Characteristics of Cerebrospinal Meningitis Cases in 2017 Outbreak, Sokoto State, Nigeria: A secondary data analysis.

ABSTRACT

Introduction: Cerebro-Spinal Meningitis (CSM) is an acute illness affecting surrounding layers of the brain and spinal cord, mostly caused by bacterial infection. The disease is responsible for the occurrence of epidemic meningitis in the African Meningitic belt. For many years, this region has experienced a large serogroup A epidemic every 7-10 years. A sharp decrease in the number of reported cases was demonstrated in countries where Men Afrivac has been introduced. However, serogroup replacement with serotype C was noted in the region, which has posed a serious threat to eliminating CSM epidemics. We describe the characteristics of cerebrospinal meningitis cases in the 2017 outbreak in Sokoto state, Nigeria.

Methodology: We obtained CSM data from the state epidemiology unit from 7th February to 24th May 2017. We extracted data on demographic characteristics, clinical features, case management and outcome of cases. We used Microsoft Excel and SPSS to analyze the data for proportions, cross-tabulations and chi-square test to find associations between variables.

Results: A total of 4969 CSM cases were recorded, with 283 deaths (case fatality rate: 5.7%). The cumulative attack rate was 96.4/ 100,000 populations. The highest proportion of cases was among ≥ the 15-year age group 2063(41.5%), and males were more affected, 2843(57.2%). Of the total 4969 suspected CSM cases, specimens were collected for only 225 (4.4%) cases, of which 58 (25.8%) were positive. Most 48 (82.8%) of the positive specimen were of NmC serotype. Only age was found to predict outcome (aOR: 1.52; 95% CI= 1.18 – 1.97).

Conclusion: Sokoto State outbreak of Cerebro-spinal meningitis in 2017 was huge and largely caused by NmC. Those aged less than 15 years might be at higher risk of dying from CSM and we therefore recommend that specific preventive interventions such as vaccination and awareness creation should target this age group.

Keywords: Characteristics, Cerebro-spinal Meningitis, Outbreak, Nigeria.

INTRODUCTION

Meningococcal meningitis, commonly referred to as Cerebro-spinal Meningitis (CSM), is a contagious disease transmitted from person to person by airborne droplets of respiratory or throat secretions of a human carrier.[1, 2] It is an acute illness characterized by inflammation of the meninges, a surrounding layers of the brain and spinal cord mostly caused by bacterial infection.[3] It is one of the epidemic-prone diseases associated with a cosmopolitan mode of distribution and seasonal variation.[4] Affected person may come down with an acute onset of fever, headache, and neck stiffness. Other symptoms like nausea, vomiting, increased sensitivity to light and altered consciousness may be observed in some patients. In neonate and younger children, fever, headache and neck stiffness may be absent or difficult to observed. However, they may present with irritability, vomiting, poor feeding and bulging of the anterior fontanelle. The commonest cause of bacterial meningitis are *Neisseria meningitidis, Streptococcus pneumoniae,* and *Haemophilus Influenza.[5] Neisseria meningitidis* (Meningococcus) is a leading cause of bacterial meningitis.[6] Differences in the polysaccharide capsule allow the definition of 13 serologically distinct meningococcal capsular groups, of which 6, designated A, B, C, X, Y and W135, are responsible for almost all cases of the disease.[7]

In Sub-Saharan Africa, especially areas located within the meningitic belt, the incidence of meningococcal meningitis can be as high as 1000 per 100,000 populations experiencing seasonal focal outbreak with recurrent large every 8-12 years for many decades.[4, 5, 8] The “African Meningitic belt” is a region of 26 countries extending from Senegal in the West to Ethiopia in the East with an estimated total population of about 500 million people.[9, 10] In Nigeria, the Meningitic belt covers all the 19 Northern states, including the federal capital territory. In recent, the belt has widened to include some Southern states, namely: Oyo, Cross River, Imo, Anambra, Enugu and Ebonyi States. A sharp decrease in the number of reported cases was demonstrated in countries where Men Afrivac has been introduced. However, serogroup replacement with serotype C was noted in the region, and this has posed a serious threat toward eliminating CSM epidemics in the meningitic belt of Africa.[11] The sequential outbreak of type C strain in Niger in 2014-2015 with more than 8500 cases and 550 deaths and in Nigeria, especially in the North-West and North-Eastern states of the country in two consecutive years, may suggest the emergence of a new strain.[9] The circumstances surrounding the frequent epidemic could be as a result of environmental factors such as dust concentration in the region, humidity and other climatic conditions.[4] Studies have shown that factors such as low socioeconomic status, immunological susceptibility, migration, behavioral factors, living in cramped and overcrowded accommodation are risk factors for epidemic meningococcal disease.[4, 8]

The integrated disease surveillance and response in Nigeria classify meningitis as one of the epidemic-prone diseases. The outbreak of the disease is detected through the case-based surveillance strategy where the cerebrospinal fluid sample is taken from each suspected CSM case.[12] Public health agencies in Nigeria led by the Nigeria Centre for Disease Control (NCDC), which is a parastatal of the Federal Ministry of Health (FMoH) and the National Primary Health Care Development Agency (NPHCDA), are supporting states in Nigeria, including Sokoto, for early detection of suspected meningitis cases, prompt reporting to higher levels and response during an outbreak of Cerebrospinal meningitis (CSM) for immediate public health control. We describe the characteristics of cerebrospinal meningitis cases in 2017 outbreak in Sokoto state, Nigeria.

METHODOLOGY

Sokoto state is located in the North-west geopolitical zone of Nigeria. It lies within the African meningitic belt with annual focal outbreaks of meningitis. The state was created in February 1976, and it is bordered to the north by the Republic of Niger, Kebbi state to the south-west and Zamfara state to the east. It has 23 local government areas, pre-dominantly rural (over 80%) with a land mass of 25,972km^2 (10,0282m), and with an estimated projected population of 5,155,973 using a population growth rate of 3.01 in 2017.[13] Sokoto state occupies the Sudan Savannah between latitudes 13^{0}01′48″ – 13^{0}06′06″ North of the equator and longitude 05^{0}14′55″ ⁻ 05^{0}16′00″ East of Greenwich, with an average annual temperature of 28.3° C (82.9° F) and an average humidity of less than 20%.[14] The annual rainfall ranges between 500mm – 1,300mm, it starts late May and ends in early October with a peak in August. The dry season is associated with hash climatic factors such as dust laden winds often accompanied by thick fog which usually starts in October and lasts up to May.

CSM is one of the priority diseases reported through the IDSR flat form in Nigeria, adopted by Sokoto State.[15] Information on suspected cases by the clinicians' flows from the health facility focal persons and report them immediately to the LGA disease surveillance and notification officers (DSNOs) designated in the PHC department, to the State DSNO, and then to the Federal Ministry of Health and Nigeria Center for Disease Control. Feedback goes in the reverse direction. However, all the health posts ensured that each suspected case in their catchment areas is linked to the treatment camps for investigation and treatment. The three designated treatment camps used during the outbreak were; Usmanu Danfodiyo University Teaching Hospital, Sokoto, The Specialist Hospital Sokoto and Murtala Mohammed Hospital, Sokoto. Case investigation forms were completed at the treatment camp, and CSF samples were collected for suspected cases. The initial serogroup confirmation was by rapid Pastorex agglutination tests. However, the remaining CSF sample from suspected cases was sent to the reference laboratory, where bacterial isolates, serogroup, and antimicrobial sensitivity testing were performed.

We conducted a secondary data analysis of CSM cases in the 2017 outbreak in Sokoto State from 7^{th} February to 24^{th} May 2017. Data on CSM cases and laboratory results from 7^{th} February to 24^{th} May, 2017 was obtained from the epidemiology and surveillance unit of the Sokoto State Ministry of Health. Standard case definitions were adapted from the WHO and NCDC as follows:[15]

Suspected CSM case: Any person in Sokoto, who presented with sudden onset of fever (>38.5°C rectal or 38.0°C axillary) and one of the following signs; neck stiffness, altered consciousness, vomiting, diarrhea and/or other meningeal signs including bulging fontanelle in toddlers during the period of outbreak.

Probable Case: Any suspected case with macroscopic aspect of CSF (turbid, cloudy or purulent; or with a CSF leukocyte count >10 cells/mm³); or with bacteria identified by gram stain in CSF. In infants, CSF leukocyte counts >100 cells/mm³, or CSF leukocyte count 10 – 100 cells/mm³ and either an elevated protein (>100 mg/dl) or decreased glucose (<40 mg/dl) level during the period of the outbreak in Sokoto.

Confirmed Case: Any suspected or probable case in Sokoto that is laboratory confirmed by culturing or identifying (i.e. by polymerase chain reaction, immune - chromatographic dipstick or latex agglutination tests) either of *Neisseria meningitides, Streptococcus pneumonia or Haemophilus influenza* type b in the CSF during the period of the outbreak.

We retrieved data in Microsoft Excel. Important variables were sorted, extracted and cleaned from the excel sheet. Variables such as age, sex, place of residence, number of cases, date of onset, vaccination status, CSF sample collected, CSF laboratory result and pathogen identified were analyzed. We used Microsoft Excel 2016 and SPSS version 23 to analyze the data for frequencies, proportions, cross-tabulations and chi-square test to find associations between variables, estimated odds ratios (OR) and 95% confidence intervals (CI) to identify factors associated with outcome among cases. Binary logistic regression analysis was done to identify independent predictors of death among CSM cases. Ethical approval was obtained to use the data from the ethical committee of the state Ministry of Health Sokoto, Nigeria with reference number SKHREC/041/2021. Confidentiality of subjects was maintained by excluding all identifying information such as name and address from the analysis. We ensured that a pass worded computer was used in accessing the data by the principal researcher.

RESULTS

The analyses identified many missing data fields on the data template. Information on age, sex, LGA of residence, date of onset of disease, CSF specimen taken and outcome of cases were complete. Whereas, variables such as vaccination status had very few missing data (0.7%), results for either positive or negative had 97.0% missing data, results on serotype had 99.0% missing data and variable for the type of test conducted had 99.1% missing data.

A total of 4969 CSM cases were recorded with 283 deaths. The overall case fatality rate was 5.7%, and urban LGAs had the highest CFR (5.8%). The cumulative attack rate was 96.4 per 100,000 populations in the state. The highest proportion of cases was among ≥ 15-year age group 2063 (41.5%), and males were more affected, 2843 (57.2%). Only about 80 (1.6%) of cases had a dose of CSM vaccine (Table 1).

Table 1: Characteristics of CSM cases, CFRs and Attack rates between February and May 2017 in Sokoto state

Variables	Number of Cases Frequency (%)	Number of Deaths Frequency (%)	CFR	Population	Specific Attack Rate
Age group (n = 4969)					**Age specific Attack rate per 100,000 population**
<5yrs	577 (11.6)	45 (15.9)	7.8	1,042,207	55.4
5-9yrs	1065 (21.4)	74 (26.1)	7.0	845,772	125.9
10-14yrs	1264 (25.4)	73 (25.8)	5.8	561,868	225.0
≥15yrs	2063 (41.5)	91 (32.2)	4.4	2,706,126	76.2
Sex (n = 4969)					**Sex specific Attack rate per 100,000 population**
Female	2126 (42.8)	110 (38.9)	5.2	2,560,754	83.0
Male	2843 (57.2)	173 (61.1)	6.1	2,595,219	109.5
Place of Residence (n = 4969)					
Urban	2116 (42.6)	123 (43.5)	5.8		
Rural	2853 (57.4)	160 (56.5)	5.6		
Vaccination status (n = 4932)*					
Not vaccinated	4852 (98.4)	281 (99.6)	5.8		
Vaccinated	80 (1.6)	1 (0.4)	1.3		
CSF Taken (n = 4969)					
No	4744 (95.5)	270 (95.4)	5.7		
Yes	225 (4.5)	13 (4.6)	5.8		
Total	4969	283	5.7	5,155,973	**Commutative Attack rate per 100,000 population = 96.4**

CFR = Case Fatality Rate; **CSF** = Cerebrospinal fluid; ***** Missing data on vaccination status = 37

There was a gradual rise in number of cases which started in week 6 and the highest peak was in week 15, 2017. There was a sharp decline in cases in the following week with another peak in week 17 of that same year. Throughout the epidemic, week 17 recorded more death as shown in Figure 1.

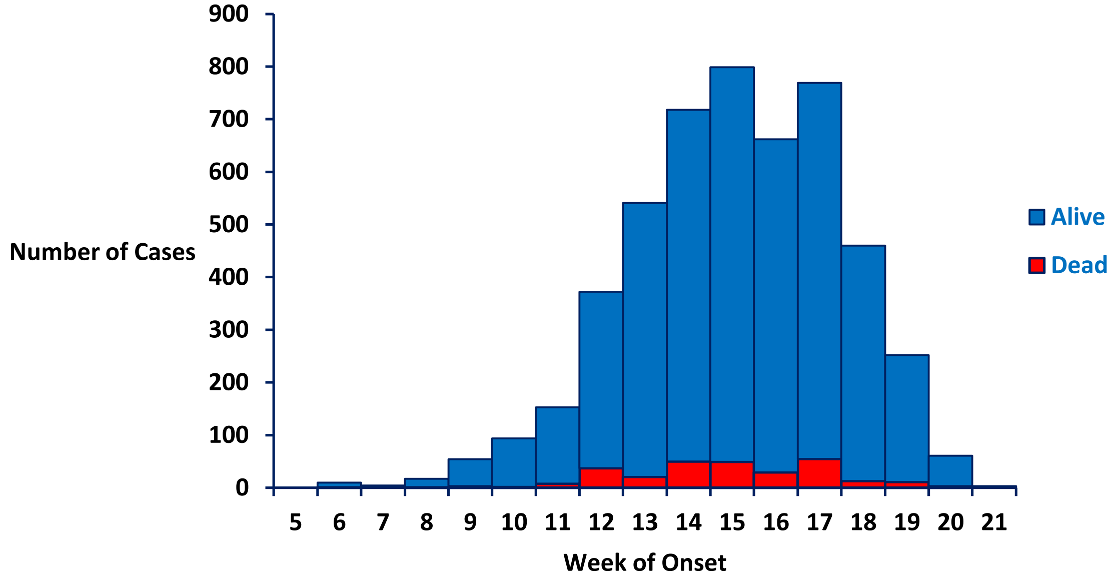

Figure 1: Distribution of CSM Cases and Death by Time Between February and May 2017 in Sokoto

The map in figure 2 shows the distribution of suspected cases during the outbreak, with Sokoto North 627 (12.6%) and Dange-Shuni 614 (12.4%) LGAs having the largest proportion of cases. Whereas, Gudu 6 (0.1%) and Shagari 33 (0.7%) LGAs with the lowest proportion of cases reported (Figure 2).

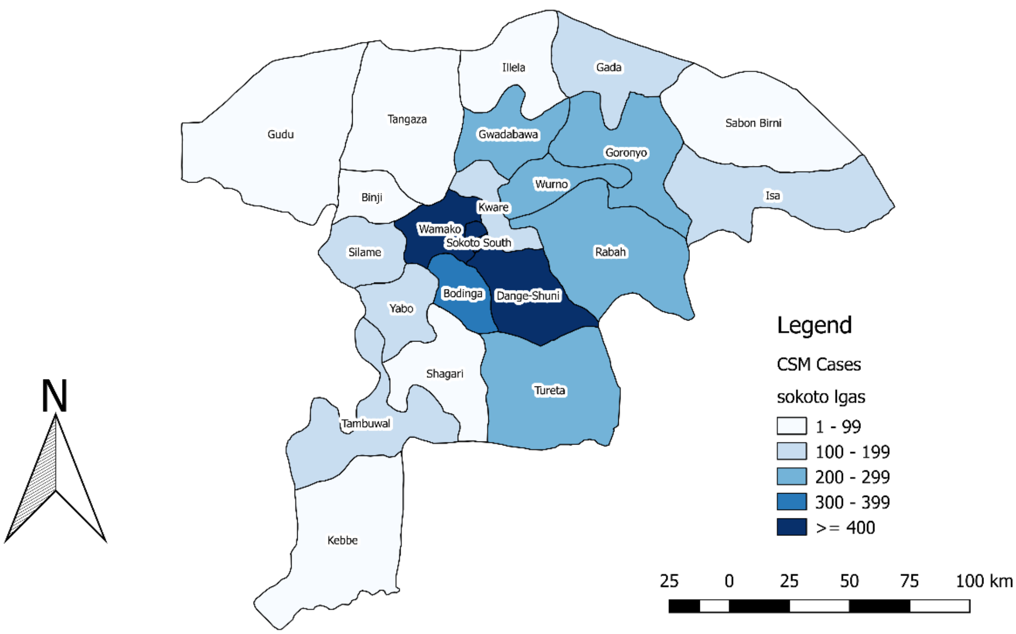

Figure 2: Map of Sokoto state showing the distribution of suspected CSM cases by LGA between February and May 2017.

Of the total 4969 suspected CSM cases, specimens were collected for only 225 (4.4%) cases, of which 58 (25.8%) were positive. Most 48 (82.8%) of the positive specimen were of NmC serotype, as shown in Table 2.

Table 2: Summary of CSF Specimen collected and pathogen identified among suspected CSM cases between February and May 2017 in Sokoto state

Variables	Frequency	Percentage
CSF Specimen Collected (n = 4969)		
Yes	225	4.4
No	4744	95.5
CSF Specimen Results (n = 225)*		
Positive	58	25.8
Negative	93	41.3
Pathogen Identified (n = 58)**		
Neisseria Meningitides serotype C	48	82.8
Streptococcus Pneumonia	1	1.7

*** Missing data on specimen results = 74; ** Missing data on pathogen identified = 9**

The proportion of death was higher among cases aged < 15 years (6.6%) as compared to those that were aged ≥ 15 years (4.4%), and the difference observed was statistically significant (χ^2 = 10.832, p = 0.001) (Table 3).

Table 3: Factors associated with outcome status among suspected CSM cases in Sokoto state between February and May 2017

Variables	Outcome		Test Statistics P value	OR (95% CI)
	Died Freq (%)	Alive Freq (%)		
Age				
< 15years	192 (6.6)	2714 (93.4)	χ^2= 10.832	1.53 (1.19 – 1.98)
≥ 15 years	91 (4.4)	1972 (95.6)	p = 0.001	
Sex				
Female	110 (5.2)	2016 (94.8)	χ^2= 1.880	1.18 (0.93 – 1.52)
Male	173 (6.1)	2670 (93.9)	p = 0.170	
Place of Residence				
Urban	123 (5.8)	1993 (94.2)	χ^2= 0.095	1.04 (0.82 – 1.32)
Rural	160 (5.6)	2693 (94.4)	p = 0.758	
Vaccination status				
Not vaccinated	281 (5.8)	4571 (94.2)	χ^2= 3.011	4.86 (0.67 – 35.03)
Vaccinated	1 (1.3)	79 (98.8)	p = 0.083	

Cases aged < 15 years are 1.5 times more likely to die than those aged ≥ 15 years, and the difference was statistically significant (aOR: 1.52; 95% CI= 1.18 – 1.97) as shown in Table 4.

Table 4: Predictors of Death among CSM Cases

Variables	aOR	95% CI	
		lower	Upper
Age (years) (< 15 vs ≥ 15*)	**1.52**	**1.18**	**1.97**
Sex (Male vs Female*)	1.15	0.89	1.47
Place of Residence (Urban vs Rural*)	1.04	0.76	1.23
Vaccination status Not vaccinated vs ≥ Vaccinated*)	4.59	0.63	33.20

aOR = adjusted Odds Ratio **CI** = Confidence Interval *** =** Reference group

DISCUSSION

In this analysis, we report the largest outbreak of NmC recorded in Sokoto state with 4969 confirmed and probable cases treated at different isolation camp in the state. This exceed the 1992 NmC cases reported between the 5th and 22nd epidemiological weeks of 2015 in Kebbi state.[16] It is also about 4289 more cases than the 680 NmC cases reported in Sokoto between February and June 2015 by Chow et al in 2016.[17] In this analysis and from previous studies, data show the continued increase in the number of meningitis cases, as it's the fifth year in a row from 2013 that similar outbreak of NmC strain has started in this region. This is not surprising as the WHO expert committee concluded in one of their meetings in Geneva that there is a high risk of the continuing expansion of meningitis due to the emergence of NmC, which was first reported in Nigeria in 2013.[18] Thus, increasing the justification for a mass vaccination campaign with a polyvalent vaccine containing NmC to prevent future spread of NmC.

Of the total cases whose CSF samples were collected, the result was missing in 32.9% of the samples, 41.3% of the samples turn out to be negative, while 25.8% of the samples tested positive, of which 82.8% were positive for NmC. The positivity rate of the samples collected could have been affected by the processes involved in the storage, transportation and testing procedures of samples at the reference laboratory. However, a more sensitive procedure like PCR may have likely yielded more positive results since all tested cases met the case definitions.

The highest proportion of cases was among ≥ the 15-year age group (41.5%), the finding is in concordance with a greater proportion of CSM cases reported in kebbi state in 2015,[16] and in Zamfara state where more cases were among the ≥ 15 years' age groups.[19] Possible explanation for this could be that youth are more likely to engage in social gatherings with their peers, which might serve as an avenue for the increased contact of a contagious person and susceptible individual, thereby increasing the risk of coming down with the disease. Therefore, the much higher presentation seen in this age group in recent epidemics may be worth considering as a problem to be investigated in future research. In addition, males were more affected (57.2%) than females, which could be explained by the fact that males were more likely to sleep in cramped, crowded and poorly ventilated rooms than the female counterpart.

This outbreak followed typical meningitis seasonal patterns in the African meningitis belt of which Sokoto is inclusive, usually began in the dry season following the Harmattan winds and stopped at the onset of the rainy season.[1, 2] According to the data obtained, the outbreak started in February 2017. It spread to all the 23 LGAs due to slow response by stakeholders in terms of public enlightenment campaigns, enhanced surveillance, proper diagnosis, and case management. The epidemiology of this CSM outbreak is closely related to climatic factors like air humidity, rainfall and dust, which are prevalent in the Sahel region of Africa.[20, 21] This is consistent with research findings that the optimal climate for transmission of the disease is the savannah climate south of the Sahel, with an annual precipitation index of 300–1,100 mm, extremely dry but warm winter seasons and a relatively abrupt onset of the rainy season.[22] In addition, outbreaks occur more frequent and severe in places with where population density is high.[23] These, may be attributed to the easy transmission of aerosols from one individual to another and the persistence of such aerosol within the same environment aiding more transmission.

The overall case fatality rate for 2017 outbreak (5.7%) was slightly above (4.0%) that was reported by Gana et, al in 2015 in Kebbi state,[16] and about half the CFR described for well managed cases (10% to 15%) in previous studies.[6, 24] This relatively lower case fatality rate could be attributed to health education, health promotion and social mobilization activities in the state through the use of mass media, training and retraining of health care providers and DSNOs on easy identification of cases through the use of pictorial case definition displayed at every health facility, improved case management and possibly strain of the organism. The CFR was higher among the age group ≤ 5 years (7.8%) and males (6.1%). Illela (15.1%) and Tangaza (14.8%) LGAs had the highest CFR, and this could be explained by the fact that the two LGAs are bordered Niger Republic with few trained health personnel and less health facilities compared to other LGAs.

Our study demonstrated a statistically significant association between age (<15years) and outcome (death). We did not find a statistically significant association between sex, those vaccinated and unvaccinated and outcome (death). However, the clinical significance of vaccination against meningitis has been documented in previous studies.[9, 25]

We were unable to carry out all but a few important analyses, especially the risk factors analysis for developing disease and outcome due to deficient data. Similarly, the data used to analyze and describe these cases and the outbreak was based solely on individuals who presented and treated at the state-based recognized case management facilities. Complete data related to NmC cases treated elsewhere were not available, and thus, suspected NmC cases are likely to have been undetected and unreported. However, the proportion of cases not included in our report is minimal as treatment is provided for free in the affected persons. Nevertheless, incomplete case ascertainment may mean that the characteristics of the cases and the outbreak described in this report are not perfectly representative of the entire NmC cases.

CONCLUSION AND RECOMMENDATIONS

Sokoto State outbreak of Cerebro-spinal meningitis in 2017 was huge and largely caused by NmC. Male and those aged 15 years and above contributed the highest proportions of cases. Cerebro-spinal fluid (CSF) specimens were collected from only a few of the suspected cases. Those aged less than 15 years might be at higher risk of dying from CSM and we therefore recommend that specific preventive interventions such as vaccination and awareness creation should target this age group to prevent future occurrence. In addition, the state should train more clinicians to conduct Lumbar puncture for CSF sample collection.

REFERENCES:

1. Agier L, Deroubaix A, Martiny N, Yaka P, Djibo A, Broutin H. Seasonality of meningitis in Africa and climate forcing: aerosols stand out. J R Soc Interface. 2013;10(79):20120814.

2. Pérez G-PC, Stanton M, Diggle P, Trzaska S, Miller R, Perlwitz J, et al. Soil dust aerosols and wind as predictors of seasonal meningitis incidence in Niger. Environ Health Perspect. 2014;122(7):679-86. .

3. Ahmad H. Inflammatory disease of the Central nervours system in:. Paediatrics and child health in a tropical region. 2nd ed. Owerri,Nigeria: African Educational services: African Educational Services; 2009. p. 525-70.

4. Salisu AB. Epidemic of Meningococcal Meningitis in Northern Nigeria Focus on Preventive Measures. Ann Afr Med. 2018;17(4):163-7.

5. Leimkugel J, Gagneux F, Pfluger S. An outbreak of serotype 1 streptococcus pneumonia meningitis in northen Ghana with features that are characteristic of nesseria meningitidis epidemics. J Infect, Dis. 2005;2:192-9.

6. Jennifer H, Andrew K, Charles W. Meningococcal Meningitis in: . Epidemiology and prevention of Vaccine preventable disease:. 13th ed. Public health foundation,: CDC; 2015.

7. Andrew J, Manish S. Neisseria meningitidis (Meningococcus) in. Nelson Textbook of Paediatrics 20th ed. Philadelphia: Elsevier; 2016. p. 1357-65.

8. Apanga P, Awoonor-Williams J. An Evaluation of Meningitis Surveillance in Northern Ghana. International Journal of Tropical Diseases & Health. 2016;12(2):1-10.

9. Obaro SK, Habib AG. Control of meningitis outbreaks in the African meningitis belt. Lancet Infect Dis. 2016;16(4):400-2.

10. W.H.O regional office. Standard operating procedures for enhanced Meningitis Surveillance. Geneva, Switzerland2009.

11. Idris M, Garba I, Abdularazaq G. Emergence and Control of epidemic meningococcal meningitis in sub-saharan Africa. pathogens and Global Health. 2017;111(1):146-8.

12. FMOH. Meningococcal Meningitis In:. Integreted Disease Surveillance and Response Technical Guidelines. 2013. p. 346-7.

13. National Population Commision (NPC) [Nigeria]. Population Disribution by Sex, State, LGA and Senatorial District. Abuja, Nigeria: The Federal Government Printer; 2010. Available from: https://www.google.com/url?sa=t&source=web&rct=j&url=http://catalog.ihsn.org/index.php/catalog/3340/download/48521&ved=2ahUKEwjMp7qY3uvsAhXXQEEAHT-oCjsQFjAAegQIARAB&usg=AOvVaw1TeZvj2pfYWGSfvo6_zMS2&cshid=1604590782086.

14. Division S. Ministry of Land and Housing Sokoto State. Sokoto2012.

15. FMoH, NCDC. Preparedness and Response to Cerebrospinal Meningitis Outbreak a Guide for Health Workers and Authorities in Nigeria. Abuja, Nigeria. October, 2017. p. 18.

16. Gana G, Badung S, Bunza A, Gidado S, Nguku P. Outbreak of cerebrospinal meningitis in Kebbi state, Nigeria. Ann Ib Postgrad Med. 2017;15(1):23-8.

17. Chow J UK, Bestman A, Kamau C, Caugant DA, Shehu A, et al. Invasive Meningococcal Meningitis Serogroup C Outbreak in Northwest Nigeria, 2015 - Third Consecutive Outbreak of a New Strain. PLoS currents. 2016;8.

18. WHO. Serogroup C in the Meningitis Belt: Facing the Challenges. Report of meeting held in Geneva. October, 2015.

19. Madu S, Abubakar U, Adeoye G. Epidemic of cerebrospinal meningitis in children at Federal Medical Centre Gusau, Zamfara state. Niger J Paed. 2013;40(2):169-71.

20. Molesworth AM, Thomson MC, Connor SJ, Cresswell MP, Morse AP, Shears P, et al. Where is the Meningitis Belt? Defining an area at risk of epidemic meningitis in Africa. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2002;96:242-9.

21. Molesworth AM CL, Connor SJ, Morse AP, Thomson MC. Environmental Risk and Meningitis Epidemics in Africa. Emerging infectious diseases. 2003;9(10):1287-93.

22. Cuevas L, Jeanne I, Molesworth A, Bell M, Savory E, Connor S, et al. Risk Mapping and Early Warning Systems for the Control of Meningitis in Africa. Vaccine. 2007;25:A12-A7.

23. Vusumuzi N, Tanya H, Nisha N, Angela M. Overcrowding and health in two impoverished surbubs of Johannesburg, South Africa. BMC Public Health. 2019;19(1358):1-8.

24. Robbins J, Schneerson R, Gotschlich E, Mohammed I, Nasidi A, Chippaux J, et al. Round Table - Meningococcal Meningitis in Sub-Saharan Africa: The Case for Mass and Routine Vaccination with Available Polysaccharide Vaccines. Bulletin of the World Health Organization. 2003;81(10):745.

25. Jacobsson S. Despite Successful Vaccines Neisseria Meningitidis Strikes Again. The Lancet Infectious Diseases. 2016;16(11):1212-3.