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Streptococcus Pneumoniae and Neisseria Meningitides X Outbreak Investigation in three Districts in Upper West Region, Ghana, 2020

Streptococcus Pneumoniae and Neisseria Meningitides X Outbreak

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Abstract:-

- ***Introduction:-* Meningitis is a severe, acute inflammation of the coverings of the brain and spinal cord (meninges). The disease is caused by different micro-organisms, viruses and bacteria and exhibits signs/symptoms including stiff neck, vomiting, nausea, severe headache, fever, seizures, altered consciousness, photophobia, and coma. In January 2020, suspected cases of meningitis were reported at the Nandom District Hospital. Eventually, many more cases were recorded in health facilities in other districts.**
- ***Objectives:-* We conducted investigations to;**

1) **identify the causative agent of outbreak**
2) **determine the magnitude and factors responsible for the outbreak**

- ***Methods:-* We defined suspected meningitis case as anyone presenting with sudden headache and fever (Temp > 38.0 °C) with one of the following signs: neck stiffness, altered consciousness, convulsions, and a bulging fontanelle (infants). We conducted case searches at health facilities and at community levels. Contacts of confirmed cases were identified, line-listed, and followed up for 21 days. Lumbar puncture was performed on all suspected meningitis cases and cerebra spinal fluid (CSF) collected for laboratory isolation of causative organism. We conducted a descriptive data analysis.**
- ***Results*:- A total of 381 suspected cases with 50 deaths (CFR = 13.1%) were recorded. Majority, 53.3% (203/381) were males. Of the 381 cases, 65 were confirmed with *Streptococcus pneumoniae* and *Neisseria meningitides* X(NmX) as the causative agents. The outbreak peaked in week 11 with 40 cases. The overall attack rate (AR) was 44.1/100,000 population. District specific ARs were; Jirapa; 66.9/100,000, Nadowli; 143.1/100,000, Nandom; 192.5/100,000. Female and male specific AR were 20.5/100,000 and 23.4/100,000 respectively. The most, 49.6% (189/381) affected age group was 15-29 years. Neck pain (57.5%), fever (73.8%), and headache (36.0%) were the main sign and symptoms.**
- ***Conclusion*:- As expected for *streptococcus* to be responsible for outbreaks, Nmx was rather established as the causative agent. We embarked on a widespread public education on mode the transmission and early reporting to health facilities and the government should collaborate with scientists to develop a vaccine against this strain.**

Keywords:- *Meningitis; Outbreak; Streptococcus Pneumoniae ; Neisseria Meningitides X(NmX)*

I. INTRODUCTION

Meningitis is a severe, acute inflammation of the coverings of the brain and spinal cord (meninges)[1]. The disease is caused by viruses and bacteria and exhibits signs/symptoms including stiff neck, vomiting, nausea, severe headache, fever, seizures, altered consciousness, photophobia, and coma [2]. About 10-20% of people who survive this disease may be left with permanent consequences including non-functional limbs, mental retardation and hearing impairment[3]. The disease also has a high case fatality rate of 70% in cases without treatment [4]. The following strains, *Haemophilus influenza*, *Neisseria meningitides* and *Streptococcus pneumoniae*, are the cause of about 80% of all causes of bacterial meningitis [5]. The Incubation periods for *S. pneumoniae* is between 2 and 4 days [6]. The disease can spread from person to person through close contact with respiratory secretions [6] [7]. The *S. pneumonia* is the major cause of acute bacterial meningitis in adults and has an average mortality rate of 25% regardless of effective antibiotic therapy and modern intensive care facilities [8].

Globally about 1.2 million cases of bacterial meningitis occur yearly, nevertheless incidence and case-fatality rates for the disease differ by region, country, pathogen, and age group [9]. The meningitis belt extends from Senegal to Ethiopia, and is distinguished by seasonal epidemics which mostly occur during the dry season [10]. Ghana lies within the African meningitis belt and accounts for the highest burden of meningitis globally [11]. There are five regions in Ghana that lie within the meningitis belt and these include Upper West, Upper East, The Northern, Volta Region and the Northern parts of Brong Ahafo.

Certain environmental factors including rainfall patterns and climate change, dust and low absolute humidity are identified as risk factors for the spread of bacterial meningitis [13] . According to WHO, travel and migration are recognized to enable the spread of bacteria that cause meningitis [9]. Between 2010 and 2015. Ghana recorded Over 3000 meningitis cases and 400 deaths [14] . The Neisseria meningitides (Nm) is accountable for more than 95% of Ghana' meningitis burden [15]. Nonetheless, fewer outbreaks of Streptococcus meningitis have been reported in Ghana in recent times [16]. The last outbreaks of meningitis in Ghana were recorded in Northern Ghana [17] and Brong Ahafo Regions in 2016 [4]. *S. Pneumoniae* is responsible for about 70% of current meningitis epidemics in Ghana [18].

The Nandom district director of Health Services in the 2nd week of January 2020 was alerted of a suspected meningitis outbreak. Two persons from Domangue, a Community in the Nandom district presented to the Nandom hospital with symptoms of fever (one with altered consciousness and the other with kenigs signs positive). The case presented with altered consciousness died a few days after admission at the hospital. Eventually, many other people across neighbouring districts presented similar symptoms at other facilities. The Regional Public Health unit upon receiving reports, suspected an outbreak of meningitis and constituted a team to investigate.

II. OBJECTIVES

We conducted this study to identify;
1) the causative agent of the outbreak
2) Determine the magnitude and factors associated with the spread of the disease and to suggest appropriate control and preventive measures.

III. METHODS AND MATERIALS

Place of Study: The outbreak was investigated in the three affected districts i.e Nandom, Jirapa and Nadowli/Kaleo districts in the Upper West Region of Ghana.
Study Design: We conducted case search at health facilities and communities in affected areas
Duration of Study: January 2020- June 2020
Method of Study: The study participants included all persons' resident in the Upper West Region who were confirmed as having meningitis or was epidemiologically linked to a confirmed case of meningitis and were line-listed (collection of data in rows and columns). We retrieved and reviewed data on the line list available. The disease control officers and other relevant health officials were trained on data collection methods. We reviewed medical records at seven hospitals and fourteen health centers in the affected districts. We also conducted active case searches at the communities and followed them up for 21 days. We abstracted data on age, sex, address, date of onset of symptoms, date of presenting at the facility, clinical signs and symptoms, type of test done and final classifications.

Statistical Methods: The data obtained was entered and analyzed using Epi info version 7.0. We performed descriptive analysis of the data of the outbreak by person, place and time. We conducted univariate data analysis and the results were presented as frequencies and rates. We computed the median age (with range), incidence rate by age group and sex, drew an epidemic curve and constructed a spot map to illustrate the spread of the disease in the various districts.

Threshold Determination: Reporting of meningitis cases in Ghana is performed using the standard clinical case definition of acute bacterial meningitis. The reporting is done independent of laboratory confirmation. Meningitis is declared as an epidemic in a district when the incidence of cases exceeds 10 cases per 100,000 populations per week (epidemic threshold) and when a laboratory confirmation is obtained after recording several cases.

IV. RESULTS

A total of three hundred and eighty-one (381) meningitis cases were reported between January 2020 and June 2020. Majority of the cases 53.3% (203/381) were males (Table 1). The median age of cases was 14 years (range, 3 weeks – 100 years). The overall attack rate (AR) was 44.1/100,000 population with a case fatality of 13.1 (50/381). A high proportion of cases 39.9% (152/381) were recorded within the age group of 1-10 years (Fig 2). Males were affected more within this age group (53.2%, 81/152). Female and male-specific ARs were 20.5/100,000 and 23.4/100,000 respectively. Out of the 381 cases, a small proportion of 12.6% (48/381) were vaccinated with the pneumococcal vaccine (PCV).

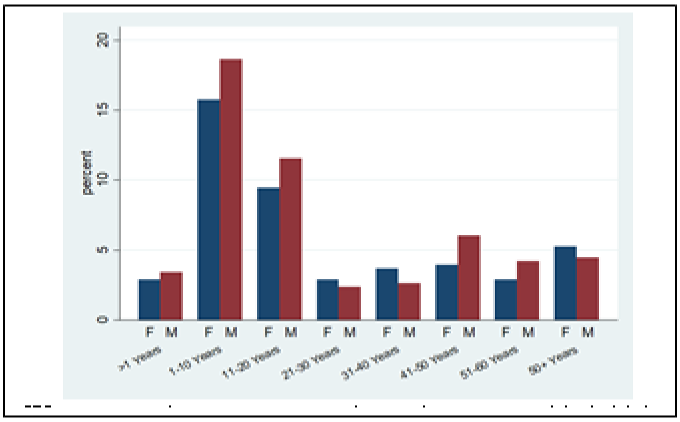


Fig. 1 Age group and sex distribution of meningitis case, UWR, 2020

Out of the eleven districts/municipalities in the region, seven reported cases. Three of the districts reported the highest number of cases. These included; Nadowli/ Kaleo 24.1% (92/381), Nandom district 20.4% (78/381) and Jirapa Municipality 18.1% (69/381 (Fig. 3). The attack rates were high in Nandom 192.5, Nadowli 143.1, Jirapa 66.9 per 100,000 populations. Others include Lambussie district 42.9, Wa Municipality 24.2, Wa West 23.9 and Sissala East 8.6 per 100,000 populations (Fig. 4).

Of the 381 cases, 65 were confirmed by Laboratory (PCR) test with *Streptococcus pneumonia* (19) and NmX (38) identified as the causative agents.

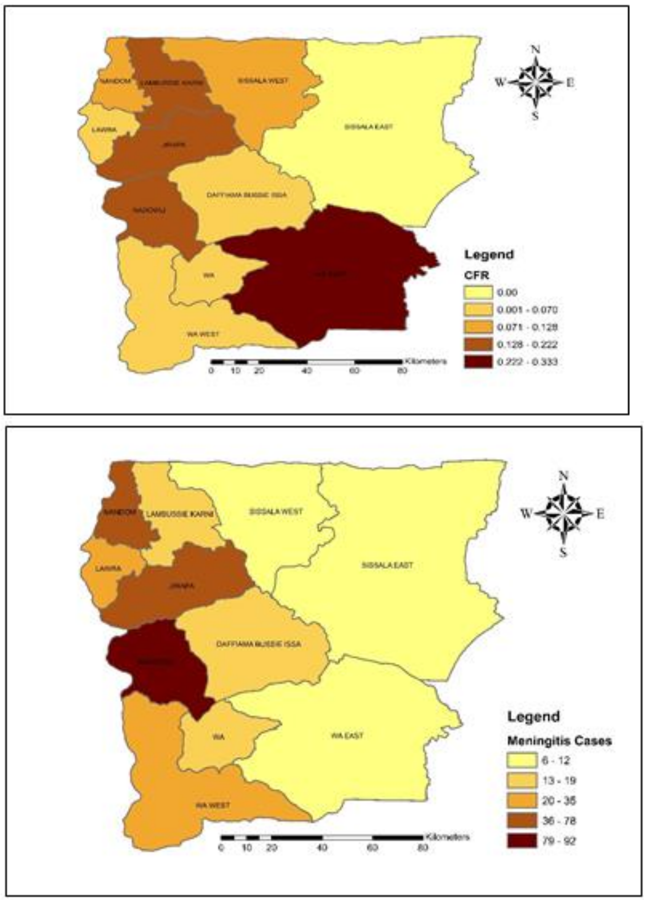
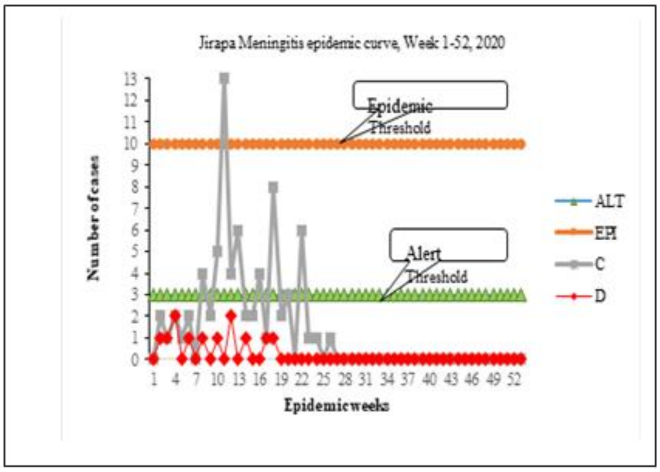


Fig. 2 Cases and CFR (lower right) of meningitis, UWR 2020, Field work, 2020



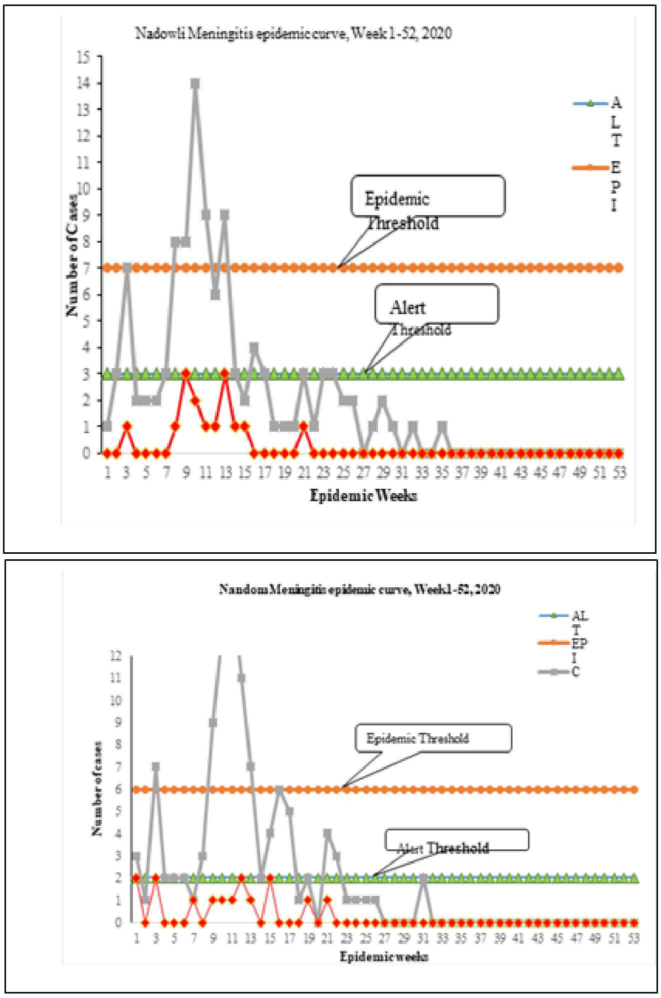


Fig 3. Alert and epidemic thresholds of meningitis by weeks in district reporting outbreaks, UWR, 2020

A. Incidence of Meningitis in UWR by Time of Onset

The index case was a 58 years old man who reported to the Nandom Hospital on 2nd January 2020 with signs/ symptoms of fever and altered consciousness. He later died. His son of 17 years also reported to the hospital with symptoms of fever.

The epidemic curve of the outbreak illustrates a propagated source. Four cases were recorded in the Nandom district during the 1st epidemiological week followed by six cases in epidemiological week two. The cases rose sharply to peak at epidemiological week 11 with 40 cases. The cases subsequently declined with the last case recorded during epidemiological week 38 (Fig 4).

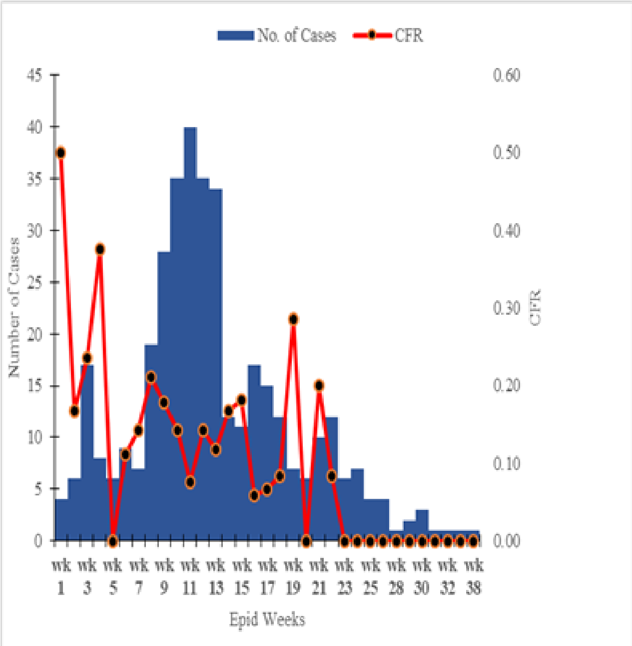


Fig. 4 incidence of meningitis by time of onset, Upper West Region, 2020

The majority of cases (80.6%, 307/381) were recorded between January and May (Dry season).We identified neck pain [aOR = 0.95, 95% (CI 0.6-1.4)], fever [aOR = 0.69, 95% (CI 0.4-1.1)] and headache [aOR = 0.71, 95%(CI 0.5-1.1)] as the most sign and symptoms associated with the disease transmission (Table 1).

B. Public health actions

Regional and District Health Management Teams in collaboration with the political leaders (district assemblies) initiated a swift investigation into the outbreak. Lumbar puncture was conducted for about 95% (261/381) of all suspected cases. The disease control officers and field technicians administered chemoprophylaxis in the form of azithromycin to all primary and secondary contacts of confirmed cases of meningitis in the region.

Health promotion officers conducted health education on causes, signs and symptoms, and prevention of meningitis in schools, churches, mosques, market places and on radio emphasizing the need for early reporting upon onset of symptoms.

Table 1. Factors associated with the spread of meningitis, UWR, 2020

Factor	**Cases (n=381)**	**(%)**	**cOR (95% CI)**	**P-Value**	**aOR (95% CI)**	**P-Value**
Sex						
Male	203	53.3	1.0		1.0	
Female	178	46.7	0.89 (0.5-1.3)	0.598	0.81 (0.5-1.3)	0.369
Age Groups (Yrs)						
>2	24	06.3	1.0		1.0	
2 – 4	55	14.4	0.72 (0.3-2.0)	0.536	0.58 (0.2-1.7)	0.336
5 – 14	113	29.7	0.56 (0.2-1.5)	0.231**	0.43 (0.1-1.2)	0.109**
15 – 29	59	15.5	0.48 (0.2-1.4)	0.167**	0.39 (0.1-1.2)	0.094*
≤30	130	34.1	1.16 (0.4-3.0)	0.759	1.13 (0.4-3.2)	0.814
Presence of Fever						
Yes	281	73.8	1.0		1.0	
No	100	26.3	0.69 (0.4-1.1)	0.126**	0.57 (0.3-1.0)	0.037*
Presence of Neckpain						
Yes	219	57.5	1.0		1.0	
No	162	42.5	0.95 (0.6-1.4)	0.800	0.87 (0.5-1.4)	0.576
Presence of Headache						
Yes	137	36.0	1.0		1.0	
No	244	64.0	0.71 (0.5-1.1)	0.125**	0.54 (0.3-0.9)	0.019*
Outcome						
Alive	331	86.9	1.0		1.0	
Dead	50	13.1	0.67 (0.4-1.2)	0.190**	0.58 (0.3-1.1)	0.101**
District						
DBI	18	04.7	1.0		1.0	
Jirapa	69	18.1	2.44 (0.8-7.2)	0.104**	2.93 (1.0-9.0)	0.060**
Lambussie	18	04.7	1.00 (0.3-3.7)	1.000	1.24 (0.3-4.9)	0.759
Lawra	35	09.2	4.80 (1.3-18.1)	0.021*	4.50 (1.1-18.1)	0.034*
Nadowli	92	24.2	1.09 (0.4-3.0)	0.872	1.12 (0.4-3.1)	0.848
Nandom	78	20.5	0.93 (0.3-2.6)	0.896	0.77 (0.3-2.2)	0.630

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S. East	6	01.6	1.00 (0.3-3.7)	1.000	1.00 (0.2-4.1)	0.759
S. West	12	03.2	1.12 (0.3-2.6)	0.880	1.21 (0.3-5.7)	0.812
Wa East	6	01.6	1.60 (0.2-11.1)	0.634	2.13 (0.3-15.8)	0.460
Wa Municipal	19	05.0	1.73 (0.5-6.6)	0.422	1.74 (0.4-7.0)	0.436
Wa West	28	07.4	1.44 (0.4-4.8)	0.554	1.52 (0.4-5.3)	0.510

Note: *=p<0.05, **=p<0.25

V. DISCUSSION

In the Sub-Sahara African meningitis belt, an enhanced surveillance system was established in 2003 to rapidly collect, disseminate and use the weekly district reported data on the incidence of meningitis to detect and manage outbreaks [19]. About 95% of meningitis outbreaks in Ghana are due to N. *meningitides* [15].

The outbreak of meningitis in the Upper West Region of Ghana in 2020 was caused predominantly by two pathogens; NmX and *S. pneumonia*. Most of the cases that occurred in the very first week were due to *S. pneumonia*. Other outbreaks that occurred in Northern Ghana in 2016 [17] and Brong Ahafo Region [4] in 2016 were also caused by *S. pneumonia*. Ghana introduced the 13-valent pneumococcal conjugate vaccine (PCV13) in 2012. The PCV13 was integrated into the national infant immunization program as a 3-dose given at ages 6, 10, and 14 weeks†; children aged >8 years during this outbreak were not age-eligible to receive PCV13 when it was introduced. However, the High coverages with PCV13 after 2012 likely resulted in the low pneumococcal infection rates observed in younger age groups [20].

The NmX strain which is responsible for the highest number of cases of meningitis among the confirmed cases has not been reported in Ghana since 2000 where nine cases were reported in Northern Ghana between 1998 and 2000. The re-emergence of the serogroup X meningococcus (Nmx) in Ghana suggests the need for the government to consider vaccines (which are not available in the country) for Nmx when making decisions about vaccinations. Epidemics due to the NmX were also detected previously in other African Countries including Niger, Uganda and Kenya in 2006 [21], Togo in 2007, Niger in 2009 and Burkina Faso in 2010 [22]. In Niger, the case fatality rate of Nmx was 12 % [23] compared to 2.6% in the Upper West Region of Ghana. The occurrence of Nmx is difficult to detect and many laboratories cannot find specific antisera for culture and by current rapid diagnostic test [21].

The results also indicated that males were more affected than females. It is suggested that men have an increased susceptibility to various pathogens due to differences in sex steroids particularly estrogen in females and androgens in males [24].

The meningitis epidemic started from Domangye, a small village in Nandom district of the Upper West Region and over time spread to the other districts in the Region. Seven out of the eleven districts recorded cases with two districts, Jirapa Municipality and Nandom districts recording outbreaks. The propagated trajectory of the outbreak signals that, the rapid spread of the outbreak in the region which traditionally lies within the meningitis belt of Africa may be due to certain critical factors.

Firstly, meningitis disease exhibits a seasonal pattern with outbreaks occurring during the dry season [25]. The current outbreak occurred between January and June and this period falls within the dry season and the beginning of the rainy season. The meningitis season is characterized by dusty and cold winds with low humidity. This increases the risk of developing upper respiratory tract infections and also increases carriers' rates of organisms and this leads into concurrent outbreaks in the various districts.

Secondly, the study may be constrained by the accurate application of case definitions to detect patience with meningitis which may result in over diagnosis or missing other cases. The current outbreak of meningitis in Ghana may be considered as the longest outbreak in recent times lasting for 38 epidemiologic weeks (week 1 to week 38) and this was as a result of delays in laboratory confirmation of cases, hence the inability of health personnel to identify the specific strain and confirm the outbreak earlier than expected. Additionally, the possibility of some false positives and negative test results were possible since the sensitivity and specificity of the various laboratory test may not have undergone quality control using more efficacious test coupled with the difficulty in testing for the Nmx strain.

Another challenge that is characteristic of the Ghana Health Service is poor records and documentary keeping and minimal data cleaning during this study could have affected the wrong classification of some of the deaths due to meningitis. Also, some cases could have been missed and or double counting as a result of the scarcity of information from the patients as provided by the clinicians. This notwithstanding, the data presented provides readers with an insight into the nature of the meningitis outbreak in the Upper West Region of Ghana in 2020.

The overall attack rate of 44.1/100,000 population could be compared to the rates in the traditional meningitis belt of Ghana which is between 10% and 120% [15] [26]. This confirms how vulnerable and susceptible the population is to meningitis. The overall case fatality rate of 13.1% recorded is however higher than that recorded in a previous outbreak in Brong Ahafo (CFR=9%) [4] .

The high susceptibility levels in addition to a weakened surveillance system in Nandom and Nadowli districts could have accounted for the high attack rates of 192.6/100,000 and

143.1/100,000 recording the high % of cases of 20.5% and 24.2% respectively. It could also be due to the new strain that was confirmed in most of the cases which are not commonly associated with outbreaks in this meningitis belt, coupled with the delays in the confirmation of cases by the laboratories.

The illustration from the epi curve as indicated earlier shows that this outbreak which lasted for 38 weeks is perhaps the longest meningitis outbreak in recent times. This may pose challenges for the surveillance system since it is suggestive that measures were not taken to prevent the spread of cases to the other districts when the first case was recorded.

It is also important to note that the Nandom district is closer to the Hamile (a border town) hence commuting between Hamile and Nandom, and traders from other districts traveling through Nandom to Hamile could have contributed to the spread of the disease.

In terms of the clinical management of cases, adherence to treatment protocols is of significance. However, this was not given the much-needed importance hence our inability to assess the quality of case management at the facility level to conclude on the case fatality rates observed. It may however suggest that the low case fatality rate observed in most of the districts may be attributed to improvement in case management.

The signs of fever and headache and other signs related to upper respiratory tract infection could be as a result of the dusty and cold winds experienced during this period.

The lumbar puncture rate of 99% points to an improvement in the skills of clinicians, specimen collection and transportation and the need to confirm cases rapidly to confirm the outbreak to institute preventive and control measures to prevent further spread. It is however not known whether standard operating procedures for CSF collection were followed hence we could not assess the quality of lumbar puncture.

The danger posed by NmX must be taken seriously because there is no vaccine against this serogroup that protects individuals. Wisdom from experience will insist that meningococcal vaccines targeting this serogroup, which can no longer be considered to be a marginal vaccine, need to be produced. Similarly, only meningococcal cultures can use present serogroup X-specific antisera; as such, their use is confined to a few laboratories in the African meningitis belt. In other countries within the African meningitis belt, the introduction of PCR targeting NmX should be encouraged for use with non-cultivable CSF specimens. There is no rapid diagnostic test to identify NmX; it would be highly desirable for this form of test to improve the collection of rapid diagnostic tools available in basic laboratories in this field.

VI. CONCLUSION

The study established a rare outbreak of meningitis due to *S. pneumoniae* and Nmx. All sex and age groups were affected. The outbreak peaked at week 11 and lasted for 38 weeks. Headache and fever where identified as signs and symptoms associated with meningitis.

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