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Serogroup Shift: *Neisseria meningitis* Out-break Investigation in Kano, Nigeria, 2017

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Abstract

Background: *Neisseria meningitis* is among the 10 top causes of death worldwide. Forecasting sero-group shift in *Neisseria meningitis* outbreak in most states in Nigeria was conducated without a proven explanatory model. We characterized the outbreak in Kano State; assessed their level of preparedness for the outbreak; and the relevant knowledge and practice of health workers in affected local government areas.

Methods: We interviewed line-listed cases; emergency response committee members; and health care workers in affected districts. Cerebrospinal Fluid samples were collected from cases for laboratory confirmation. Data were analyzed using descriptive statistics, spot map and chi-square at 5% level of significance.

Results: A total of 295 cases were line listed with a Case Fatality Rate of 8%. Children aged 5-14 years had the highest number (34.9%) of cases. Outbreak lasted from epidemiologic week 1 to 20, affecting 34 of 44 districts with varied attack rates, ranging from 0.3 per 100,000 population in Dambatta to 14.4 per 100,000 population in Fagge. 'Latex particle agglutination test' was 'sero-group C' positive for 17 of 51 samples collected. Mass vaccination was delayed until the 16th week of the outbreak. Most (62.5%) health workers had good knowledge concerning meningitis. However, only a few (27.1%) practice droplet precaution. There was no statistically significant association between level of knowledge of Health Workers and the practice of droplet precaution (OR: 1.99; 95% CI: 0.96-4.11; p-value: 0.06).

Conclusion: The 2017 *Neisseria meningitis* outbreak affected most districts in Kano and majority of the cases were children. Regular evaluation of the national vaccine program and further research on the impact of mass vaccination on sero-group selection and meningococcal carriage are recommended.

Keywords: Kano; *Neisseria meningitis*; Outbreak; Sero-group C; Preparedness

Abbreviations: AFENET: Africa Field Epidemiology Network; AKTH: Amino Kano Teaching Hospital; CFR: Case Fatality Rate; CSF: Cerebrospinal Fluid; CSM: Cerebrospinal Meningitis; EHO: Environmental Health Officer; EOC: Emergency Operation Center; FMOH: Federal Ministry of Health; HCW: Health Care Worker; HE: Health Educator; ICG: International Coordinating Group; LGA: Local Government Area; NFELTP: Nigeria Field Epidemiology and Laboratory Training Programme; NHREC: National Health Research Ethics Committee; NPHCDA: National Primary Health Care Developmental Agency; PHEIC: Public Health Emergency of International Concern; PPE: Personal Protective Equipment; RRT: Rapid Response Team; SMOH: State Ministry of Health

Background

About 90% of bacterial meningitis is caused by *Neisseria meningitidis*. Twelve sero groups of *Neisseria meningitidis* have been identified, of which six (sero-group A, B, C, X, Y and W135) have been implicated as major cause of epidemics [1-6]. Multivalent vaccines are expensive for low resource settings and may not cover all the strains in an epidemic. The cost and availability may result in prioritization causing delayed mass vaccination in some affected areas. This practice contradicts World Health Organization's (WHO) recommendation of immediate mass vaccination for cerebrospinal meningitis (CSM) threshold [7-12]. Bacterial meningitis is among the 10 top causes of death worldwide. It has a case fatality rate (CFR) of 90% to 100% if un-treated. Although sporadic cases of meningitis occurs worldwide all year round, large scale epidemics is typical of the meningitis belt of sub-Saharan Africa which has been found to be extending further south due to the climate changes associated with global warming. There may be a hypothetical explanatory model for the recurrence of large scale CSM epidemics in sub-Sahara African. However, the explanatory variables in these models are not explicit. A proven explanatory model is required to accurately predict epidemics and inform vaccine strategy [13-17].

Previous epidemics in Nigeria were dominated by *Neisseria meningitidis* type A. Nigeria recorded *Neisseria meningitidis* type C in epidemic proportion for the first time in 2017. The first case of *Neisseria meningitidis* type C in Nigeria was in 2013, although it was a relatively small outbreak. In 21st November 2016, an outbreak of CSM with predominantly *Neisseria meningitidis* sero-group C was first reported in Zamfara State and later spread to involve 22 other States in Nigeria in 2017 [18]. Kano State reported her first confirmed CSM case of the outbreak in March 22nd, 2017. The state eventually convened an epidemic preparedness/response meeting, and activated her Emergency Operation Center (EOC).

We described the CSM outbreak in Kano; assessed the level of preparedness of the Kano State Ministry of Health to contain the CSM outbreak; assessed the knowledge and practice of health care workers in Kano State in regard to CSM; and collected specimen to determine the sero-groups implicated in the outbreak in order to inform vaccine strategy.

Methods

Study area

Kano State is in North-Western Nigeria. The State borders Katsina State to the north-west, Jigawa State to the north-east, Bauchi State to the south-east and Kaduna State to the south-west. Kano State has 44 local government areas. The projected population of the state was 13,076,892 (projected from the 2006 census figure) making it the most populous state in the country. The state has a tropical savanna climate which is very hot throughout the year. However, December to February tends to be cold with very low humidity favoring the transmission of CSM. The states dry season is characterized by very low humidity and nighttime temperature (11 to 15°C (52 to 59°F) especially in the months of December, January and February [12].

Case definitions

Suspected case: A person with sudden onset of fever (>38.5°C (>100.4°F) for rectal or 38.0°C (99.1°F) for axillary temperature) and one of the following meningeal signs: neck stiffness, altered consciousness or other meningeal signs including bulging anterior fontanel in toddlers.

Probable case: A suspected case with turbid, cloudy or purulent cerebrospinal fluid (CSF); or with a CSF leukocyte count >10 cells/mm^3 or with bacteria identified by Gram stain in CSF. In infants: CSF leucocyte count >100cells/mm^3; or CSF leucocyte count 10-100 cells/mm^3 and either an elevated protein (>100 mg/dL) or decreased glucose (<40 mg/dL) level.

Confirmed case: A suspected or probable case that is laboratory confirmed by culture, polymerase chain reaction, immune chromatographic dipstick or latex agglutination [13-16,18].

Data collection

We reviewed line list of cases in affected LGAs from 1st March to 20st May 2017. Additional information was obtained through Disease Surveillance and Notification Officers (DSNOs) who conducted active surveillance and active case search. A semi-structured interviewer administered questionnaire was used to collect information from suspected cases. We collected information on socio-demographic characteristics, risk factors of CSM, knowledge of CSM, clinical presentation and history of treatment/chemoprophylaxis. A semi-structured interviewer administered questionnaire was also used to collect information from conveniently selected members of the public health emergency management committee (PHEMC) and rapid response team (RRT). Information on preparedness for the outbreak; integration of available services; and forecasting of the predominant *N meningitidis* serogroup in the CSM outbreak was collected these group. Health care workers in affected LGAs were also interviewed to determine their knowledge and practice concerning CSM.

Laboratory methods

Sample collection and transportation: Cerebro-Spinal Fluid (CSF) samples were collected from case-patients who were fit for Lumbar Puncture. Blood samples were also collected from some suspected cases. A total of 51 CSF specimens were collected as at 20th April 2017. Specimens were transported *via* trans-isolate media, to the Aminu Kano Teaching Hospital.

Diagnostic procedure: The samples were also tested using the Pastorex (Latex Particle agglutination) or Directigen (Rapid Imunoassay) rapid diagnostic test kit for *N meningitidis*, *Streptococcus pneumonia*, and Haemophillus influenza type B.

Measurement of variables

The primary outcome variable of the third objective of this study was the proportion of Health Care Workers who use the personal protective equipment (PPEs) appropriately. The dependent variables of interest include whether or not health care worker (HCW) had good knowledge about CSM. The Level of knowledge of HCW was determined by the number of correct choices made out of the 10 objective questions designed to test knowledge about CSM. The questionnaire used was face validated. Scoring 7/10 (70%) and above was classified as good knowledge while below was poor knowledge. Good practice was when the HCW self-reported adherence to the use of PPEs for droplet precaution by scoring 7/10 (70%) in the objective questions testing for practice of droplet precaution, given that he/she had good knowledge and was observed to be consistent in the use of PPE.

Selection of 7/10 (true score) as the cut-off point for 'good knowledge' was based on the 'Modified (adjusted) Angoff method of selecting cut-off'. The cut-off was initially set at the normal expectation of acceptable proficiency 10/10 (true score). Note, for effective 'infection prevention and control' HCW must satisfy all the ten requirements (represented by the ten questions testing for knowledge/practice). Experts recommend 10/10 (true score), but because of the measurement error expected of all tests, 'Conditional standard error of measurement' (CSEM) was used to adjust for minimum cut-off by applying ± 3 standard deviation to the critical score of 10/10.

Data analysis

Descriptive analysis of line listed cases was conducted. Epidemic curve was drawn and proportion of cases for each age group was determined. Spot map was computed, showing the distribution of cases within the state. Frequency distribution of the responses of the health care workers was computed to generate count and percent, reflecting the level of knowledge and practice of the HCW. Chi-square was used to test the association between the level of knowledge and the practice of the respective cadre of health care providers at 5% level of significance.

Results

Descriptive epidemiology

A total of 295 cases, were line listed (suspected/probable cases: 273; and confirmed cases: 22). Males constituted 60% of the cases. Median age of the cases was 11 years (range: 1 month-65 years. with the age group 5-14 years constituting the highest number (34.9%) of the cases (Figure 1).

Twenty four deaths documented (CFR: 8%). The onset of the Kano State CSM outbreak was in epidemiologic week one of 2017. The outbreak was propagated as evident by progressively taller peaks with the tallest peak at epidemiologic week 15, before a sharp decline from epidemiologic week 16 to week 20 (Figure 2).

Cases were distributed across 34 LGAs in Kano State. As at 20th April, 2017, Dala, Gwale, Nassarawa, Kumbotso, and Ungogo LGAs already had the highest number of cases, while Dala, Gwale, Kumbotso, Tsanyawa and Kabo LGAs were found to have crossed the alert threshold. At the end of the outbreak (20th May, 2017) 34 LGAs exhibited varied attack rates, ranging from 0.3 per 100,000 population in Dambatta LGA to 14.4 per 100,000 population in Fagge LGA. Most of the cases were concentrated within the Metropolitan LGAs and those bordering Katsina State (Figure 3).

Level of preparedness

Public health emergency management committee successfully coordinated the establishment of a rapid response team; the risk mapping; the stock piling of drugs, vaccines and other supplies needed for the outbreak. However, the committee did not specify the valence of the vaccine that will be needed most. Moreover, contingency stock was not set-up immediately after risk mapping due to delayed arrival of vaccines from National Primary Health Care Developmental Agency (NPHCDA). The committee designated a reference laboratory: Amino Kano Teaching Hospital (AKTH) to confirm cases. However, there was not enough stock of basic laboratory meningitis test kits. Moreover, there were not enough preparations to surmount the challenge of paucity of clinicians who could perform lumber puncture. Reactive vaccination was eventually delayed until the 16 epidemiologic weeks, approximately 15 weeks after the onset of the first case.

Knowledge and practice of health workers concerning CSM

At the close of work on the 20th April, 2017, a total of 145 health workers ranging from 19 to 54 years of age had already been interviewed to determine their knowledge and practice concerning CSM. Mean age of health workers was 34.6 years ± 9.2 SD. Male constituted 58.6% (n=145) of the respondents. Most HCW responded appropriately to the questions testing for level of knowledge of CSM (Table 1). However, a relatively low proportion responded appropriately to questions testing for practice of droplet precaution (Table 2). The practice of droplet precaution was fair amongst doctors (50.0%); worse amongst Health Educators (HE) (20.0%); and Environmental Health Officers (EHO) (12.5%) (Figure 4). Chi-square test of the association between the level of knowledge concerning CSM and the practice of droplet precaution of health care workers at 5% level of significance was not statistically significant (OR: 1.99; 95% CI: 0.96- 4.11; p-value: 0.06) (Table 3).

Laboratory investigation

Examination of laboratory results revealed that the predominant etiologic Neisseria meningococcal sero-group is C, which accounts for 77.3% of the confirmed cases. Other sero groups implicated in the Kano CSM outbreak of 2017 included the following in descending order of frequency: W135, B, and A/Y (Table 4).

Discussion

The duration of the Kano State outbreak was epidemiologic week one to week 20. These findings were consistent with other related

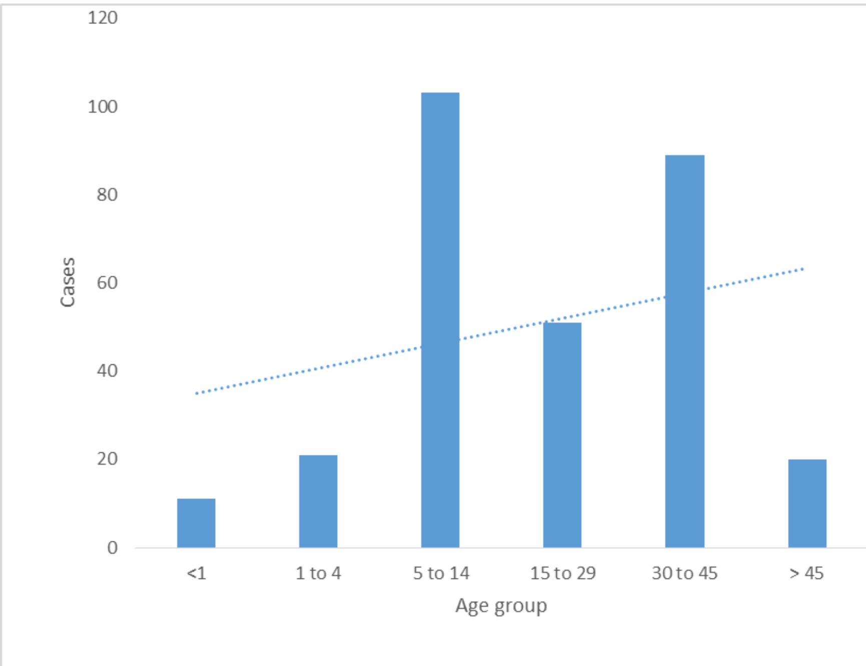

Figure 1: Age distribution of Cerebrospinal Meningitis cases in Kano, as at 20th April 2017.

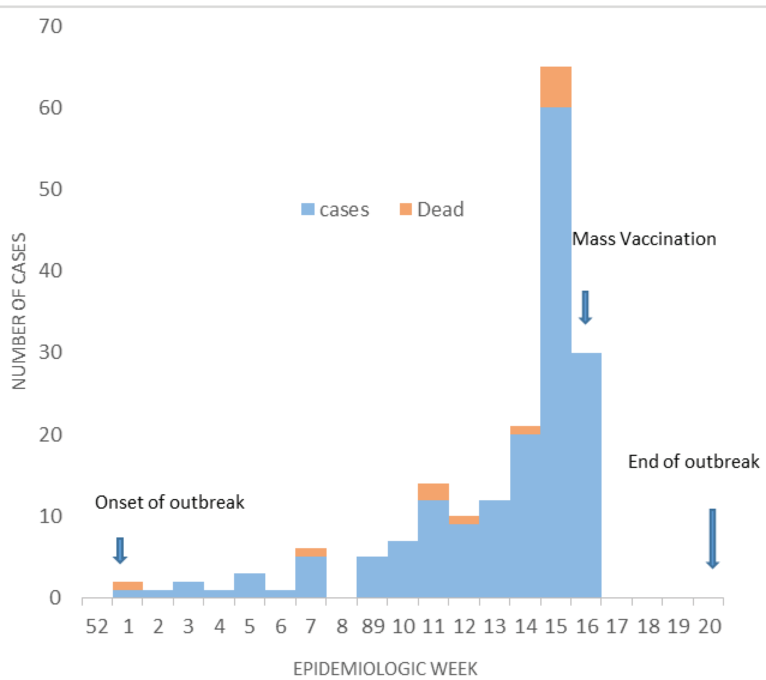

Figure 2: Epicurve of Cerebrospinal Meningitis cases in Kano by epidemiologic week last updated 20th April 2017 (four epidemiologic weeks to end of outbreak).

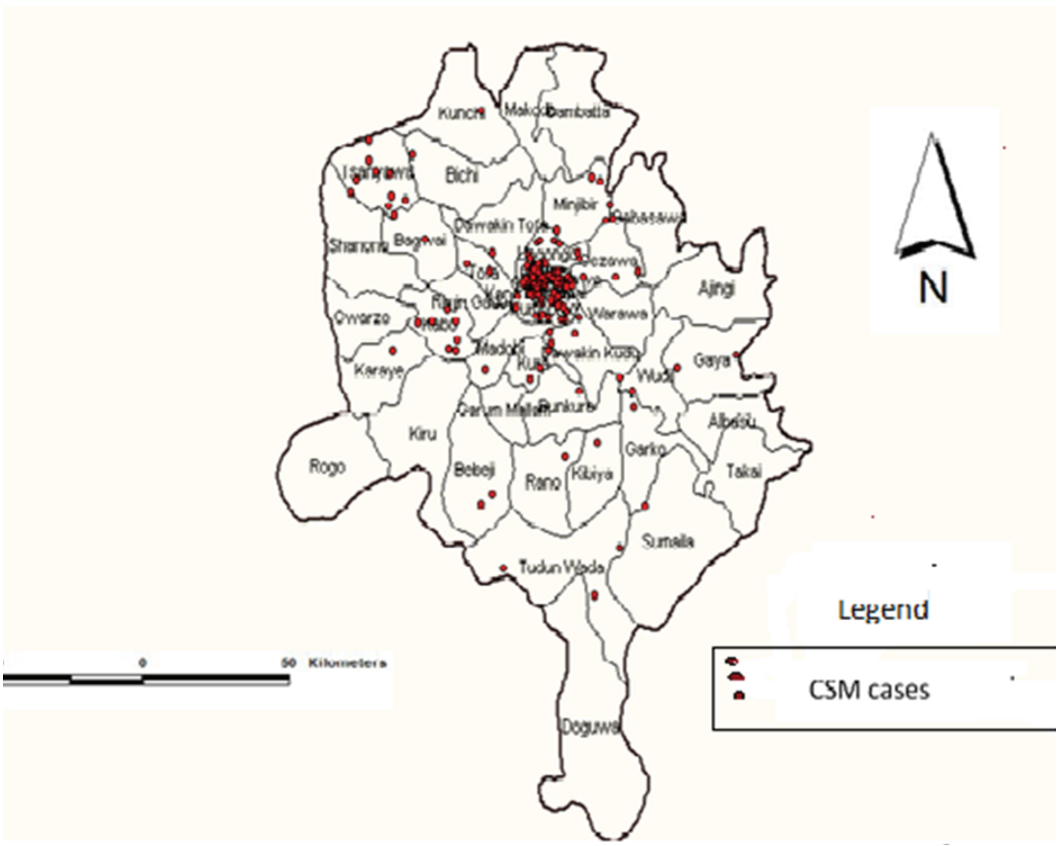

Figure 3: Distribution of Cerebrospinal Meningitis cases among the Local government areas in Kano State, 20th April, 2017.

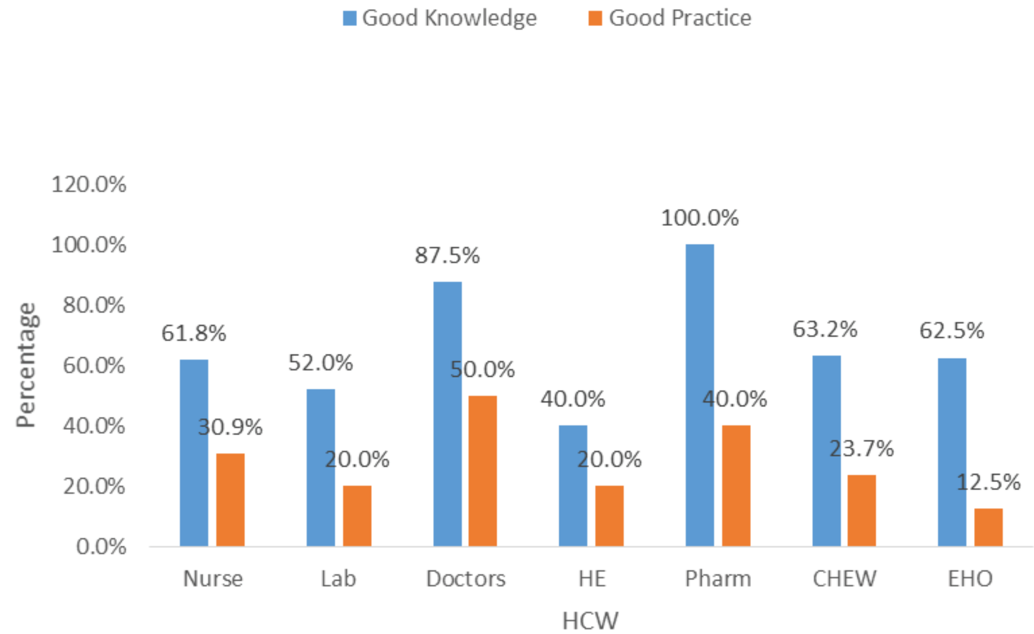

Figure 4: Proportion or health care workers (HCW) with good knowledge concerning cerebrospinal meningitis compared to the proportion that actually practice droplet-precaution, Kano State, 2017. [The different cadre of HCW: community health extension worker (CHEW); environmental health officer (EHO); and health educator (HE)].

Table 1: Proportion of Health Care Worker (disaggregated by gender) who responded appropriately to questions testing for knowledge concerning Cerebrospinal Meningitis, Kano State, April, 2017 (n=145).

Interview Knowledge	Male		Female	
	n	%	n	%
Neck stiffness is a typical symptom?	82	96.5	47	78.3
Fever is a typical symptom?	81	95.3	51	85
Overcrowding is a risk?	33	38.8	22	36.7
Poor ventilation is a risk?	41	48.2	22	36.7
CFR may rise if not reported on time	68	80	55	91.7
Prevention is by protecting against respiratory droplet	57	67.1	45	75
Transmission is by person-to-person?	68	80	53	88.3
Transmission is by contact with nasal secretion?	58	68.2	46	76.7
Transmission is from rat's	85	100	60	100
Transmission is from cat's	85	100	60	100

Male (n=85) and female (n=60)

Table 2: Proportion of Health Care Workers (disaggregated by gender) who responded appropriately to questions testing for practice of droplet precaution, Kano State, April, 2017 (n=145).

Practice	Male		Female	
	n	%	n	%
Use well-fitting face mask	35	41.2	24	40
Isolate case-patients (barrier nursing)	81	95.3	59	98.3
Use eye protection (goggles)	5	5.9	2	3.3
Use hand gloves	34	40	20	33.3
Use gown	12	14.1	8	13.3
Consistent use of PPEs	69	81.2	52	86.7
Regular hand washing	82	96.5	59	98.3
Avoiding contact with secretions/specimen	80	94.1	56	93.3
Use boots	73	85.9	45	75
Avoiding contact with infected objects	74	87.1	52	86.7

Male (n=85) and female (n=60)

studies. Nnadi C, et al. [18] revealed timing from epidemiologic week one to week 21. Anecdotal evidence implicated the following as the cause of the delay in reactive vaccination: absence of a national stockpile of emergency vaccine; delay in requesting for vaccine by the NPHCDA; and delayed response from ICG (International coordinating group). The implication in public health practice of the prolonged duration of the 2017 outbreak in Kano, and some other northern Nigerian states, is that more effort is required in terms of ensuring that mass vaccination, as a response activity, is not delayed unnecessarily, but should be initiated with immediate effect once the epidemic threshold in each LGA is reached. National protocol prescribes immediate mass vaccination once epidemic threshold is reached per LGA based on the objective of 100% coverage [19,20]. Timely mass vaccination will impact on the CFR. However, the scenario painted by the CFR of 8.0% obtained in this study, is that the outbreak was well managed, given a virulent pathogenic agent like *N meningitidis*. In poorly managed CSM outbreak, CFR may be as high as 50.0%. Case Fatality Rate is a direct measure of the virulence of a pathogen, but it indirectly measures the quality of outbreak management.

Table 3: Association between the level of knowledge concerning Cerebrospinal Meningitis and the practice of droplet precaution of the respective cadre of health care providers during the Cerebrospinal Meningitis Outbreak in Kano, April, 2017 (n=145).

Health Care Workers	Good Practice	Poor Practice	OR (95% CI)	p-value
	n (%)	n (%)		
HCW				
Good knowledge	39 (43.3%)	51 (56.7%)	1.99 (0.96-4.11)	0.06
Poor knowledge	15 (27.8%)	39 (72.2%)		
Doctors †				
Good knowledge	4(57.1%)	3 (42.9%)	Fisher exact (0,00-65.00)	0.63
Poor knowledge	1(100.0%)	0(0.00%)		
Nurses †				
Good knowledge	17(33.6%)	27 (61.4%)	0.84 (0.29-2.41)	0.75
Poor knowledge	9(42.9%)	12 (57.1%)		
Laboratory technician †				
Good knowledge	5 (58.5%)	8 (61.5%)	3.12 (0.47-20.58)	0.23
Poor knowledge	2 (16.7%)	10 (83.3%)		
CHEW †				
Good knowledge	9 (37.5%)	15 (62.5%)	3.60 (0.65-19.90)	0.12
Poor knowledge	2 (14.3%)	12 (85.7%)		
Environmental Health Officer †				
Good knowledge	0 (0.0%)	5 (100.0%)	Fisher Exact (0.00-23.4)	0.38
Poor knowledge	1 (33.3%)	2 (66.6%)		
Health Educator †				
Good knowledge	1 (50.0%)	1 (50.0%)	Fisher Exact (0.01-234.50)	0.7
Poor knowledge	1 (33.3%)	2 (66.6%)		

†Doctors (n=8); Nurses (n=55); Laboratory technician (n=25); Community Health Extension Worker (CHEW) (n=38); Environmental health officers (n=8); and Health Educators (n=6)

Although the level of preparedness of the Kano State Health System to control the CSM outbreak was encouraging, more effort is required on the part of the Kano State Emergency Operation Center (EOC) in terms of addressing the gaps in surveillance; preparedness and response; and the pre-existing 'adaptation' strategies expected of the communities within the state. Assessment of the preparedness of the state revealed that the following impacted the course of the 2017 CSM outbreak in Kano State: the collaboration of Kano state with partner organizations; the zeal of SMOH (Epidemiology unit) staff to control both outbreaks (CSM and Lassa Fever, occurring concurrently); cooperation of traditional leaders and their community; and the timely response of the SMOH. Moreover, the timely provision of fund by the state government for routine surveillance activities; and the

Table 4: Sero-groups of *Neisseria meningitidis* implicated in the Kano State CSM Outbreak: April, 2017.

Positive Cases	Frequency	Percentage
Neisseria meningitidis A/Y	1	4.5
Neisseria meningitidis W135	2	9.1
Neisseria meningitidis C	17	77.3
Hemophilus influenza type B	2	9.1
Total	22	100

team spirit at play between partner agencies and the SMOH assisted considerably in the response coordination and quality. In addition, the timely purchase and prepositioning of relevant antibiotics in health facilities by SMOH enabled effective CSM case management. Kano State also supported radio jingles providing health education and enabling risk communication. However, information to educate the masses on the long term effect and the need for adaptation strategies in responding to recurring seasonal outbreaks like CSM was not included in the jingles. Adaptation strategies may involve the adjustment of ecological, social and economic systems in response to expected climatic stimuli and their impacts, in the bid to moderate harm. These include anticipatory, reactive, autonomous and planned adaptations strategies. The only reactive adaptation strategy Kano Sate employed was annual mass CSM vaccination, although it was not timely. The radio jingles did not emphasize moderation of socio-cultural activities that require mass gathering and mass movement. Also autonomous adaptation involving modifying dwelling places; avoiding overcrowding; encouraging sleeping in the open to enable effective ventilation where not emphasized.

This study revealed that most of the health care workers in Kano State had good knowledge about the typical clinical features of CSM. Moreover, majority knew that transmission of CSM is usually person-to-person. However, only a few of the HCW knew that contact with infected respiratory secretions could transmit the pathogen, and that overcrowding and poor ventilation are known risk factors of CSM. Concerning practice of health care workers, this study revealed that most health care workers in the affected LGAs use personal protective equipment (PPE) and employ barrier nursing (isolation of case) during case-management. However, only a few of them used well-fitting face mask, goggles, hand gloves and gowns. The implication of this finding in public health practice is that more effort is required in terms of health education, intensive media involvement, training and retraining of health care workers. In addition, preventive vaccination for all health workers before redeployment to worksites/fields should be mandatory.

This study revealed that the predominant sero-group implicated in the 2017 meningococcal meningitis outbreak in Kano State was sero-group C. Epidemiologic studies conducted in other states in northern Nigeria affected by CSM outbreak also revealed a predominantly sero-group C meningococcal meningitis outbreak [11,18,21]. The meningococcal meningitis outbreaks occurring in Nigeria prior to 2013 were predominantly sero-group A. Sero-group C emerged in Nigeria during the 2013 dry season (December, 2013-June, 2014), albeit implicated in a relatively small outbreak. The proportion of cases attributed to sero-group C in subsequent meningococcal meningitis outbreaks has progressively increased [22-24]. The implication of this finding is that there is the need for a proven explanatory model to predict CSM epidemics and its attendant serogroup-shift and to inform vaccine strategies. This cannot be overemphasized considering the extent of vaccine shortage for sero-groups other than sero-group A in the 2016/2017 outbreak in Kano. Ensuring availability of multivalent vaccine, as an alternative strategy, may not be economically feasible in a developing economy like Nigeria. This underpins the need for proven explanatory model to enable accurate prediction as prescribed by some related studies who argued that competition between strains may play a role in defining which sero-group will be predominant during an epidemic, and that mass vaccination (example, using group A conjugate vaccine) is expected to impact on meningococcal carriage (carrier states) and could select for the spread of other Neisseria meningitis sero-groups [25-32].

Study Limitation

The following may have affected the results of this study: Lack of Laboratory reagents, trans isolate medium and lumber puncture kit in most health facilities visited. This may have affected the total number of laboratory confirmed cases recorded for the outbreak. Poor documentation of records in some health facilities visited may have affected the total number of line listed cases for the outbreak (suspected/probable cases were 273; confirmed cases were 22). Absence of written case definitions of epidemic prone diseases in some of the Health Facilities visited may have resulted in missed diagnosis. Most patients were on antibiotics before presenting at health facility, they were therefore not subjected to laboratory test, which may have affected the number of laboratory confirmed cases. Lack of personnel with capacity to do Lumber Puncture in most health facilities visited may have affected the total number of laboratory confirmed cases recorded for the outbreak. In determining association between level of knowledge and practice of droplet precaution of HCWs some assumptions were made. These assumptions may have adversely affected the result of the study to an extent, because these assumptions were made about things we were uncertain about. For example, the assumption that scoring 70.0% in the objective questions testing for level of knowledge and practice signifies good knowledge and good practice respectively. Moreover, the assumption that the response of participants to questions testing for knowledge and practice of HCW concerning CSM is the truth.

Conclusion

The 2017 CSM outbreak affected most LGAs in Kano and majority of the cases were children. Regular evaluation of the national vaccine program and further research on the impact of mass vaccination on sero-group selection and meningococcal carriage are recommended.

Public Health Actions

The NFELTP team supported the Kano State government by carrying out the following public health actions: advocacy visit to decision makers and sensitization of health workers at the health facilities in affected LGAs in Kano State.

Recommendations

1. FMOH should ensure early pre-positioning of CSM vaccines in the states based on their capacity to identify potential serogroup shift from risk mapping/forecasting;
2. FMOH/SMOH should ensure regular training/retraining of relevant health workers to improve their capacity in CSF collection.
3. FMOH/SMOH should ensure that health education on adaptation strategies is included in the public health enlightenment campaign.
4. FMOH/SMOH should ensure mass vaccination is initiated immediately epidemic threshold is reached as prescribed by national protocol.
5. The epidemiology unit of the federal and state ministry of health should ensure regular evaluation of the vaccine program.

Declarations

Availability of data and materials

All data supporting the conclusions of this article are included within the article.

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Authors' Contributions

GBE conceived the study, designed the study, Contributed in acquisition of data, analysis and interpretation of data and wrote the draft manuscript. SA, TV, MMA contributed in data collection, entry and analysis. BE, MSB, ASA, AU and CU made substantial contributions in the critical revision of the manuscript for important intellectual content.

Ethics Declarations

Ethics approval and consent to participate

The study was an outbreak investigation. A waiver was obtained from the National Health Research Ethics Committee (NHREC). Appropriate verbal informed consent was obtained from each respondent before recruitment into the study. All respondents were free to withdraw from the study without any negative consequences. No respondent was denied any privilege/benefit (treatment for cases) because of failure to enroll or provide response to all or part of the questions in the questionnaire.

Consent for Publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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