Predictive Signs and Symptoms of Bacterial Meningitis Isolates in Northern Ghana

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ABSTRACT

Objective: Cerebrospinal Meningitis (CSM) is a public health burden in Ghana that causes up to 10% mortality in confirmed cases annually. About 20% of those who survive the infection suffer permanent sequelae. The study sought to understand the predictive signs and symptoms of bacterial meningitis implicated in its outcomes.

Materials and methods: Retrospective data from the public health division, Ghana Health Service (GHS) on bacterial meningitis from 2015 to 2019 used for this study. A pre-tested data extraction form was used to collect patients information from case based forms kept at the disease control unit from 2015 to 2019. Data were transcribed from the case based forms into a pre-designed microsoft excel template. The data was cleaned and imported into SPSS version 26 for analysis.

Results: Between 2015-2019, a total of 2446 suspected bacterial meningitis cases were included in the study. Out of these, 842 were confirmed. Among the confirmed cases, males constituted 55.3%. Children below 14 years of age were most affected (51.4%). The pathogens commonly responsible for bacterial meningitis were *Neisseria meningitidis* and *Streptococcus pneumoniae* with their respective strains especially Nm W135, Nm X, Spn St. 1 and Spn St. 12F/12A/12B/44/4 being responsible for most of the confirmed cases. The presence of neck stiffness (AOR=1.244; C.I=1.026-1.508), convulsion (AOR=1.338; C.I=1.083-1.652), altered consciousness (AOR=1.516; C.I=1.225-1.876) and abdominal pains (AOR=1.404; C.I=1.011-1.949) or any of these signs and symptoms poses a

higher risk for testing positive for bacterial meningitis cases adjusting for age.

Conclusion: Patients presenting one and/or more of these signs and symptoms (neck stiffness, convulsion, altered consciousness and abdominal pain) have a higher risk of testing positive for bacterial meningitis adjusting for age.

INTRODUCTION

Bacterial meningitis is one of the most prevalent public health diseases affecting approximately 1.7 million people with roughly 170,000 deaths yearly in the world's population [1]. It remains one of the most serious kinds of meningitis known to attack the focal sensory system in people. The four main causes of acute bacterial meningitis are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Streptococcus agalactiae*. The most prevalent strains remain to be *Neisseria meningitides* serogroups A, B, C, W135 and Y, *Streptococcus pneumoniae* serotype St 1, St 14, St 19A and *Haemophilus influenza* type b. Bacterial meningitis is a substantially a more serious disease and more likely to cause death compared to viral meningitis and its 100% lethal if untreated [2]. Survivals of bacterial meningitis can experience the ill effects of genuine neurological confusions for instance, deafness, visual deficiency, mental and scholarly disability which frequently is endured over the lifetime of the person [3]. A key factor that contributes to this high morbidity is our incomplete understanding of the pathogenesis of the disease resulting in it being one of the leading causes of mortality in the world due to its mode of transmission [4]. The African Meningitis Belt (AMB) consists of 26 nations extending between Senegal toward the west to Ethiopia in the east. These nations are known for having a high yearly incidence of bacterial meningitis [5].

It is estimated that, frequency rates during pandemics have reached as high as 100 cases-1000 cases for every 100,000 population which are remarkably high rates for an obtrusive bacterial infection. The case fatality rates ranges from 6.6%-10.0% and about 30%-50% of the survivors sustain neurological sequelae [6].

In Ghana, *Neisseria meningitidis*, *Streptococcus pneumonia* and *Haemophilus influenzae* are the most common species found around the meningitis belt spanning from Brong Ahafo through to upper east regions [7]. Bacterial meningitis is a public health problem in Ghana contributing to the high burden of disease and can cause mortality up to 10% of the victims yearly [7]. Approximately 20% of the people who get the infection experience disorders or neurological sequelae [1]. The review pointed toward giving quantitative evaluation of the prescient signs and symptoms of bacterial meningitis in Ghana and to give results that are summed up over the entire ghanaian populace.

MATERIALS AND METHODS

Study design

This was a retrospective, cross-sectional study conducted using a consolidated database from the disease control and surveillance unit and the zonal public health laboratory, Tamale-Ghana. The study was an experimental design that sought to identify the association between sign and symptoms of bacterial meningitis. The study was quantitative design that involves capturing of data using case investigation forms.

Study setting

The study data covered all the districts and regions in northern Ghana. The population of Ghana is 30,800,000 with the northern zone having an 8,237,660 population [8]. The northern zone of Ghana consists of northern region, upper east, upper west, Brong Ahafo and some part of volta region. The study was carried out at the Zonal Public Health Reference Laboratory (ZPHRL), Tamale-Ghana. The facility is a reference laboratory for bacterial meningitis in Ghana and West Africa which serves as the reference public health laboratory for the northern zone of Ghana.

Study population

All patients who presented with signs and symptoms suggestive of bacterial meningitis per the Ghana Health Service case definition for bacterial meningitis were included in the study. All samples collected across the country were brought to the ZPHRL for RT-PCR testing and or confirmation.

Case definition

The study classifies the cases according to the clinical case presentation, laboratory criteria for diagnosis and case identification.

Clinical case definition: An illness with sudden onset of fever (>38.5°C rectal or >38.0°C axillary) and one or more of the following: neck stiffness, altered consciousness, another meningeal sign or petechial or purpureal rash [9]. In patients less than one year, suspect meningitis when fever accompanied by bulging fontanelle [9].

Laboratory criteria for diagnosis: Lumbar puncture was performed at peripheral facilities in the districts level, aliquoted and sent to the ZPHRL for RT-PCR analysis. Positive CSF rapid test (i.e. Latex agglutination test, Wellcogen test, Gram stain) or positive culture test for screening at district or health facility level and confirmed by RT-PCR test within 72 hours of disease presentation at the ZPHRL [9].

Case classification: Suspected case is that which meets the clinical case definition, probable case is a suspected case as defined (with or without positive rapid test results) or ongoing epidemic and epidemiological link to a confirmed case and confirmed case is a suspected or probable case with polymerase chain reaction positive outcome at the ZPHRL [9].

Outcome of cases: The outcome of cases in the study is defined by the RT-PCR results for each suspected case. The outcomes are binary in nature and are described as “negative” or “positive”.

Sample size determination

No sample size was determined as all suspected cases of bacterial meningitis were included in the study from 2015-2019.

Patient and public involvement

Data collected by the Ghana Health Service on patients information was investigated by clinicians and necessary data collected in a predesigned case investigation form by GHS. Patient information and laboratory outcomes were key in the findings and results. Patients were involved in the recruitment process but not with researcher since the

study was retrospective. Results and findings of the study will be made available to the Ghana Health Service, health promotion department to share the findings to communities during health promotion talks.

Data analysis

Data was extracted from the case reporting forms unto a pre-designed microsoft excel template. The data was cleaned twice and exported to SPSS Version 25, for analysis. Descriptive analysis was performed and presented in graphs and tables. A chi-square analysis was performed for associated signs/symptoms of bacterial meningitis whiles binary logistics regression model was adopted to determine the clinical signs and symptoms that are predictive of a person likely to be tested positive for bacterial meningitis using the five years retrospective data. The dependent variable remained to be the test outcomes for the Polymerase Chain reaction (RT-PCR) (Positive and Negative).

Inclusion criteria

All patients that fulfilled the case definition criteria for bacterial meningitis were included to the study as collated by the disease control and surveillance unit and the ZPHRL.

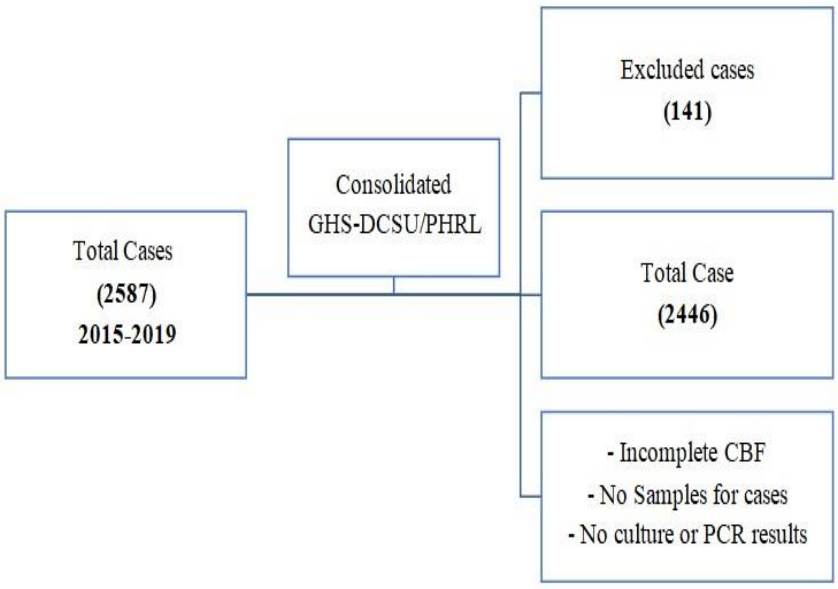
Exclusion criteria

All patients with inadequately filled case investigation forms, cases that were not having samples accompanying the case investigation forms and cases that had no culture and RT-PCR results.

Selection criteria summary

The diagram below gives a breakdown of the summary of the selection criteria and data screening processes as shown in Figure 1.

Figure 1. Represents case criteria summary for all suspected case.



RESULTS

A total of 2587 suspected cases were identified over the period with 2446 (94.6%) suspected cases included in the study; males were predominant (52.7%), the upper west and northern regions recorded the highest suspected cases within the study period (40.6%) with northern region having the highest positivity rate (Table 1). Majority of the study population were within 15 years-49 years (40.1%) but age group 5 years-14years with highest positivity rate (Table 1).

Table 1. Demographic characteristics of the cases recorded over the five years period.

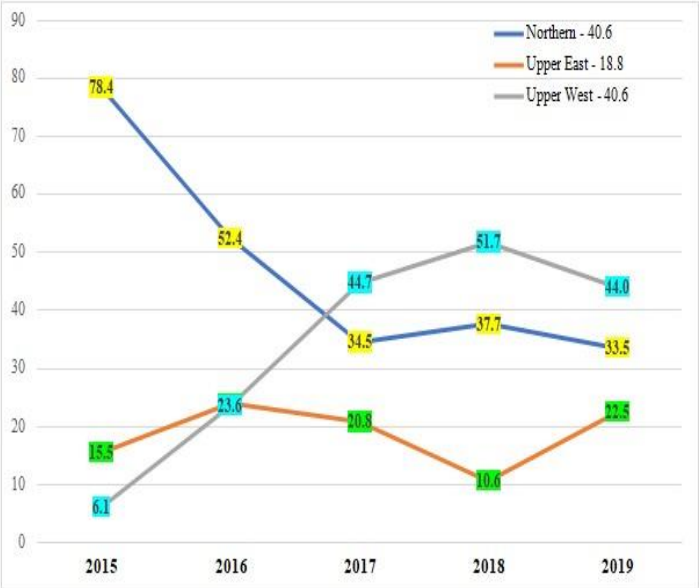
Indicator	Negative (n=1604)	Positive (n=842)	Case count (n=2446)	Percentage
Sex				
Male	822 (63.8)	466 (36.2)	1288	52.7
Female	782 (67.5)	376 (32.5)	1158	47.3
Regions				
Northern	566 (57.0)	427 (43.0)	993	40.6
Upper east	283 (61.5)	177 (38.5)	460	18.8
Upper west	755 (76.0)	238 (24.0)	993	40.6
Age grouping				
Under 5	316 (71.5)	126 (28.5)	442	18.1
5-14	366 (54.4)	307 (45.6)	673	27.5
15- 59	811 (69.7)	352 (30.3)	1163	47.5
60+	123 (73.2)	45 (25.8)	168	6.9
Vaccination (MenAfriVac or MenAC/WY)				
Vaccinated	160 (58.8)	112 (41.2)	272	11.1
Not vaccinated	153 (63.8)	87 (36.2)	240	9.8
Unknown	1291 (66.8)	643 (33.2)	1934	79.1

Regional distribution of suspected bacterial meningitis cases

The northern and upper west regions recorded the highest and lowest suspected cases of meningitis in 2015 and 2016 respectively in Figure 2 between 2017-2019. However, the upper west region consistently recorded more suspected cases than the other two regions (Figure 2).

Geographical distribution of confirmed cases across the five-year period denoted a general increase in confirmed cases of bacterial meningitis. The study revealed that over the five-year period, the northern and upper west regions reported the highest number of suspected cases 993 (40.6%) respectively whiles upper east had the least suspected cases with 466 (18.8%). Further analysis reveals that, out of these suspected cases across the three regions, the northern region had 50.7% of confirmed cases of bacterial meningitis compared to the upper east region which recorded a positivity rate of 21.0%. The UWR also recorded significant positivity rate of 28.3%.

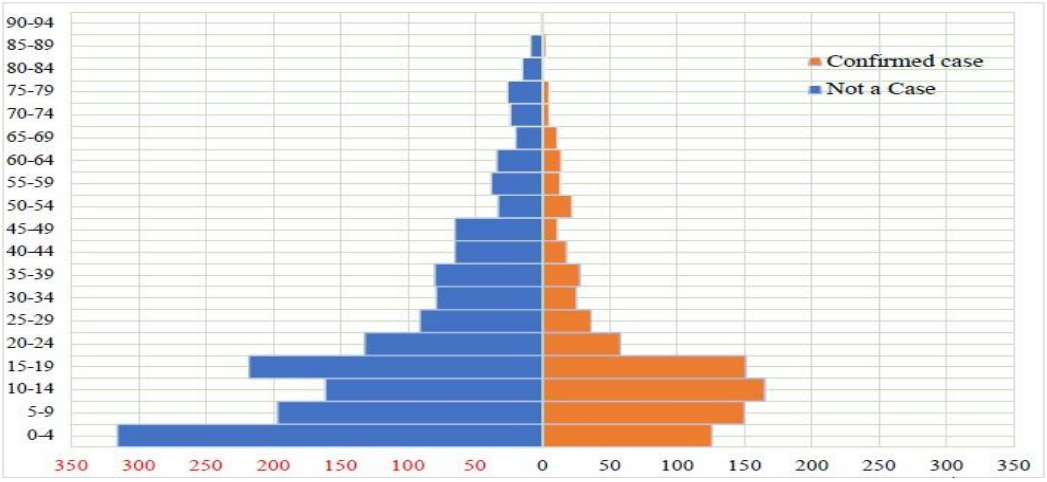
Figure 2. Regional counts of suspected cases across the years under review. **Note:** Northern-40.6; Upper east-18.8; Upper west-40.6.



Trend of confirmed bacterial meningitis cases from 2015-2019

Figure 3 graphically represent population of "not a case" and "confirmed case" RT-PCR outcomes for suspected bacterial meningitis cases across the northern zone of Ghana. Greater proportion of the population of confirmed and not a case is dense within the ages of 0 to 24 years. Positivity rates are also higher in the ages ranging from 0 to 24 years.

Figure 3. Population pyramid for patient bacterial meningitis RT-PCR result outcomes. **Note:** Confirmed case; Not a case.



The case incidence rate for the population at risk is 10.4775 per 100,000 populations within the study period with a 34.4% (842/2446) positivity rate. However, 2017 recorded the highest positivity rate of 35.7% (3.9210/100,000) and 2015 the lowest positivity rate of 6.9% (0.7915/100,000) shown in Table 2. Northern region recorded more

cases than the other two regions across the study period. Overall, the 0-14 years and 60+ year's age category had the highest incidence rate across the study period (Table 2).

Table 2. Shows the distribution of cases across the years (RT-PCR outcomes).

RT-PCR outcomes	2015 (n=58)	2016 (n=151)	2017 (n=301)	2018 (n=172)	2019 (n=160)	Total
Outcomes of suspected cases						
Yearly incidence	58	151	301	172	160	842
Percentage of cases	27.2	61.4	38.1	30.9	25	34.4
Incidence rate/100,000	0.7915	1.9896	3.921	2.1896	1.991	10.4775
Regional distribution of confirmed cases						
Northern	49	88	142	95	53	427
Percentage of NOR	84.5	58.3	47.2	55.2	33.1	50.7
Upper east	7	27	61	31	51	177
Percentage of UER	12.1	17.9	20.3	18	31.9	21
Upper west	2	36	98	46	56	238
Percentage of UWR	3.4	23.8	32.6	26.7	35	28.3
Age category of confirmed cases						
0–14	31 (53.4)	76 (50.3)	168 (55.8)	89 (51.7)	67 (41.9)	433 (51.4)
Incidence rate	0.2627	0.6441	1.4237	0.7542	0.5678	3.6695
15–59	25 (43.2)	59 (47.1)	111 (36.9)	76 (44.2)	81 (50.6)	352 (43.3)
Incidence rate	0.133	0.3138	0.5904	0.4043	0.4309	1.8723
60+	2 (3.4)	4 (2.6)	22 (7.3)	7 (4.1)	12 (7.5)	45 (5.3)
Incidence rate	0.1539	0.3077	1.6923	0.5385	0.923	3.4615

Note: Incidence rate calculated based on population dynamics of Ghana.

Signs and symptoms associated with bacterial meningitis

Fever (72.9%), neck stiffness (69.3%), headache (56.6%), Convulsion (22.9%) and altered consciousness (21.5%) were the most reported signs and symptoms for suspected bacterial meningitis. However, signs and symptoms that were associated with bacterial meningitis were neck stiffness (72.6%), fever (71.3%), headache (60.1%), convulsion (26.5%) and altered consciousness (26.0%). Notwithstanding that, neck stiffness (X^2=6.215; p<0.05), headache (X^2=6.233; p<0.05), convulsion (X^2=14.687; p<0.001), altered consciousness (X^2=15.033; p<0.001), abdominal pain (X^2=12.038; p<0.001), back pain (X^2=6.509; p<0.05) and kenning signs (X^2=6.523; p<0.05) were found to be statistically significantly associated with bacterial meningitis RT-PCR outcomes (Table 3).

Table 3. Shows the signs and symptoms presented by patients across the five years period.

Signs and symptoms	Present sign (N=2446)		Presence of BM (N=842)		X^2 (Yate's correction)	
	Frequency	%	Frequency	%	X^2	Sig.
Fever	1783	72.9	600	71.3	1.6146	0.204
Neck stiffness	1695	69.3	611	72.6	6.215[a]	0.013*
Headache	1384	56.6	506	60.1	6.233[a]	0.012*
Bulging fontanelle[b]	137	5.6	40	4.8	1.52	0.218
Convulsion	538	22	223	26.5	14.687[a]	0.000***
Altered consciousness	526	21.5	219	26	15.033[a]	0.000***
Breathing difficulty	158	6.5	53	6.3	0.024	0.878
Abdominal pains	197	8.1	90	10.7	12.038[a]	0.001***
Diarrhoea	300	12.3	114	13.5	1.761	0.184
Dizziness	264	10.8	84	10	0.765	0.382
Vomiting	327	13.4	125	14.8	2.228	0.136
Waist pains	130	5.3	53	6.3	2.228	0.136
Loss of appetite	247	10.1	73	8.7	2.65	0.104
Back pain	181	7.4	78	9.3	6.509[a]	0.014*
Cough	254	10.4	90	10.7	0.083	0.773
Kenning signs	272	11.1	113	13.4	6.523[a]	0.011*
Photophobia	268	11	83	9.9	1.423	0.233

Note : ***=0; **=0.001 ; *=0.01 ; .=0.1. [a]=Denotes significant chi-squared values. [b]=Denotes signs and symptoms assessed with/without children below 15 years of age.

Signs and symptoms predictive of bacterial meningitis

The statistical model for prediction of bacterial meningitis adjusting for age in the model indicates that suspected cases with neck stiffness (AOR=1.244; C.I=1.026-1.508) has a 24.4% more likely to test positive than others. Patients with convulsion (AOR=1.338; C.I=1.083-1.652), altered consciousness (AOR=1.516; C.I=1.225-1.876), and abdominal pains (AOR=1.404; C.I=1.011-1.949) has to greater risk of 33.8%, 51.6% and 40.4% respectively (Table 4).

Table 4. Shows the binary logistics model summary for COR and AOR in the equation.

Variables in the equation	95% C.I. for OR			95% C.I. for OR		
	COR(B)	Lower	Upper	AOR(B)	Lower	Upper
Fever	0.882	0.732	1.063	0.824	0.678	1.001
Neck stiffness	1.269	1.055	1.525	1.244[a]	1.026	1.508
Headache	1.245	1.051	1.475	1.165	0.972	1.395
Bulging fontanelle[b]	0.775	0.531	1.131	0.82	0.541	1.243
Convulsion	1.474	1.211	1.794	1.338[a]	1.083	1.652

Altered consciousness	1.485	1.218	1.81	1.516[a]	1.225	1.876
Breathing difficulty	0.959	0.682	1.349	1.012	0.701	1.461
Abdominal pains	1.674	1.248	2.246	1.404[a]	1.011	1.949
Diarrhoea	1.194	0.93	1.532	1.129	0.857	1.488
Dizziness	0.877	0.667	1.153	0.844	0.623	1.142
Vomiting	1.21	0.951	1.539	0.977	0.752	1.271
Waist pains	1.332	0.93	1.91	1.395	0.953	2.044
Loss of appetite	0.78	0.586	1.04	0.844	0.615	1.158
Back pain	1.488	1.095	2.022	1.22	0.879	1.694
Cough	1.051	0.801	1.38	0.969	0.715	1.313
Kenigns signs	1.409	1.089	1.822	1.204	0.909	1.595
Photophobia	0.839	0.638	1.103	0.776	0.569	1.058

Note: [a]=denotes statistically significant predictor of bacterial meningitis signs and symptoms. [b]=denotes signs and symptoms assessed with/without children below 15 years of age. Adjusted Odds Ratio for age ranges (0-14 and 15+).

DISCUSSION

The burden of bacterial meningitis is disproportionately distributed by place, time and age but nearly equally distributed by sex. Within the study period, a total of two thousand four hundred and forty six (2446) cases were recorded and tested by both culture and Real Time Polymerase Chain Reaction (RT-PCR) methods for pathogens responsible for bacterial meningitis. The trends of the suspected cases increased over the years with 2015 recording 8.6% of the cases to 25.9% in 2019. The results further revealed that 52.7% of the suspected cases were males. In addition, the RT-PCR testing confirmed 34.4% of the suspected cases as bacterial meningitis. It further showed that, 55.3% of the confirmed bacterial meningitis cases were males whiles 44.7% were females. It was worth noting that 2017 had the highest total case positivity rates of 30.7%, while 2015 had the least total case positivity rate of 8.6%. This finding clearly shows that males in all instances have higher rates compared to females and this could be as a result of population dynamics of the respective regions under the study where males to females ratio is estimated at approximately 93% [10]. Also, it could be as a result of stronger immune system in women than men against viruses and bacteria infections [11]. This finding is discordant with a similar study conducted by Kwambana Adams, et al. on pneumococcal meningitis outbreak and its associated factors in six districts of Brong Ahafo region, Ghana [12]. The researchers documented that 55.9% of the confirmed cases were females compared to 44.1% males. This disparity could be due to the study period within which both studies were conducted. Whilst our study stands a five-year period (2015-2019), the other was done within a year (2015-2016).

Geographical distribution of confirmed cases across the five-year period denoted a general increase in confirmed cases of bacterial meningitis. The study revealed that over the five-year period, the northern and upper west regions reported the highest number of suspected cases 993 (40.6%) respectively whiles upper east had the least suspected cases with 466 (18.8%). Further analysis reveals that, out of these suspected cases across the three regions, the northern region had 50.7% of confirmed cases of bacterial meningitis compared to the upper east

region which recorded a positivity rate of 21.0%. The UWR also recorded significant positivity rate of 28.3%. These findings are consistent with a study done by Codjoe and Nabies. The authors shared that the suspected and confirmed case of bacterial meningitis were highest in northern region and upper west regions within the meningitis belt in Ghana [13].

Meningitis cases were higher among younger age groups and adults below 44 years. This could be due to the increased likelihood of these groups of people participating in activities within overcrowded places such as schools, markets and other workplaces as well as type of settlement. The finding is in line with Amadu, et al. who had similar outcomes and trends in the demographic features of the cases [14]. The most suspected and confirmed cases of the bacterial meningitis in these regions remains among the 15 years–44 years age group with a total of 981 cases (40.1%). The confirmation of suspected cases by RT-PCR denoted that child within the 0-14 years age bracket had a total of 52.4% positivity rate compared to adults within the 15 years-60 years age group that had a positivity rate of 41.8% [14]. These outcomes might be as a result of the vulnerability of children to infectious diseases of which bacterial meningitis is not an exception. This supports the argument that children younger than 15 years of age accounts for majority of all infections across the world [15-19]. Our finding is also consistent with that of Nyarko who identified that 77.3% (761/980) of the confirmed meningitis cases were among children below the ages of 30 years in the upper west region [20].

In 2016 a total of 61.4% of the suspected cases were positive for bacterial meningitis compared to the other years. The number of confirmed positive cases over the period denoted an increased pattern from 2015 with 6.9% of the total positives to 35.7% in 2018. This pattern dropped sharply in 2019 to 19.0% indicating a significant decline in cases over the one year period. This patterns and trends seen over the period is in congruent with a study conducted on the US Centres for Disease Control and prevention's (CDC) surveillance data on bacterial meningitis from 1998 to 2003, where there was a significant reduction in the incidence of cases of bacterial meningitis cases [21]. The common signs and symptoms being neck stiffness (72.6%), headache (60.1%), convulsion (26.5%), altered consciousness (26.0%), abdominal pain (10.7%), back pain (9.3%) and kenning signs (13.4%) were associated with bacterial meningitis. However, binary logistics regression revealed that the presence of one or more of the following signs and symptoms; neck stiffness (AOR=1.244; C.I=1.026-1.508), convulsion (AOR=1.338; C.I=1.083-1.652), altered consciousness (AOR=1.516; C.I=1.225-1.876) and abdominal pains (AOR=1.404; C.I=1.011-1.949) as risk factors of confirmed bacterial meningitis cases. This aligns with little variation with an earlier publication by the CDC team in 2012 who found fever, headache, stiff neck, nausea, vomiting, photophobia, altered mental status remain as the major signs and symptoms of bacterial meningitis [22].

CONCLUSION

Bacterial meningitis continues to be an important cause of morbidity and mortality throughout the world, with differential risk among gender, age and geographic location. There is an increase in the rates of the disease pathogen over the period of the study. Children aged 0-14 years, males and northern region are the most affected. Neck stiffness, convulsion, altered consciousness and abdominal pains are risk factors associated with bacterial meningitis. We recommended that peripheral health facilities should be keen in the identification of predictive signs and symptoms with particular attention to associated risk factors identified in the study. This study could also inform

Ghana Health Service in the review of protocols stipulated for managing suspicion levels of clinicians in managing cases of bacterial meningitis.

ETHICAL CONSIDERATION

Ethical clearance for the study was sought from the kwame nkrumah university of science and technology ethical review board with a reference number of CHRPE/AP/469/20. Permission was also sort from the Regional Health Administration and the Zonal Public Health Laboratory with reference number of GHS/ZPHL/0014/20.

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DECLARATIONS

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Competing interests

The authors declare that they have no competing interests in the research study conducted.

Author contribution

The author contributed to the study conception and design. The data collection and analysis were performed by DKT. The first draft of the manuscript was written by DKT and DKT commented on previous versions of the manuscript. HD read and approved the final manuscript.

Data sharing statement

The data collected was retrospective data gotten from the Ghana Health Service for the purposes of the study. Data obtained was given the necessary permission and ethical consideration. The data was strictly guarded by policies and cannot be shared to any third party involved.

Ethics approval

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