Original Article

Uncommon mixed outbreak of pneumococcal and meningococcal meningitis in Jirapa District, Upper West Region, Ghana, 2016

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Ghana Med J 2017; 51(4): 149-155 DOI: http://dx.doi.org/10.4314/gmj.v51i4.2

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Conflict of interest: None declared

SUMMARY

Objective: The Jirapa District in Ghana falls within the African meningitis belt where over 500 million people are at risk of epidemic meningitis. The district suffered an outbreak of Neisseria meningitides, W (NMW) in 2012 and a mixed outbreak of Streptococcus pneumonia and NMW in early 2016. We investigated the outbreak to identify the source, causative agents, and magnitude and assess health facility preparedness and propose control measures.

Design and Setting: We conducted a descriptive study in all sub-districts of Jirapa, between 28th February to10th April 2016. We reviewed records at health facilities, assessed health facility preparedness, searched for cases, traced contacts of case to administer chemoprophylaxis and collect CSF for laboratory analysis. Data were entered in Microsoft excel cleaned, and exported to stata-13 for analysis by person place and time.

Results: A total 233 meningitis cases were reported with mean age of 22.4years and standard deviation 21.6. Males were (57%), females (43%) and 60.8% were less than 19 years. Attack rate of meningitis was 214/100,000 with case fatality rate (CFR) of 12.4% (29/233). Causative agents were NMW (69.5%) and streptococcus pneumonia (27.1%), mainly serotype STN1 and H. influenza (3.4%). The index case had travel history to dollar power, close to Tain District which is the epicentre for the 2016 meningitis outbreak in Ghana.

Conclusion: The Jirapa district experienced a mixed outbreak of streptococcal and meningococcal meningitis in early 2016, facilitated by migration. Active surveillance and mass vaccination with multivalent vaccines is required to protect the population.

Funding: Ghana Field Epidemiology and Laboratory Training Programme (GFELTP)

Keywords: Meningitis, outbreak, surveillance, Jirapa, CSF

INTRODUCTION

The upper west region of Ghana falls within the African meningitis belt where over 500 million people are at risk of meningitis thus making the region prone to outbreaks of the disease.[1,2] Epidemic meningitis continues to be a major public health problem in the extended African meningitis belt which comprises 26 countries stretching from Ethiopia in east Africa to Senegal in the west.[3] It has been observed that climate changes are affecting the areas that fall under this belt with meningitis outbreaks been reported in areas that were not part of this belt.

Ghana recorded a major outbreak in 1997 in which 18,703 cases and 1356 deaths were reported in the three northern regions.[4]

In 2010 the Jirapa District and other parts of the Region experienced an outbreak of meningitis caused by *N meningitides* Y/W135 (NMW) Species. The disease is an inflammation of the brain and spinal cord coverings (Meninges) caused by microorganisms (Bacteria, parasites, viruses and fungi). It can also be caused by non-infectious agents including toxins, drugs and trauma.

Meningitis is characterized by symptoms ranging from fever, headache, neck stiffness, photophobia, muscle pains to vomiting and diarrhoea. Long term effects (sequelae) of meningitis include loss of hearing, brain damage, learning disability and seizures among others.[5]

Bacterial meningitis is caused mainly by *Neisseria* and *Streptococcus* species. However other bacteria can also cause the disease and causative agents vary with age and immune status. *Haemophilus influenzae* type b, Group B streptococci and *E. coli* are among agents of meningitis especially among children. Echoviruses, coxsackie viruses and fungi such as *Cryptococcus* are also known to cause meningitis.[6]

Out of twelve (12) serotypes of *N. meningitidis* known to cause meningitis, six of them are associated with epidemics. These are serotypes, A, B, C, X, Y and W135/MNW.[3] Transmission of the disease is mainly by direct person to person contact, through inhaling air droplets with infectious agents from infected persons via sneezing, coughing, talking and kissing.[3] About 5-20% of some populations are carriers of N. meningitis who serve as sources of infection.[1,6,7]

About 10% of all bacterial meningitis results in death, however case fatality rates (CFR) for meningitis resulting from *Streptococcus pneumoniae* infections could be as high as 44%.[8] About 10% patients infected with streptococcus pneumonia who receive effective antibiotics and intensive care still die.[3] Factors that can increase a person's risk of bacterial meningitis include: age, community setting, other medical conditions, working with meningitis causative agents and travel to meningitis endemic/epidemic areas.

Prevention and control: key strategies for control are vaccination, public education and early diagnosis and treatment as well as continuous surveillance. Three major types of vaccines targeting various causative agents of bacterial meningitis are available for prevention. They include meningococcal A conjugate vaccine, C conjugate vaccines, tetravalent A, C, Y and W135 conjugate vaccines.

Meningococcal polysaccharide vaccines have all also been shown to be effective and immunogenic among adults and children above 2years.[9] Polysaccharide vaccines can however not be developed for group streptococci due to antigenic mimicry with polysaccharides in humans neurologic tissues.[1] As a result of this antigenic mimicry, scientist have resorted to the use of outer membrane protein (OMP) vaccines for prevention of Group B streptococcal meningitis. A new meningococcal conjugate vaccine, Men A which was introduced in 2010 with mass vaccinations among of people aged 1- 29 years in many African countries accounts for the drastic reduction in cases of Meningitidis A within the African meningitis belt.[3,10] This vaccine which is reported to have several advantages including being effective among children under two years, less expensive and able to reduce meningococcal carriage in vaccinated populations.[3]

Penicillin, Ceftriaxone Ciprofloxacin, Rifampicin, Gentamicin are antibiotic that are commonly used for treatment and prophylaxis. Other preventive measure includes respiratory isolation of cases for 24 hour following commencement of treatment and tracing of contacts.[6,11]

The Jirapa District as part of integrated disease surveillance trained key staff, in the district on meningitis surveillance and case management prior to the beginning of the meningitis season. This led to high index of suspicion and all persons with suspected meningitis were screened. On the 28th of December 2015, a 22-year-old male from Jeffere, Kandieyiri a farming community, reported to the St Joseph's hospital in Jirapa with symptoms of meningitis. Medical staff suspected meningitis and performed lumber puncture to collect CSF for Laboratory testing, the results were positive.

Surveillance officers in the Jirapa District reported the first laboratory confirmed case of meningitis (Streptococcus pneumonia) for 2016 on 28th December. The District Health Management Team (DHMT) continued to monitor the situation in the District using the 2015 WHO revised standard operating procedure for epidemic meningitis.[11] The District reached an alert thresh hold when it reported 9 suspected cases and confirmed three (3) of them in the second epidemiological reporting week of 2016. This threshold was reached based on the current projected population of the district (98,700)[12] and the 2015 WHO standard operating procedures for meningitis surveillance.[13] In the seventh week of 2016 the Jirapa District reached the epidemic threshold when it reported 30 suspected meningitis cases and confirmed 10 of them with laboratory test. As of 16th February 2016, 96 suspected cases of meningitis were reported and 26 were confirmed. Two main agents *N. meningitides* W135 and *Streptococcus pneumoniae* were isolated.

A team of public health officials from the Ghana Field Epidemiology and Laboratory Training program (GFELTP) and a Joint team of Regional and District Public Health Officials investigated the outbreak to: Identify the source and causative agent(s), determine the

geographical spread, assess health facility preparedness, and propose measure to control the outbreak.

METHODS

Study design

We conducted a descriptive epidemiological study, by reviewing records, defining cases and conducting cases search as well conducting interviews with health staff and patients. Health records at the St. Joseph's Hospital in Jirapa and Jirapa District Health Directorate were reviewed to identify all reported cases of meningitis in the district between December 2015 and April 2016. We also assessed health facility preparedness using a check list.

Study area

The outbreak investigation was conducted in Jirapa District of the Upper West Region of Ghana between 23rd February and 20th April 2016. The region is located in northwest Ghana (longitude 1º 25'' W and 2º 45'' and latitudes 9º 30'' N and 11ºN) and falls within the African meningitis belt. The District just like the rest of the region experiences a short raining season from June to October, followed by a long hot dry season from November to May. Maximum temperature is 22ºC in the raining season and up to 40ºC in the dry season. Humidity is typically between 70% to 90% in the raining season but can fall as low as 20% in the dry season[14] which make the district prone to meningitis outbreaks. The projected population of the District is approximately 98,700[12]. The district shares boundaries with Lawra, Lambusie-Karni, Nadowli- Kaleo, Sisala East and Dafiama-Busie- Issah Districts.

Participants

Cases definition and case search

We formulated a surveillance case definition and used it to search for cases. We defined meningitis case as follows:

Suspected case*:* Any person with sudden onset of fever (>38.5ºC rectal or38.0ºC axillary) and one of the following signs: neck stiffness, altered consciousness or other meningeal signs and photophobia. In babies a bulging fontanel.

Probable Case**:** A suspected case as define above with turbid CSF confirmed by a clinician and a positive gram stain result

Confirmed case: A suspected case confirmed by isolation of *N. meningitides or Streptococcus pneumonia, H. Influenza* or any other agent of meningitis.

Based on the working definition, we searched new cases in health facilities and traced their contacts in communities. We continued line listing of cases and contact tracing. All close contacts of meningitis cases were given Ciprofloxacin as chemoprophylaxis.

Health facilities were also assessed using a structured questionnaire and check list. We asked for presence of epidemic management team, displayed definitions, evidence of staff training, interventions for case management and availability of logistics and laboratory capacity.

CSF collection and laboratory testing

Cerebrospinal fluid (CSF) samples were collected at Jirapa Hospital into sterile cryo vials (tubes), (Greiner Bio-ine GmbH- Germany), tested by gram stain, culture, and serology (Pastorex, BIORAD- France and Wellcogen TM M. meningitidis ACY W135, REMEL Europe Ltd, UK.) at the Jirapa hospital Laboratory and later transported to the Public Health Reference Laboratory in Tamale for PCR.

Data Analysis

Line list of cases was entered into Microsoft Excel 2013, cleaned and exported to Stata software, Version 13, (Texas, USA) for analysis. Data was analysed by person place and time to show age and sex groups, cases by sub-districts and time trends in the form of an epicure. We also calculated attack rates and case fatality rates. Laboratory results were presented as frequencies and percentages.

Ethical issues

This was an outbreak situation and no formal clearance was obtained from an institutional review board, however permission was obtained from the Ghana Health Service regional and district health directorates.

RESULTS

General Characteristics of meningitis cases

A total of 233 cases of suspected meningitis were reported in the Jirapa district of the upper west region of Ghana between December 28th 2015 and April 10th 2016. Males were 133(57%) while females were 100 (43 %). The mean age of cases was 22.4 years with a standard deviation of 21.6 years. Ages of cases ranged from 0.04 years (two weeks) to 87 years. Children below five years were most affected constituting 23.9 % of all cases, and those between 10 and 19 years (23.9%) of the total cases. Up to 60.8% of all the cases were less than 20 years (Figure 1). Out 233 cases 29 people died from meningitis representing a cases fatality rate of 12.4%. The attack rate of meningitis in the District is 214/100,000.

Causative Agent and Laboratory Findings

Out of 233 CSF samples collected, gram staining results were available for 232(99.6%). Out of 232, 21 (8.6%)

were gram positive cocci presumptively identified as Streptococcus pneumonia, 50 (21.6) were gram negative cocci and 162 (69.8%) did not show any organism. Overall, 70 out 232 (30.1%) of CSF samples tested by gram technique were positive.

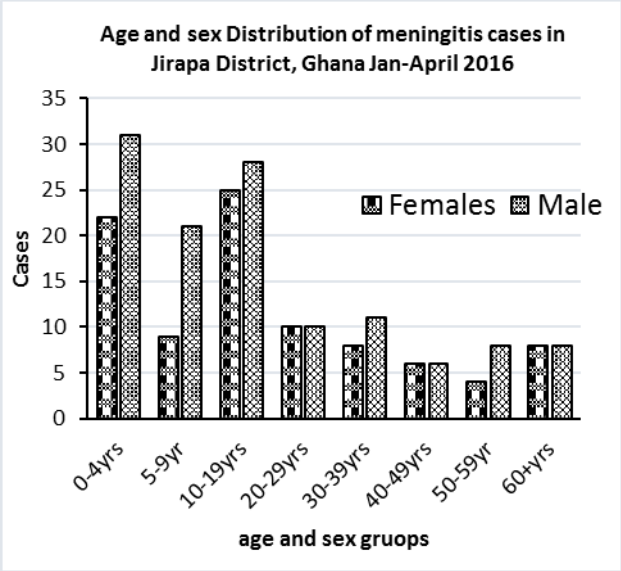

Figure 1 Age and Sex Distribution of Meningitis cases, Jirapa District Upper West Region, Ghana, Jan-April 2016

Two key Pathogens were isolated from CSF samples collected from suspected meningitis cases; *Streptococcus pneumoniae* and *Neisseria meningitides*. There was a case of *N. meningitidis* A. One person had a mixed infection with *N. Meningitides* W and *Streptococcus pneumonia* and died. All CSF samples were tested by gram stain, culture, serology (Pastorex BIORAD- France) in Jirapa hospital Laboratory and later transported to the special meningitis Laboratory in Tamale for PCR. Lumber puncture rate was 100% and 73/233 (31.3%) CSF tested positive for meningitis.

A total of 150 CSF sample from suspected meningitis cases collected from four Districts in the region including 102 (68%) from Jirapa District were transported to the Public health Reference laboratory in Tamale for PCR testing. Fifty-nine (39.3%) were confirmed and serotyped as follows:Out of the 59 PCR isolates 18 (31%) were *Streptococcus pneumoniae* and 41(69%) were *Neisseria meningitides* W 135.

Source of Outbreak

The index case was identified as a 22-year-old male from Jeffere, Kandieyiri who reported to the St. Joseph's Hospital Jirapa hospital 28th December 2015. Cerebrospinal fluid was collected from the patient and sent to the laboratory for testing the same day. Gram positive diplococci was isolated and finally identified as *Streptococcus pneumoniae*. He had a travel history and was reported to have returned from a popular surface mining site called "Dollar Power" in the south-western part of Northern region which shares boundary with Tain district in the Brong Ahafo region which is the epicentre for the 2016 meningitis outbreak in Ghana.

Magnitude and geographical spread of Cases

A total of 233 cases were reported in the district within the period, with 212/233(90.9%) and of them resident in the District, while 21 (9.1%) were from other districts. Out 233 cases 29 people died from meningitis representing a cases fatality rate of 12.4%. The attack rate of meningitis in the District is 214/100,000. Pathogen specific attack rates were 51.4/100,000 population for *N. meningitides* and 21.6/100,000 populations for *Streptococcus pneumonia*. Cases were reported from all sub-districts, however Jirapa Urban-Tizza sub district contributed 130 (55.7%) of total reported cases. Out of fifty cases with confirmed Neisseria Meningitides ten died (10/50) representing a case fatality rate of 20%. Streptococcus Pneumonia was isolated from 20 patients and six of them died giving a CFR of 30%. Cases were reported from all sub-districts within the region and also from other Districts in the region, however most cases were from Jirapa urban (Figure 2).

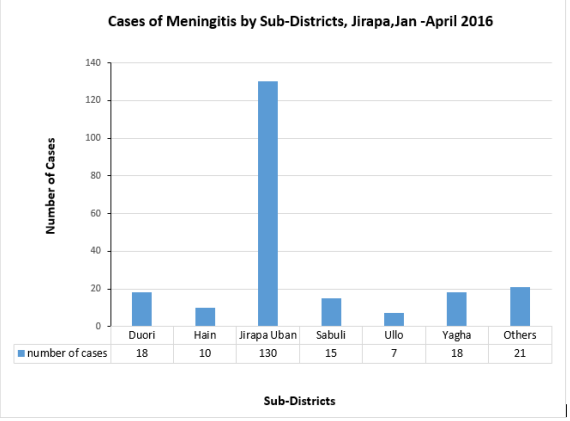

Figure 2 Distribution of meningitis cases by Sub-districts in Jirapa District, 28th December 2015 -10th April 2016

Distribution of cases by time

The Jirapa District started to report cases of meningitis from 28th December 2015, and went a pre-epidemic and epidemic phases within a space of two months or 8 epidemiological reporting weeks.

The index case, a 22-year-old male from Jeferi with travel history from a popular surface mining site called "dollar power" was reported on the 28th of December 2015 in the first epidemiological week of 2016.

Other cases were detected within the vicinity close to the index case in the subsequent weeks. Based on the 2015 WHO revised S.O.P for epidemic meningitis management[11], the district reached alert threshold alert threshold in the second epidemiological week of 2016 with 9 reported cases and confirmed three of them. The District reached it epidemic threshold in week 7 when 30 cases were reported and 10 of them confirmed. There has been a marginal drop in the number of cases from 30 in week 7 to 29 in week 8. The epicurve (Figure 3) suggest a propagated outbreak that reached its Peak in the 7th week. The cases started to decline by week 9 and by the end of week 14, on one case of meningitis was reported (Figure 4).

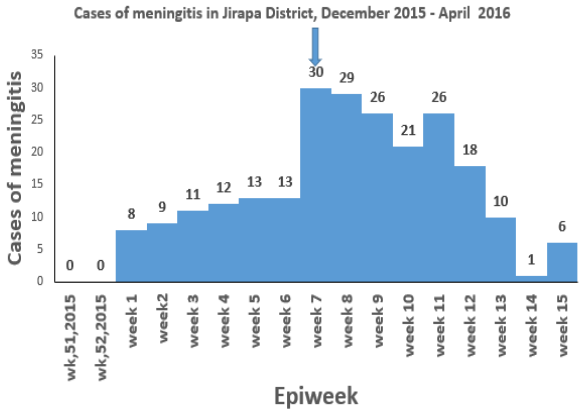

Figure 3 Epicurve: Cases of Meningitis in Jirapa District 28th December- 10th April 2016

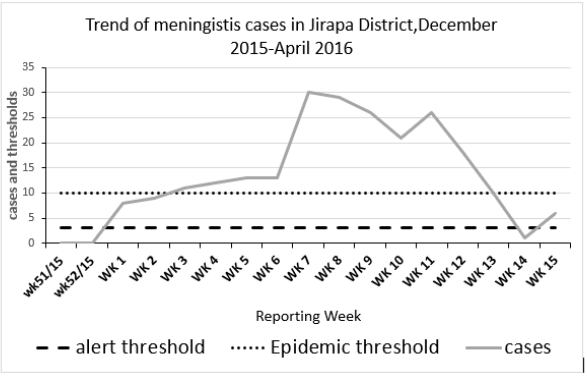

Figure 4 Trend of Meningitis cases in Jirapa District December 2015-April 2016, with epidemic and alert thresholds

Case management and Facility Assessment.
All cases have been managed with ceftriaxone and dexamethasone/mannitol as adjunctive treatment. Lumber was performed for all suspected meningitis case and Chemoprophylaxis in the form ciprofloxacin was given to all contacts of confirmed cases.

All health workers working on patients were given ciprofloxacin as prophylaxis. Ceftriaxone and dexamethasone ere procured from through the national and regional medical stores

Cases of meningitis were referred and reported from eight health facilities (6 health centers, one polyclinic and one district hospital). Only two (the polyclinic and district hospital) had capacity to perform lumber puncture and laboratory testing. There was an active epidemic management team in the district and evidence of training at all facilities. There was adequate supply of medicines (ceftriaxone) but lack laboratory reagents for serological testing. Health education was carried out in the community. The community members were educated on the preventive measures to reduce the spread of meningitis and detection of early signs of meningitis.

DISCUSSION

Our result indicate that Jirapa District experienced an outbreak of meningitis within the first quarter of 2016. This outbreak is unique due to the mixed nature agents (*Streptococcus pneumonia* and *Neisseria meningitis*) that are associated with it. Though literature suggest that pneumococcal outbreak often pre-cede meningococcal meningitis out breaks, both outbreak seem to be occurring concurrently.

Cases of *Streptococcus Pneumonia* started increasing from the year 2000 to 2003 in northern Ghana with serotypes ST 217, ST 303 and ST 615[8]. The types of *Streptococcus Pneumonia* serotype isolated in this outbreak *Streptococcus Pneumonia* serotype 1 (SPN ST1). This same serotype was isolated from the outbreak in the south. There is a possibility that these two serotypes might be epidemiologically linked since the index case visited the epicentre of the outbreak in the Brong Ahafo region.

A case of *Neisseria meningitidis* serogroup A NMA isolated from one case despite massive vaccination campaigns in the past suggest that some population may not be covered.[15] From the results only one case each of *H. influenzae* and NMA were confirmed. A similar observation of few cases of the two agents was also observed by Opare and others who reviewed surveillance data in the upper east region of Ghana[16] and

could be attributed to the success of previous vaccination programmes. The emergence of new strains of agents of meningitis in Ghana and the re-emergence of NMC in Niger indicate a greater potential of larger outbreaks in the meningitis belt.[10] This calls for concerted efforts to tackle the disease through enhance surveillance and protection of the population with multivalent vaccine that target the agent isolated.
Public education to encourage easy identification and early reporting to health facilities is best option for controlling the current outbreak. Targeting a pneumococcal vaccine for the population could be difficult since different serotypes of *Strep. Pneumonia* are isolated in this outbreak. The possible source of cases of N meningitis W135 in this current outbreak could be due to immigration of non-immune subjects who have moved in from other districts.

This is because in 2012, a massive immunization exercise was carried out in the Jirapa district for all those below and routine immunization continued in the district. Hence the resurgence of this could be explained by immigration of non-immune subjects into the district. A single case of meningitides A isolated from one patient could also be due this patient missing vaccination. Until 2010 most epidemics have been due to *Neisseria meningitidis* serogroup A (NmA), with others due to serogroups W, X and C. Since 2010, countries in the extended meningitis belt have started to introduce a new serogroup A meningococcal conjugate vaccine (MenAfriVac®) through mass campaigns[16]. While NmA has declined since 2010, as evidenced by fewer confirmed cases, the proportion of cases due to NmW, NmX and *Streptococcus pneumoniae* has risen. The proportion of suspected cases with laboratory confirmation across the belt has been rising (from 2–3% in 2003 to 6–7% in 2013)[13], but is still at a relatively low level. However up to thirty percent of case in this outbreak were confirmed by laboratory test and this suggest improvements in laboratory capacity.

Cases seem to have been imported from other districts and most of them reported that they have travelled from the southern part of the country. Our index case in this outbreak particularly had a travel from to popular surface mining site called dollar power. The poorly ventilated surface mine pits could also be a source of spread. The Tian district which report the first outbreak of meningitis in Ghana and later became the epicentre is closer to dollar power and also host a significant proportion of these surface miners.

The high numbers of children of school going age, involved in this outbreak suggest that school could be a potential source of infections and must be particularly targeted in educational campaigns. From the epicurve, the district is still within alert threshold and there is the need to keep active surveillance.

A major key limitation, of this study is our inability to conduct an analytical study to identify setting specific risk factors associated with the spread of meningitis in the district. We propose a case control study to determine the possible role of traditional funeral and burial rites, migration to and from surface mining sites and type of housing, in the spread of meningitis in the District.

CONCLUSION

In conclusion, the Jirapa district suffered an outbreak of Meningitis in the first quarter of 2016, which was caused by streptococcus pneumonia and Neisseria meningitides. The spread of this outbreak is by direct person to person contact facilitated by migration and surface mining activities. We recommend to health authorities to maintain surveillance, continue to analyse data to monitor the situation engage in public education on the need to avoid overcrowding and complete all childhood immunisation schedules. All close contacts of confirmed cases should be traced and given chemoprophylaxis. There is also a need for health facilities to prepare with adequate logistics and reagents ahead of the meningitis season in the future. In the long term multivalent vaccines targeting NMW and streptococcus pneumonia serotype one (SPN ST 1) should be acquired for the protection of the general population.

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