due to close social interactions [1,6].

Outbreak
On 6th July, 2015 the directorate of Disease Surveillance Control & Research (DSCR), Ministry of Health of Zambia, received notification from Kabompo District Community Medical Office (DCMO) of six suspected cases of MM, including three deaths. Cases were reported through IDSR from facility to the DCMO. The sudden deaths reported from 20th June through 3rd July, 2015 from Kabompo Secondary School in Kabompo district caused the community to panic and accused the headmaster of inciting witchcraft. They then vandalized the boarding school, breaking window panes and doors, causing the student body to vacate the premises out of fear.

The Ministry of Health assembled an investigation team to support the Kabompo District response to the outbreak. The team included ZFETP residents, an epidemiologist, and an infectious disease specialist. The team travelled to Kabompo District on 12th July 2015 to assist other health professionals already at the scene.

The team investigated the outbreak to describe the epidemiological characteristics, confirm the aetiology of the outbreak, and to generate hypotheses for MM risk factors.

Methods
This was a retrospective descriptive study based on data extracted from medical records of students from Kabompo Secondary School who were admitted at Kabompo District Hospital between 20th June and 17th July 2015. Kabompo District Hospital is a 1st level hospital offering preventive, promotive, and curative services. Kabompo district is in North Western Province of Zambia, and is 1,267 km from the capital city Lusaka. The
cases were reported through the IDSR weekly reporting. The six case-patients were students from a district boarding school with 683 registered students, of which 443 were boarders, and 240 were day-students. The boarders lived in seven dormitories where they either shared bunk beds, or slept on mattresses on the floor.

Case definitions

We defined a suspected case as acute onset of fever (≥38°C) and one of the following signs: headache, neck stiffness, or altered consciousness from 20th June – 17th July 2015 in any student or close contact to a student of Kabompo Secondary School. A probable case was a suspected case that was epidemiologically linked to another clinically compatible case, but did not have laboratory confirmation. A confirmed case was defined as a suspected or probable case confirmed by identification of the causal pathogen (Neisseria meningitidis) from CSF.

Data and laboratory specimen collection

We reviewed the medical records for the six reported cases for symptoms, date of disease onset, hostel of residence, and laboratory specimen collected. We interviewed two discharged patients from their homes using a structured questionnaire to capture exposure history. Additionally, we visited all seven school dormitories where we observed, and recorded bed space allocation, and compared it to the number of students living in each dormitory. We also spoke to school officials about general conditions, and policies regarding boarding and off-campus populations.

Prior to the arrival of the investigative team, a senior resident medical officer collected one CSF and five blood specimens from six students with suspected MM who were hospitalized at Kabompo District Hospital. Malaria test by Giemsa staining was performed on four out of five blood specimens, and one out of five was performed by Rapid Diagnostic Test (RDT) SD Bioline.

Due to lack of culture facility and specific transport medium for CSF (trans Isolate) at the district laboratory, two smears were prepared from 1–2 mLs of CSF, which was collected in one plain tube container. The dried smears and the remaining portion of the CSF in the container were packed according to guidelines outlined in World Health Organization Laboratory Biosafety Manual of 2004 [7]. The specimens were shipped from Kabompo district to Solwezi General Hospital, a level 2 hospital, for Gram staining and culture. Four days later the same CSF
sample was then sent to the national reference laboratory at University Teaching Hospital (UTH) in Lusaka for serotyping. One other CSF specimen was collected upon admission at UTH from a student who discharged himself from Kabompo hospital against medical advice. At UTH, CSF processing for cell count and Gram staining was carried out following standard microbiological methods [8,9,10]. Inoculated Mac Conkey agar plates were incubated overnight at 37°C in aerobic atmosphere, while blood and chocolate agar plates (Oxoid – UK) were incubated at 37°C in 5% carbon dioxide (CO2) [11,9]. Detection of soluble antigens and identification of Neisseria meningitidis was performed using Pastorex™ Meningitis complete kit (Bio-Rad) whose sensitivity is 100% and specificity of about 97 – 100% . The testing was done following manufacturer’s instruction [12]. Chemical composition of the CSF was measured using Cobas Integra 400 plus chemistry analyzer (Roche Diagnostics).

Data analysis
The data obtained from the record review, questionnaires, and laboratory results were entered into Epi Info version 7 to calculate attack rates for the general school population and boarders.

Ethical considerations
Zambia has a waiver for ethical approval of outbreak investigations under the Ministry of Health’s directorate of DSCR. However, oral consent was obtained from the patients interviewed after explaining to them that participation was voluntary and their identifying information would remain confidential. Oral permission was also sought from the hospital administration to review the patients’ medical records.

Results
Epidemiological results
Six cases of MM occurred during an outbreak in Kabompo District Boarding School, between 20th June and 17th July 2015. Three deaths occurred (one male, two females),
resulting in a case fatality rate of 50%. The overall school population attack rate was 0.9% (6/683), and all case-patients were boarding students, with an attack rate of 1.4% (6/443). The age of the case-patients ranged from 14 to 21 years, with a mean of 16.3 years. Four (67%) of the six case-patients were male (Table 1). Clinical characteristics included headache, fever, neck stiffness, vomiting, comatose, and confusion (Table 1).

All six cases were admitted to Kabompo District Hospital and treated with intravenous gentamycin and benzyl penicillin, chloramphenicol and erythromycin, and some were treated with antimalarial.

Cases occurred between 20-29 June, 2015 (Figure 1). The first case-patient presented to Kabompo hospital on 20\textsuperscript{th} June 2015 around 03.45hrs and the second case on the same date later in the day 2015. Four days after the third and fourth cases, two more case-patients were seen on the 30\textsuperscript{th} June (fifth case) and the 3\textsuperscript{rd} of July (sixth case) (Figure 1)

Environmental results

Two dormitories had greater than 100% occupancy, and all cases were in the 3 dormitories with the highest occupancies (Table 2). One dormitory had 72 sleeping spaces occupied by 100 students (139% occupancy), where all sleeping spaces were mattresses on the floor. In all other dormitories, the students slept in bunk beds (one per bunk bed)

Laboratory results

Two CSF samples (3\textsuperscript{rd} and 4\textsuperscript{th} cases) were positive for \textit{Neisseria meningitidis} serotype W135 with the Pastorex™ Meningitis kit.

Both CSFs were clear colourless on macroscopic examination, and no polymorphonuclear cells were seen upon microscopic examination of stained Gram smears prepared directly from the specimens. There was no growth of any bacteria after 24 to 48 hours incubation. One CSF sample that was sent for chemistry analysis showed elevated protein levels 0.59g/L (Ref range:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
</tr>
<tr>
<td>Deaths</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
</tr>
<tr>
<td>Age group in years</td>
<td>Count</td>
</tr>
<tr>
<td>10 – 14</td>
<td>1</td>
</tr>
<tr>
<td>15 – 20</td>
<td>5</td>
</tr>
<tr>
<td>Class</td>
<td></td>
</tr>
<tr>
<td>9\textsuperscript{th}</td>
<td>1</td>
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<tr>
<td>10\textsuperscript{th}</td>
<td>2</td>
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<tr>
<td>11\textsuperscript{th}</td>
<td>1</td>
</tr>
<tr>
<td>12\textsuperscript{th}</td>
<td>2</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>6</td>
</tr>
<tr>
<td>Fever \geq 38 C</td>
<td>4</td>
</tr>
<tr>
<td>Neck stiffness</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
</tr>
<tr>
<td>Confusion</td>
<td>2</td>
</tr>
<tr>
<td>Laboratory results</td>
<td></td>
</tr>
<tr>
<td>CSF positive for \textit{Neisseria meningitidis} W135</td>
<td>2</td>
</tr>
<tr>
<td>Malaria positive by Giemsa stain thick smear</td>
<td>3</td>
</tr>
<tr>
<td>Malaria positive by \textit{BD} IMF method</td>
<td>1</td>
</tr>
</tbody>
</table>
0.20-0.4 g/L), low glucose levels 1.83 mmol/L (Ref range: 2.20-4.20 mmol/L) while chloride was within the reference range 122.0 mmol/L (Ref range: 120-130 mmol/L). Three out of five (60%) blood slides examined for malaria parasites were positive.

Discussion
At the time of this investigation, there was no prior description of a MM outbreak in a boarding school in Zambia. Reports in other countries have documented the increased risk of MM among boarding schools where students live in close proximity, and are therefore more vulnerable to the spread of infectious disease [1, 6]. Because this outbreak was located at a secondary boarding school, the age distribution of cases was higher (mean age of cases was 16.3 years) than in prior community-based outbreaks in Zambia and other countries where more infants and young children were affected [5, 3, 13]. All six cases were among boarding students, as opposed to day students, and it appears that being a boarder may have been a risk factor for developing MM, although this was not statistically evaluated. MM is typically spread via droplets, long periods and close social interactions, and living in crowded conditions may increase the risk of transmission of MM [17, 2].

The school’s student housing policy stated that 75% of the school population should be boarders, and at the time of the outbreak, only 65% (443/683) of the school population were boarders. Although the school was not at maximum boarder capacity, overcrowding did occur in two dormitories. Because the school’s housing policy grouped students by grade and gender, students were distributed unevenly in dormitories, and the junior girls located in Dormitory A was at 139% of its maximum occupancy (Table 2). All six cases from this outbreak were housed in overcrowded or near-crowded hostels, and two of the three deaths occurred in Dormitory A (Table 2).

<table>
<thead>
<tr>
<th>Dormitory</th>
<th>Sleeping capacity</th>
<th>Sleeping arrangements</th>
<th>Occupancy A of students in dormitory</th>
<th>Occupancy %</th>
<th>Case (s)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>A - Girls</td>
<td>72</td>
<td>Mattresses on the floor</td>
<td>100</td>
<td>139</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>B - Boys</td>
<td>50</td>
<td>Bunk beds</td>
<td>71</td>
<td>90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C - Girls</td>
<td>50</td>
<td>Bunk beds</td>
<td>41</td>
<td>50</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F - Girls</td>
<td>72</td>
<td>Bunk beds</td>
<td>81</td>
<td>101</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

Feasible capacity standards as provided by Sub-moPH (Boarding 1/100)
Another case-patient discharged himself from the district hospital against medical advice, so that he could stay with his parents in Lusaka. The parents brought this case-patient to the national reference hospital because he continued to suffer from his symptoms.

This outbreak exemplifies several challenges in diagnosis and microbiologic confirmation of outbreaks in rural Zambia. First, only one CSF specimen tube was collected at Kabompo district hospital, instead of the recommended 2-3 tubes according to MoH standard operating procedures for hospital laboratories [10]. The district hospital had no capacity to perform the necessary microbiology procedures, thus the CSF specimen was transported to a level 2 hospital 365 km away, arriving more than 13 hours after collection, without appropriate transfer medium. Finally, the level 2 hospital received the sample, refrigerated it overnight, and did not process it until more than 12 hours after receipt. All of these non-adherences to standard protocol made it unlikely that organisms would have survived to be cultured.

Among the five specimens tested for malaria, four specimens tested positive, including one death in a case-patient who did not have a lumbar puncture done. All the cases were treated with antimalarial combined with one or two antibiotics. The recommended treatment for MM include ceftriaxone or penicillin (five-day course) given parenterally with oral rifampicin or ciprofloxacin upon discharge to ensure elimination of organisms from the nasopharynx [3]. In this outbreak, only three out of six (50%) patients were treated with penicillin. The rest were treated with gentamycin, erythromycin and chloramphenicol, but none were given rifampicin or ciprofloxacin upon discharge. The fact that a lumbar puncture was not done on all the cases to identify MM also indicates a diagnostic problem.

According to Zambian Ministry of Health Malaria treatment guidelines, combining malaria treatment with antibiotics is a recommended regimen for severe diseases [15]. Although health workers at Kabompo District Hospital adhered to the country’s treatment protocol, they should have also been aware of the possibility of co-infection in patients presenting with fever. A delay in diagnosis, and treatment of bacterial co-infections with appropriate antibiotics, can result in poor outcomes [16].

This outbreak investigation has limitations in completeness and generalizability. None of the six cases were available for interview or
medical examination by the investigating team because half had died (3), and the rest had returned to their homes outside of the district. Thus, the investigators relied on medical records, which often had missing and incomplete laboratory data, to classify the cases. Second, the small size of this outbreak limited our ability to identify, and quantitatively analyze risk factors for developing MM. Third, only two CSF specimens were collected and analyzed, and although both were positive for \textit{Neisseria meningitidis}, we cannot exclude the possibility that the other four cases might have been misdiagnosed as MM. Finally, we were also limited in pursuing a broader community investigation of the source of infection, and identifying potential additional cases due to the heightened public anxiety around sudden student deaths, vandalization, and subsequent school closure.

\textit{Recommendations and Conclusions}

One does not have to wait for future outbreaks and fatalities to consider implementing preventative public health interventions for MM among boarding schools. First, there is need for enhanced surveillance by school authorities and local hospital staff to regularly screen boarding school students, and to identify early signs and symptoms of MM. Health workers should not assume malaria to be the final diagnosis for all fevers, and should be re-oriented to the treatment guidelines for malaria. The DCMO should create an emergency response plan to control the spread in a future outbreak, by giving prophylaxis to close contacts of cases. Students should be annually sensitized to the causes and risk factors for MM to avoid fear and panic in the event of a future outbreak. Given the known association of MM with student living in dormitories, personal hygiene education including cough etiquette should also be encouraged in order to reduce MM transmission. School authorities should review hostel conditions and better utilize their existing dormitory space for girls to make sure overcrowding will not exacerbate transmission.

Although there is not enough data in this outbreak investigation to analytically determine whether crowding in dormitories was a key risk factor, future research should examine crowding in closed settings as a transmissibility factor. Additional research is required to develop appropriate strategies to prevent and control this highly infectious disease.

In the long term, the Zambian government should strengthen continued surveillance in order to detect, understand, and predict the
changes in the epidemiology of meningococcal diseases and consider prioritizing boarding students for vaccination against MM. This precaution has been taken in other countries and would greatly reduce the risk of MM among boarding students in Zambia [17]. In addition, diagnostic microbiology capacity must be built in rural laboratories to enable quick confirmation of disease, so that appropriate treatment can be administered as soon as possible.

**Authors’ contributions**

Loveness Moonde, Ernest Kateule, Dr Muzala and Dr Malama were involved in conceptualization and design of the study, data collection and drafting/finalization of manuscript. Loveness Moonde, Ramya Kumar were involved in analysis, interpretation, and finalization of the manuscript. Rene Kapinga contributed on laboratory tests done on the cases at Kabompo District Hospital John. Mwaba contributed to laboratory analysis done at UTH. All authors have read and agreed to the final version of this manuscript and have equally contributed to its content.

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**Competing interests**

The authors declare no competing interests.

**CDC authorship disclaimer**: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centres for Disease Control and Prevention
References


