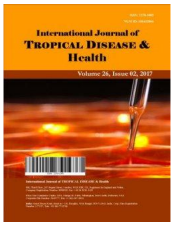

International Journal of TROPICAL DISEASE & Health

28(3): 1-11, 2017; Article no.IJTDH.38252
ISSN: 2278–1005, NLM ID: 101632866

Analysis of Bacterial Meningitis Surveillance Data, 2011-2015, East Mamprusi District, Ghana

Atasige Awin-Irigu Stephen[1,2*], Emmanuel Jejete Kandoh[1] and Adam Bukari[1,2]

[1]Ghana Health Service, University of Ghana, Accra, Ghana.
[2]Ghana Field Epidemiology and Laboratory Training Program, University of Ghana, Accra, Ghana.

Authors' contributions

This work was carried out in collaboration between all authors. Authors EJK and AB performed the data collection and statistical analysis. Authors AAIS and EJK managed the drafting of the manuscript. Author AAIS managed the literature searches. Author AAIS took responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2017/38252
Editor(s):
(1) Giuseppe Murdaca, Clinical Immunology Unit, Department of Internal Medicine, University of Genoa, Italy.
Reviewers:
(1) J. A. A. S. Jayaweera, Rajarata University of Sri Lanka, Sri Lanka.
(2) Soon Ae Kim, International Vaccine Institute, South Korea.
Complete Peer review History: http://www.sciencedomain.org/review-history/22700

Original Research Article

Received 20th October 2017
Accepted 3rd January 2018
Published 12th January 2018

ABSTRACT

Background: Globally meningitis mortality ranges between 2% and 30% and that of in Ghana it is estimated in range between 36% to 50%. The East Mamprusi district in Ghana reports cases due to its location in the meningitis belt. This study assessed the distribution of cases in the district by person, place and time from 2011-2015.

Methods: Meningitis surveillance data in the East Mamprusi district in northern Ghana from 2011-2015 was analyzed. Case based forms, laboratory tests, results and weekly line lists were reviewed. MS excel was used to analyze the data. We calculated the incidence of the disease and assessed the trend using the alert and epidemic thresholds. We determined the distribution of cases by persons history. Case fatality rates and prevalence of etiological agents were estimated.

Results: The Northern Region recorded a total of 961 suspected meningitis cases from 2011-2015. Numerous subjects are identified, amongst them 205 were confirmed of various organisms with 77 deaths. Between 2011 and 2015, 293 suspected and 83 confirmed meningitis cases were reported from East Mamprusi district. Males are representing 57.5% (216/376) of the total population. About

**Corresponding author: Email: atasigestephen@yahoo.co.uk;*

20% (75/376) of the cases were below one year. The median age of cases was 15 (range 1-77years). The highest numbers of cases were 36.7% (138) reported from Nalerigu Sub-district. Every year, meningitis incidence increased between January and May. The case fatality rate increased from 4.0% in 2012 to 13.3% in 2015. *N. meningitides, S. pneumonia* were the common etiological agents in the East Mamprusi District. In 2011 nearly 111 and in 2012, 101 cases were recorded respectively. However in 2012 there was a vaccination campaign in the district. Subsequently after the campaign, in 2013, 2014 and 2015 the number of cases declined from 73, 61 and 30 respectively.

Conclusion: Most of the cases were reported among the venerable age group of 1-15 years and from the district capital. There is an observed impact of a 2012 vaccination campaign in the district. There have been reported outbreaks over the period and most outbreaks were reported during the dry and windy season. Case fatality rate is on the increase though incidence is declining of N. meningitides which is the prevalent etiological agent isolated.

Keywords: Meningitis; surveillance; analysis; data; Mamprusi east district.

1. INTRODUCTION

Meningitis is an inflammation of the meninges. The meninges are the three membranes that cover the brain and spinal cord. Meningitis can occur when fluid surrounding the meninges becomes infected [1]. Viral and bacterial meningitis are contagious. They can be transmitted by coughing, sneezing, or close contact [1].

Bacterial meningitis remains a source of substantial morbidity and mortality in childhood [2]. Meningitis is a life threatening central nervous system infection that is prevalent worldwide [3]. Pneumococcal meningitis continues to be associated with high rates of mortality and long-term neurological squeal. The infection starts commonly by nasopharyngeal colonization by *Streptococcus pneumonia* [4].

1.1 Case Definitions

The following case definitions are used for suspected, probable and confirmed meningitis cases for meningitis surveillance in Ghana.

1.1.1 Suspected meningitis case

Any person with sudden onset of fever (>38.5ºC rectal or ≥38.0ºC axillary) and one of the following signs: neck stiffness, bulging fontanelle, convulsions, altered consciousness or other meningeal signs [5].

1.1.2 Probable meningitis case

Any suspected case with macroscopic aspect of Cerebrospinal fluid turbid, cloudy or purulent or with microscopic test showing Gram negative diplococcic, Gram positive diplococcic, Gram positive bacilli; or leukocyte count of more than 10 cells/mm3 [5].

1.1.3 Confirmed meningitis case

Isolation or identification of causal pathogen (Neisseria meningitides, Streptococcus pneumoniae, Haemophilusinfluenzae b) from the Cerebrospinal fluid of a suspected or can b e cultured by, Polymerase Chain Reaction or agglutination test [5].

1.2 Methods of Meningitis Diagnosis

Meningitis can be diagnosed based on a medical history, a physical exam and certain diagnostic tests.

- **Blood cultures:** Blood samples are placed in a special dish to see if it grows microorganisms, particularly bacteria. A sample may also be placed on a slide and stained (Gram's stain), then studied under a microscope for bacteria.
- **Imaging:** Computerized tomography (CT) or magnetic resonance (MR) scans of the head may show swelling or inflammation. X-rays or CT scans of the chest or sinuses may also show infection in other areas that may be associated with meningitis [6].
- **Spinal tap (lumbar puncture):** For a definitive diagnosis of meningitis, you'll need a spinal tap to collect cerebrospinal fluid (CSF). In people with meningitis, the CSF often shows a low sugar (glucose) level along with an increased white blood cell count and increased protein [6].

CSF analysis may also help identify which bacterium caused the meningitis. If viral meningitis is suspected, DNA-based test known as a polymerase chain reaction (PCR) amplification or a test to check for antibodies against certain viruses to determine the specific cause and determine proper treatment [6].

The causative organism varies with age, immune function, immunization status, and geographic region, and empiric therapy for meningitis is based on these factors [7]. The disease epidemiology is changing rapidly due to immunization practices and changing bacterial resistance patterns [7]. As a part of the United Nations Millennium Development Goal 4, the WHO has introduced a new vaccine policy to improve vaccine availability in resource poor countries [7].

1.3 Categorization of Countries by Risk of Meningococcal Disease

High risk countries are those with >10 cases/100,000 population) and/or> =1 epidemic over the last 20 years. Moderate risk countries are categorized as those with 2–10 cases/100,000 population per year. Low risk countries report with <2 case/100,000 population per year. Classification is based on country-specific epidemiological data with pre-defined cutoffs of high, moderate, and low endemicity categories as used by the WHO's Strategic [8]. The categorization was done by the Advisory Group of Experts on Immunizations (SAGE), in its recently updated recommendations on the use of meningococcal vaccines.

Meningococcal disease is found worldwide, with the highest incidence of disease found in the 'meningitis belt' of sub-Saharan Africa. In this region, major epidemics occur every 5 to 12 years with attack rates reaching 1,000 cases per 100,000 population. Other regions of the world experience lower overall rates of disease and occasional outbreaks, with annual attack rates of around 0.3 to 3 per 100,000 population [9].

Ghana experienced widespread Cerebral Spinal Meningitis (CSM) epidemics with high morbidity and mortality in 1984/85 and 1996/97 [10]. During the 1996/97 epidemic, about 19,000 people were affected with 1,200 deaths in almost all districts of the three northern regions of the country including the East Mamprusi district. Ghana has since experienced minor focal outbreaks each year during the dry season in the three regions which lie within the Meningitis belt of Africa [10]. Between 2011 and 2015, the Northern Region recorded a total of 961 suspected meningitis cases. Out of this number, 205 were confirmed of various organisms and out of that, 77 deaths were recorded. During December 9, 2015-February 16, 2016, a total of 432 suspected meningitis cases were reported to health authorities in the three northern regions. The Ghana Ministry of Health, with assistance from CDC and other partners, tested cerebrospinal fluid (CSF) specimens from 286 patients [11].

Accurate estimation of global, regional, and national burden meningitis in children is problematic for some reasons. The incidence of meningitis in populations can be adequately estimated generally only by longitudinal studies in the community. Such studies are not common in developing countries, where the burden of meningitis is higher, partly because such studies require a greater commitment of researchers and investors over a longer period [12].

Meningitis is one of the epidemic prone diseases in Ghana and it is being reported weekly, including zero reporting. Surveillance of this condition like other priority diseases such as measles and acute flaccid paralysis (AFP) is mainly passive. However, periphery services that generate, collate and transmit the data to higher levels do not conduct rigorous data analysis and hence sometimes overtaken by seasonal focal outbreaks. The analysis of a five-year meningitis data will help determine the magnitude, trend and distribution of cases to make recommendations for effective surveillance and control.

1.4 Data Flow

Meningitis cases are suspected on the field/community or in the health facility either through active or passive surveillance by applying the standard case definition. Data on suspected cases are recorded in case base forms by disease surveillance officers. Samples from suspected cases are collected for laboratory confirmation. Feedback on laboratory results are sent to the reporting health facility. Data on laboratory results are recorded in the case base forms. Data on cases are reported to the next level (region) and entered into the District Health Information Management System (DHIMS). The reporting facility also keeps records of cases. The DHIMS data cannot be altered after entry. The data is audited to ensure it is valid.

2. METHODS

2.1 Study Type

This study was a secondary data analysis of meningitis surveillance data in East Mamprusi district (EMD) between 2011 and 2015. All reported and recorded cases of meningitis over the five year period was analyzed.

2.2 Study Area

The East Mamprusi District (EMD) is one of the oldest districts in the Northern Region of Ghana with a land mass of 3,037 Km^2. It lies within the imaginary boundaries of the meningitis belt of sub-Sahara Africa that extends from Senegal in West Africa to Ethiopia in East Africa and experiences annual dry and dusty northeastern trade wind from November to March. Hence, it is one of the meningitis epidemic prone districts in Ghana. Projected population of the district was 139,606 in 2015 and majority of the people are subsistence farmers. The district is divided into five (5) health sub-districts namely Gambaga, Gbintri, Langbensi, Nalerigu and Sakogu. A sub-district has at least a health centre as the first periphery referral point and a number of Community-Based Health Planning and Services (CHPS) compounds manned by health personnel. Baptist Medical Centre (BMC) in Nalerigu – a mission health facility is the major health facility that serves the district and beyond including southern districts of the Republic of Togo.

2.3 Data Collection

We reviewed reported Integrated Disease Surveillance and Response (IDSR) case based forms, laboratory test results of Cerebrospinal Fluid (CSF) and weekly line lists of meningitis incidence in East Mamprusi District. A Microsoft Excel softcopy template for meningitis data was adopted from the East Mamprusi District Health Administration and modified for data abstraction. Demographic data captured included age, sex and residence (proxy: sub-district). Other variables collected included time of onset, etiological agents (from laboratory test results of CSF specimens), and treatment outcome and immunization status of cases. We interviewed the District Disease Control Officer on meningitis surveillance and on any record of outbreak between 2011 and 2015. The data was obtained from disease surveillance and health information departments of the East Mamprusi Health Directorate.

2.4 Data Analysis

We initially sorted the data set by date of onset and aggregated case incidence by epidemiological weeks. The data was entered into Microsoft Excel 2010 for the analysis. We further summed the incidence by month and year to observe monthly and annual trends respectively. We determined the weekly incidence of meningitis and compared with the alert and epidemic thresholds. When 5 cases per 100000 inhabitants are recorded in a population greater than or equals 30000 per week then incidence of the disease is at the alert threshold. However when it is 10 cases recorded per 100000 inhabitants for the same population per week, the incidence of cases is at the epidemic or outbreak threshold and an outbreak is declared and a definite response triggered. These thresholds are indicators for monitoring the weekly incidence of meningitis disease to identify possible outbreaks. In addition, we determined the annual incidence. Proportion of cases by age was calculated. Proportion of etiological agents isolated from cases was determined for the study period. We also calculated annual case fatality rates. The results were presented in tables and graphs.

2.5 Methods of Calculating Rates and Proportions

2.5.1 Identifying numerators and denominators

A simple count of cases does not provide all of the information needed to understand the impact of a disease on the community, health facility or district. Simple percentages and rates are useful for comparing information reported to the district. The first step in analyzing person data is to identify the numerator and denominator for calculating percentages and rates [13].

- The numerator is the number of specific events being measured (such as the actual number of cases or deaths of a given disease, for example the number of cases of Guinea worm that occurred during the year in school age children[13].
- The denominator is the number of all events being measured (such as the size of the population in which the cases or

deathsof a given disease occurred, or the population at risk [13].

Therefore the rates and proportions
= Numerator/denominator

2.6 Methods for Setting Thresholds

We used the Cumulative Sum (CUSUM) method to set seasonal thresholds for meningitis in the study area. The CUSUM was used originally in manufacturing to measure production quality in the 1950s. It is designed to detect sudden changes in the mean value of a given count. One of the newer forms is the C2 which require limited amounts of baseline data in weeks or months. These methods have been shown to be as sensitive and specific as methods requiring historical data [14].

C2 = Mean + 3* standard deviations of 7 past surveillance points prior to a 2-day lag.C2 is a common method used in the United States of America to analyze surveillance data [14].

3. RESULTS

3.1 Socio-demographic Distribution of Cases

Between 2011 and 2015, three hundred and seventy six (376) suspected and confirmed meningitis cases were reported from EMD, with males representing 57.5% (216/376) (Table 1). About 20% (75/376) of the cases were below one year. The median age of cases at one year and older was 15 (min 1 and max 77). The commonest affected age group across the study period was 1 to 15 years (Fig. 1). The incidence of meningitides in this age group increased from 2011 to 2013 and decreased in the subsequent two years. Averagely, meningitis incidence was low in the age group of 60 years and older (Fig. 1).

Nalerigu Sub-district recorded the highest incidence rates of meningitis for the period. The fall in rates was systematic in Gambaga and Gbintri Sub-districts from 2011 to 2014 (Fig. 2). The incidence rate of meningitis remained virtual same from 2011 to 2015 in the other sub-districts (Fig. 2).

3.2 Annual Trend of Meningitis Cases

A decrease in incidence was observed within the surveillance data period. Between 2011 and 2012, meningitis incidence decreased marginally from 89.1/100,000 population to 87.8/100,000 population in the East Mamprusi District. The annual incidence rate decreased sharply from 87.8/100,000 population in 2012 to 55.4/100,000 population in 2013. A continued downward incidence rates was observed in the subsequent two years but not comparable to the 2013 record (Fig. 3). In absolute figures, for 2011 and 2012,111 and 101 cases were recorded respectively. However in 2012 there was a vaccination campaign in the district. Subsequently after the campaign, in 2013, 2014 and 2015 the number of cases declined from 73, 61 and 30 cases respectively.

Table 1. Socio-demographic characteristics of meningitis cases, East Mamprusi District, Ghana, 2011 – 2015

Characteristic	Frequency	Proportion (%)
Gender		
Male	216	57.5
Female	160	42.5
Total	376	100%
Age/yrs		
< 1	75	20
1 – 15	157	41
16 – 30	77	21
31 – 45	35	9
46 – 60	14	4
≥ 61	18	5
Total	376	100%
Sub-district		
Nalerigu	138	36.7
Gambaga	68	18.1
Sakogu	62	16.5
Langbensi	60	16.0
Gbintri	48	12.8
Total	376	100%
Year		
2011	111	29.5
2012	101	26.9
2013	73	19.4
2014	61	16.2
2015	30	8.0
Total	376	100%

Socio-demographic data of meningitis cases, east Mamprusi district, 2011-2015

3.3 Monthly Trend of Cases

Every year, meningitis incidence increased between January and May (Fig. 4). In 2012 and 2013, meningitis cases were more than expected from March to May and February to March respectively. In addition, for these two years, cases increased after October.

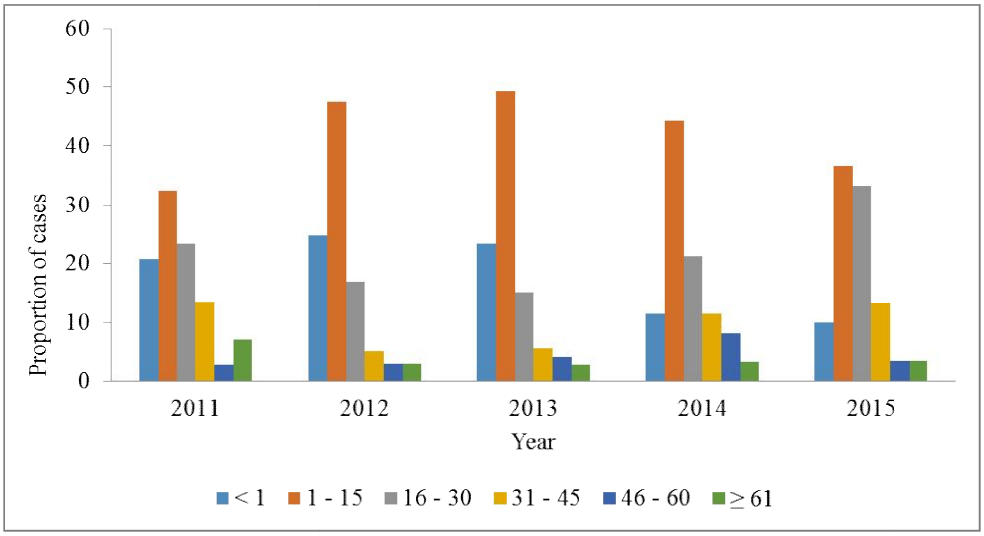

Fig. 1. Annual distribution of meningitis cases by age, East Mamprusi district, Ghana, 2011-2015

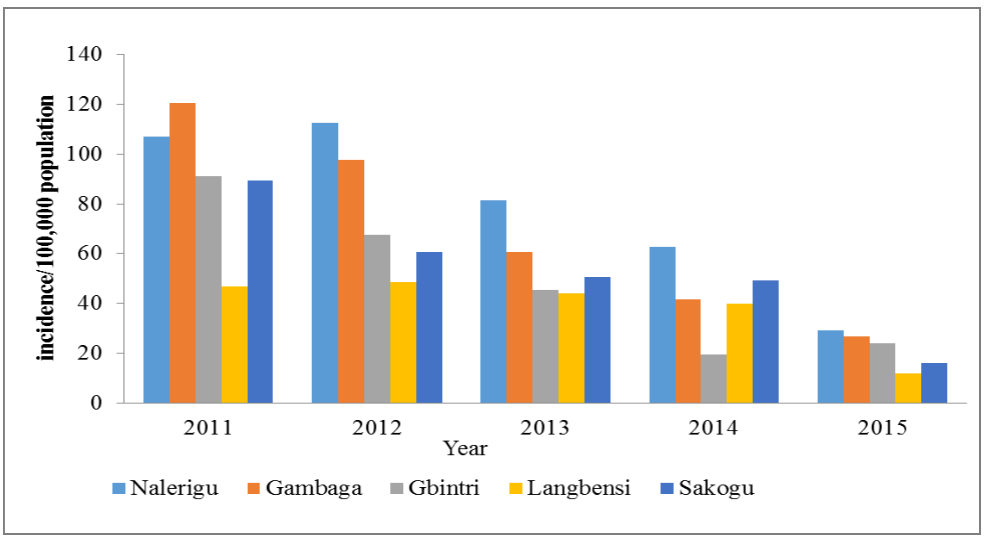

Fig. 2. Annual incidence rate of meningitis by sub-districts, East Mamprusi district, Ghana, 2011-2015

3.4 Trend of Cases by Weeks

In 2012, meningitis incidence (12 cases) exceeded the epidemic threshold in week 12.The weekly meningitis cases reached or exceeded the alert threshold at least twice annually with the exception of 2014. Averagely, cases increased between weeks 5 and 20 every year (Fig. 5). The population in the EastMamprusi District exceeds 30000, therefore 5 cases per 100000 inhabitants is the alert threshold and 10 cases is the epidemic threshold [13].

An alert threshold suggests to health staff and the surveillance team that further investigation is needed. Depending on the disease or condition, an alert threshold is reached when there is one suspected case(as for an epidemic-prone disease or for a disease targeted for elimination or eradication) or when there is an unexplained increase for any disease or unusual pattern seen over a period of time in weekly or monthly summary reporting [13].

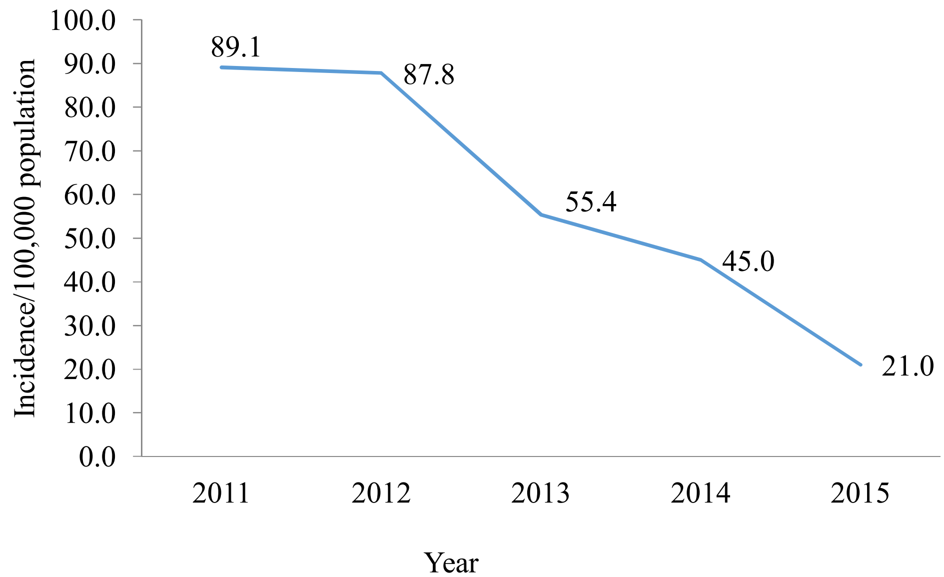

Fig. 3. Trend of annual incidence of meningitis, East Mamprusi District, Ghana, 2011-2015

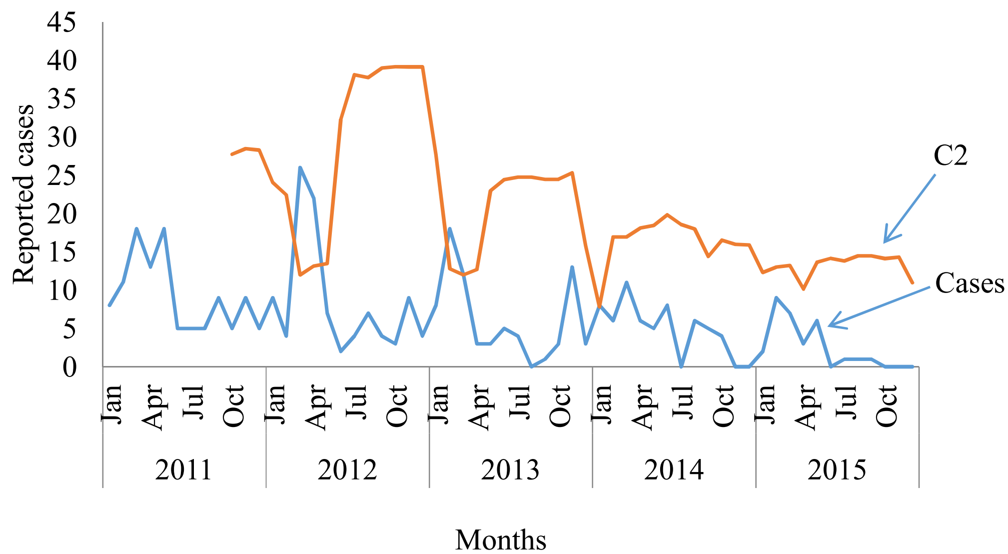

Fig. 4. Monthly meningitis incidence, East Mamprusi district, Ghana, 2011-2015

An epidemic/action threshold triggers a definite response. For meningitis it is 10 cases in a population. It marks the specific data or investigation finding that signals an action beyond confirming or clarifying the problem. Possible actions include communicating laboratory confirmation to affected health centers, implementing an emergency response such as an immunization activity, community awareness campaign, or improved infection control practices in the health care setting [13].

3.5 Trend of Case Fatality Rate (CFR)

Fig. 6. shows the annual CFR of meningitis cases in the East Mamprusi District. The highest CFR (13.3%) was recorded in 2015. In 2011, the CFR was 12.6% and decreased steeply to 4.0% the following year. CFR rose gradually in the subsequent two years after 2012, but a sharp increase occurred between 2014 and 2015 (6.6% and 13.3% respectively).

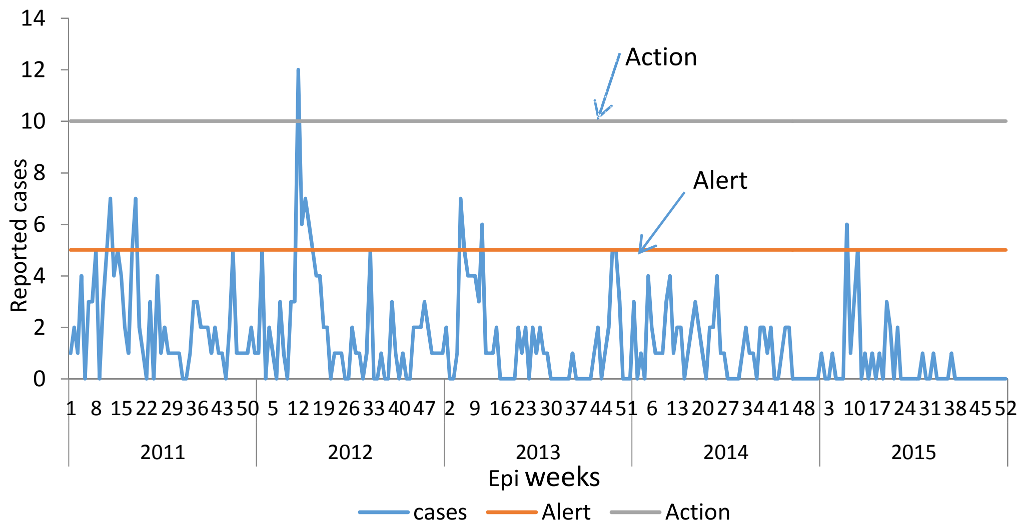

Fig. 5. Weekly reported suspected and confirmed meningitis incidence, East Mamprusi district, Ghana, 2011-2015

3.6 Distribution of Etiological Agents of Meningitis

As shown in the Fig. 7, organisms were not reported in most of the annual CSF specimens. *N. meningitides, S. pneumonia* and *Nm W135* were the common etiological agents in the East Mamprusi District. Streptococcal pneumonia was the commonest agent isolated in 2011. Neisseria meningitides was the prevalent microbial agent in the district between 2012 and 2014. No viral, parasitic and fungal agents were isolated from cases for the study period.

4. DISCUSSION

The study relied on secondary data for the five year period. Hence we were not in control of the data. Age group categorization and other variables are based on the existing data forms of the Ghana health service. Therefore based on the available data we analyzed, we discuss our results.

The age group 1-15 years were most affected because they are a venerable age group due to their low immunity. A study in Burkina-Faso showed that annual national incidence of meningococcal meningitis was highest among infants aged <1 years [15]. Pneumococcal bacteria are also spread by close contact with an infected person and by coughing, sneezing etc. However, in most cases they only cause mild infection, such as a middle ear infection (otitis media). Those with a poor immune system may develop a more severe infection such as meningitis [16].

Nalerigu sub-district is the capital and has a higher population. The relatively higher population density may be a factor for the higher incidence compared to the other sub-districts.

The continuous decline of cases can be attributable to improved vaccination coverage and control measures. In 2012, MenAfriVac conjugate vaccine was introduced in the district and children between 1 and 29 years were vaccinated. Subsequent years recorded a continuous decline in the number of cases. In Calgary Canada, a study on the impact of vaccination showed that invasive pneumococcal disease in children decreased from an average of 17 cases/100,000/year in 2000/2001 to 4 cases/100,000/year in 2015 after the vaccination program [17].

The monthly trend of cases shows peaks from February to May, possibly due to the weather conditions during this period when the infection can thrive and spread. In 2012 and 2013, there were outbreaks between "March and June" and February 2013 respectively. The system was able to detect the 2012 outbreak but failed in 2013. This could be due to the reduction in annual incidence or inadequate peripheral data analysis.

Though the incidence of cases has declined over the period, the case fatality rate is on the increase possibly due to poor case management and or late case reporting. Periodic stock out of materials (rapid kits and reagents) in first-line laboratories responsible for confirmation of causal agents might have resulted to delay in appropriate treatment and fatalities.

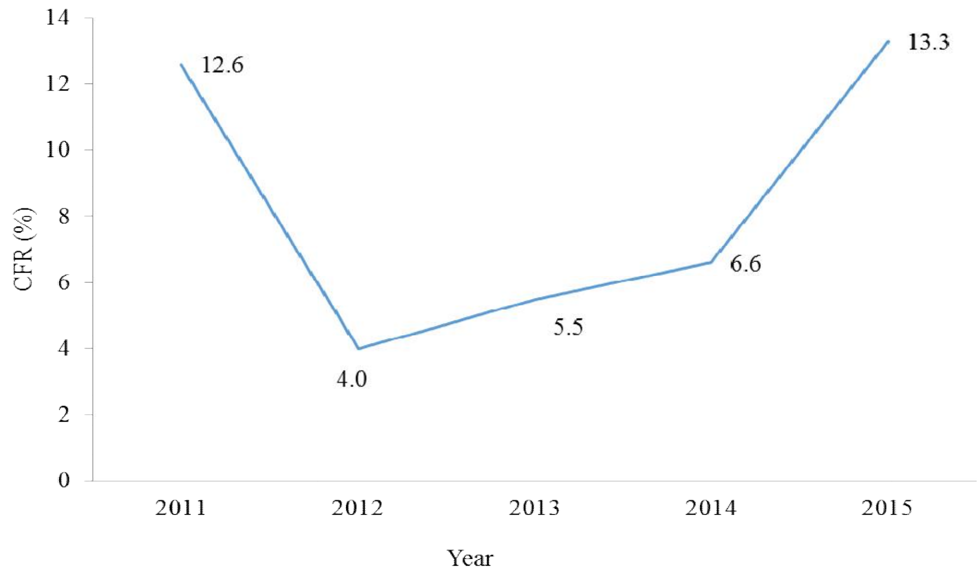

Fig. 6. Annual CFR of meningitis cases, East Mamprusi district, Ghana, 2011-2015

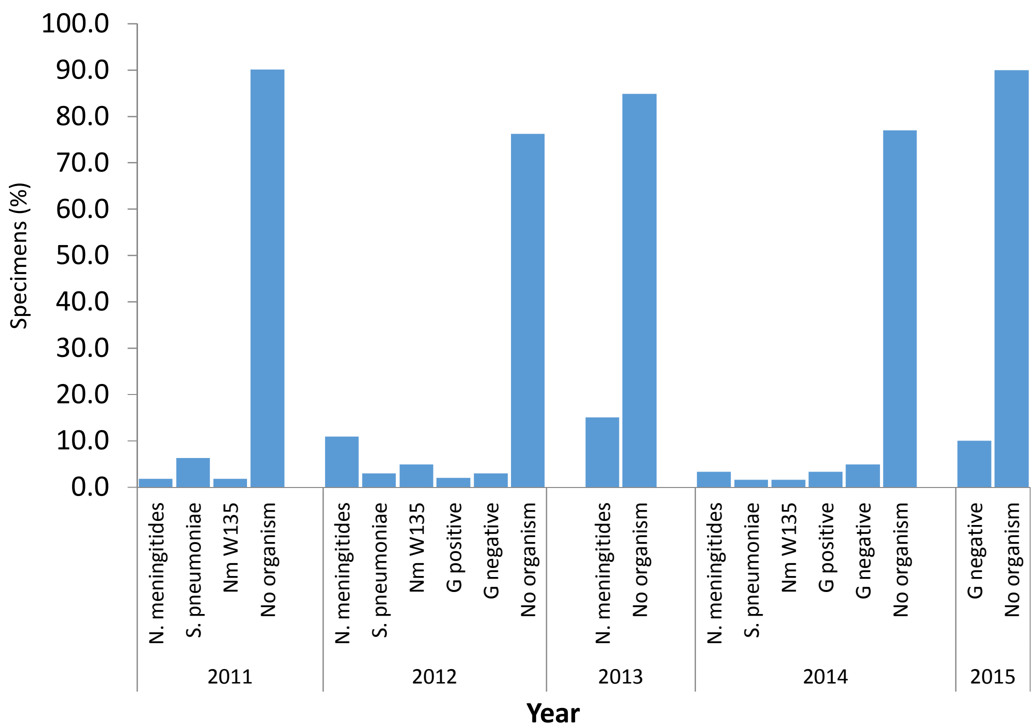

Fig. 7. Annual distribution of pathogens (latex, culture, PCR) in CSF specimens, EMD, Ghana, 2011-2015

N. meningitides was the prevalent etiological agent isolated from CSF specimens within the period (2011 – 2015). Other agents included *S. pneumonia* and *Nm. W135*. The poor understanding of meningitis causal agents' epidemiology in Ghana resulted to unexpected seasonal focal outbreaks in recent years. Also, CSF specimens were not totally typed for other strains of Neisseria due to inadequate logistics.

The population is vaccinated against the disease periodically especially during outbreaks. In addition, cases are isolated and managed in health facilities. Also all contacts of cases are closely monitored within the incubation period for symptoms and response. These actions are taken to prevent as well as control cases.

5. CONCLUSION

Most of the cases were reported among the venerable age group of 1-15 years and from the district capital. There is an observed impact of a 2012 vaccination campaign in the district. It has led to a decline of meningitis cases in the district. There have been reported outbreaks over the period and most outbreaks were reported during the dry and windy season. Case fatality rate is on the increase though incidence is declining. N. meningitides is the prevalent etiological agent that has been isolated.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

ACKNOWLEDGEMENT

We acknowledge the Ghana Health Service the Ghana Field Epidemiology training Program and the East Mamprusi District Health Directorate.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Brouwer MC, McIntyre P, Prasad K, van de Beek D. Corticosteroids for acute bacterial meningitis. Cochrane Database Syst Rev. 2015;(9):CD004405.
2. Theodoridou MN, Vasilopoulou VA, Atsali EE, Pangalis AM, Mostrou GJ, Syriopoulou VP, et al. Meningitis registry of hospitalized cases in children: Epidemiological patterns of acute bacterial meningitis throughout a 32-year period. BMC Infect Dis. 2007;7:101.
3. Yerramilli A, Mangapati P, Prabhakar S, Sirimulla H, Vanam S, Voora Y. A study on the clinical outcomes and management of meningitis at a tertiary care centre. Neurol India. 2017;65(5):1006–12.
4. Mook-Kanamori BB, Geldhoff M, van der Poll T, van de Beek D. Pathogenesis and pathophysiology of pneumococcal meningitis. Clin Microbiol Rev. 2011; 24(3):557–91.
5. Apanga P, Awoonor-Williams J. An evaluation of meningitis surveillance in Northern Ghana. Int J Trop Dis Health. 2016;12(2):1–10.
6. Mayo foundation for medical education and research. Meningitis Diagnosis and Treatment. 2017.
7. Agrawal S, Nadel S. Acute bacterial meningitis in infants and children: epidemiology and management. Paediatr Drugs. 2011;13(6):385–400.
8. Jafri RZ, Ali A, Messonnier NE, Tevi-Benissan C, Durrheim D, Eskola J, et al. Global epidemiology of invasive meningococcal disease. Popul Health Metr [Internet]. 2013;11(1). Available:http://pophealthmetrics.biomedcentral.com/articles/10.1186/1478-7954-11-17[cited 2017 Sep 29]
9. Wilder-Smith A. Meningococcal disease: Risk for international travellers and vaccine strategies. Travel Med Infect Dis. 2008; 6(4):182–6.
10. Minister briefs MP's on meningitis situation in Ghana; 2016. NewsGhana.com.Gh.
11. Aku FY, Lessa FC, Asiedu-Bekoe F, Balagumyetime P, Ofosu W, Farrar J, et al. Meningitis outbreak caused by vaccine-preventable bacterial pathogens — Northern Ghana, 2016. MMWR Morb Mortal Wkly Rep. 2017;66(30):806–10.
12. Lukšić I, Mulić R, Falconer R, Orban M, Sidhu S, Rudan I. Estimating global and regional morbidity from acute bacterial meningitis in children: Assessment of the evidence. Croat Med J. 2013; 54(6):510–8.

13. WHO and CDC. Integrated Disease Surveillance and Response in the African region 2nd edition; 2010.
14. Tokars JI. Enhancing time-series detection algorithms for automated biosurveillance. Emerg Infect Dis. 2009;15(4):533–9.
15. Diallo AO, Soeters HM, Yameogo I, Sawadogo G, Aké F, Lingani C, et al. Bacterial meningitis epidemiology and return of *Neisseria meningitidis* serogroup A cases in Burkina Faso in the five years following MenAfriVac mass vaccination campaign. PloS One. 2017; 12(11):e0187466.
16. Ananya Mandal. Meningitis causes. News medical; 2017.
17. Ricketson LJ, Conradi NG, Vanderkooi OG, Kellner JD. Changes in the nature and severity of invasive pneumococcal disease in children, Before and after the 7-Valent and 13-Valent pneumococcal conjugate vaccine programs in Calgary, Canada. Pediatr Infect Dis J; 2017.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/22700