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ORIGINAL ARTICLE

Seasonal Variation in Admissions of Bacterial Meningitis at a Tertiary Care Hospital: A Time Series Study using Wavelet Analysis

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ABSTRACT

Background: Bacterial meningitis is one of the most feared infectious diseases, being an important cause of death and long-term neurological disability. Various studies have observed seasonality of occurrence of bacterial meningitis most commonly in dry and cold seasons. Studies of seasonal variation contribute to understanding the etiology of infections, health-care planning for prevention, and rational use of hospital resources. **Objectives:** The objectives of the study were to know the seasonal variations and trend in the admissions of community-acquired acute bacterial meningitis in Karnataka Institute of Medical Sciences (KIMS) Hospital. **Methods:** A time series analysis by compiling monthly data of bacterial meningitis cases admitted in KIMS, Hubli, from the reports of medical records department for a period of 5 years from January 2014 to December 2018. **Results:** The peaks for hospitalizations were predominantly in March–May and even the seasonality for aggregate years occurs as peak effect in summer. Hospitalizations for bacterial meningitis showed a periodicity of 3–4 months in each year along with cyclical trend over the years studied. **Conclusion:** This study found evidence of seasonality for bacterial meningitis, thereby suggesting that hospitals should be prepared for providing clinical services round the year; however, more resources may be required during the peak months of March–May.

Key words: Bacterial meningitis, seasonal variation, tertiary care hospital, time series analysis, wavelet transform

INTRODUCTION

Time trends and fluctuations in occurrence have been observed in many diseases. Short-term fluctuations in the form of outbreaks and medium-term seasonal and cyclical fluctuations are commonly observed in infectious diseases. Different methods to study seasonality of diseases occurrence have been used such as comparison of disease occurrence between seasons, modeling by the use of a sine curve, and generalized linear models. Simple methods may overlook important seasonal peaks that would have been identified if more advanced methods had been applied. A recent and more advanced method like wavelet analysis has been used to study many diseases. In spite of all these advancements, cyclic variation is often neglected in both etiological and prognostic research and health services research.[1] Meanwhile, infectious diseases remain a major cause of mortality in the developing countries among which meningitis being the most dreadful.

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Meningitis is an inflammation of the thin lining that surround the brain and spinal cord, called meninges.[2] A variety of organisms, including different bacteria, fungi, or viruses, can cause meningitis.[3] However, bacterial meningitis is the most serious infection comparatively which leads to sudden onset of fever, headache, stiff neck, nausea, vomiting, and altered mental status, and can rapidly result in death. *Neisseria meningitidis*, *Streptococcus pneumoniae,* and *Haemophilus influenzae* are the leading causes of bacterial meningitis worldwide.[4]

Globally, meningitis is one of the most feared infectious diseases, and it can result in a devastating impact on the entire

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population in case of any outbreaks.[5] The risk of secondary cases of meningococcal disease among close contacts of someone with the disease (i.e. household members, day-care center contacts, or anyone directly exposed to the patient's oral secretions) is high. Antimicrobial resistance has been identified for all three bacterial meningitis pathogens, which has affected the treatment of patients and chemoprophylaxis of close contacts.[2]

N. meningitidis meningitis is commonly seen in children <5 years of age and in adolescents. *N. meningitidis* can also cause a severe bacteremia, called meningococcemia.[2] In case of *H. influenzae* meningitis, which is rare in adolescents and adults, the incidence rates are highest in children <5 years of age, with an estimated incidence rate of 31 cases/100,000 in young children.[6] Meningitis due to *S. pneumoniae* occurs most commonly in the very young and the very old, with an estimated incidence rate of 17 cases/100,000 populations in children <5 years of age.[7] Although vaccination programs have been implemented in many countries and there has been a considerable impact on the disease,[8] more than 1.2 million cases of bacterial meningitis are estimated to occur each year.[9] Incident cases globally increased from 2.5 million (95% CI 2.19–2.91) in 1990 to 2.82 million (95% CI 2.46–3.31) in 2016.[10] The case-fatality rate is high for all three pathogens (ranging from 5% to 50%) and neurological sequelae occur in up to 50% of survivors.[9]

For reducing the incidence of bacterial meningitis, it is important to understand its epidemiological behavior completely. The frequency of the different etiologic organisms of bacterial meningitis and their fatality rates varies with age, region, and country. India is endemic for meningitis caused by these organisms. Various studies have observed seasonality of occurrence of bacterial meningitis most commonly in dry and cold seasons. This may be because of changes in human behavior throughout a year and also annual cycles in the appearance/virulence of pathogen which are secondary to annual climatic cycles that affect temperature, rainfall, and humidity.[11] Despite a strong seasonality, the temporal dynamics of bacterial meningitis, including the seasonality, interannual variation, and secular trends are poorly understood. Studies of seasonal variation contribute to understanding the etiology of infections, health-care planning for prevention, and rational use of hospital resources.[1] Hence, this study was conducted to know the seasonality in admissions of cases of bacterial meningitis.

METHODS

Database Compilation

In the study, a time series analysis of bacterial meningitis had been developed by compiling monthly data for a period of 5 years from January 2014 to December 2018. After prior permission, the data were obtained from the reports of Medical Records Department in Karnataka Institute of Medical Sciences (KIMS), Hubli. The data of cases of all ages and both genders were included. While collecting the data, only confirmed cases of bacterial meningitis had been considered, thereby excluding any other varieties. Hence, for enlisting the specific categories, the codes of 10th Revision of International statistical Classification of Diseases and related health problems (ICD-10),[12] a medical classification list by the WHO, were used. The study data included the total number of patients admitted in the hospital and total number of bacterial meningitis cases falling under the codes G-00 and G-01 as per ICD-10.[12]

Description of the Concepts Used in the Study

Seasonal variation/seasonality is defined as a periodic variation in the occurrence of disease/disease outcome with calendar time.[1] The occurrence of disease can be measured either as a count of cases per unit time, a rate that relates cases to a denominator of person time, or an incidence proportion that relates cases to the number of persons at risks.[1] With a single annual cycle, there will be a single peak in occurrence during the year, and ordinarily a single trough, or time of low occurrence, often assumed to be 6 months from the peak. The amplitude of seasonal pattern is defined as the difference in occurrence between the peak and trough times.[1]

Statistical Analysis

Data collected were entered into Microsoft Excel and converted into time series data. Monthly data for bacterial meningitis for 5 years were standardized for 1 lakh in-patients during the same time, that is, 2014–2018. Data were tested for seasonality by Edward's model,[13] using Episheet,[14] which is freely available Excel sheet for various statistical calculations. Time series data were decomposed using local polynomial regression, Wavelet analyses was performed, and a wavelet power spectrum was plotted using the package WaveletComp[15] in R Software version 3.1.[16]

RESULTS

The study database contained the total number of bacterial meningitis cases admitted in KIMS, Hubli, over a period of 5 years from 2014 to 2018. These data have been standardized for 1 lakh in-patients for further analysis which are shown in Table 1.

The time series plot shown in Figure 1 shows repetition of a pattern every year. Here, exactly three peaks can be observed in each year and these peaks correspond in a similar fashion suggesting increase in the number of bacterial meningitis cases in specific months of a year.

It is also observed that there is an increased frequency in the number of bacterial meningitis cases in April comparatively which can be appreciated in Figure 2 with radial plot where the centroid is deviated toward April.

Seasonality

Edward's model[12] is based on converting monthly data into a simple sinusoidal harmonic curve. In Figure 3, "μ" is the mean number of meningitis cases over the 12-month cycle, "θ" is phase angle indicating month of maximum frequency of meningitis cases, and "α" is the amplitude of the seasonal effect, interpreted as the increase in number of cases over the mean during θ. To identify the seasonality, a null hypothesis that amplitude (α) = 0 (no seasonality) was tested using Edward's test.

Table 2 illustrates the estimated peak-to-low ratios, including 95% confidence intervals, when the entire study period was summed up. The peak day for consecutive 3 years from 2015 to 2017 was in summer season. However, in 2014 and 2018, the disease did not follow the peak in the same seasons.

Table 1: Actual and adjusted number of cases of bacterial meningitis for 5 years (2014–2018)

Months	Adjusted number of cases (per lakh)	95% CI
January	187	123–250
February	231	158–303
March	227	158–297
April	268	193–343
May	201	138–264
June	196	132–261
July	188	127–248
August	209	145–274
September	178	117–238
October	193	133–254
November	166	110–223
December	155	97–214

Table 2: Seasonal distribution (Edward's model) of bacterial meningitis cases for 5 years (2014–2018)

Year	Peak to low ratio	95% CI	Peak day	Theta	Alpha	*P*-value (Edward's test)
2014	1.175	1.054–1.31	October 23	292	0.0804	<0.05
2015	1.698	1.513–1.905	March 19	77	0.2586	<0.05
2016	1.285	1.154–1.432	April 19	108	0.1249	<0.05
2017	2.655	2.323–3.035	May 10	129	0.4528	<0.05
2018	1.356	1.169–1.574	December 1	330	0.1512	<0.05
All Years	1.335	1.19–1.499	April 19	108	0.1436	<0.05

Table 3 explains the number of bacterial meningitis cases admitted during each season in every year of the study. Here also, it is clearly appreciated that the maximum number of cases were admitted in summer season.

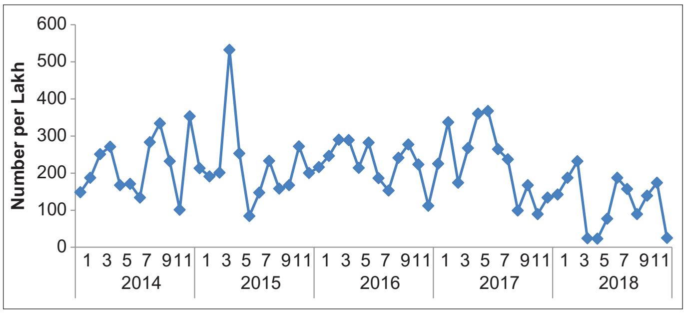

Figure 1: Time series data of bacterial meningitis (2014–2018)

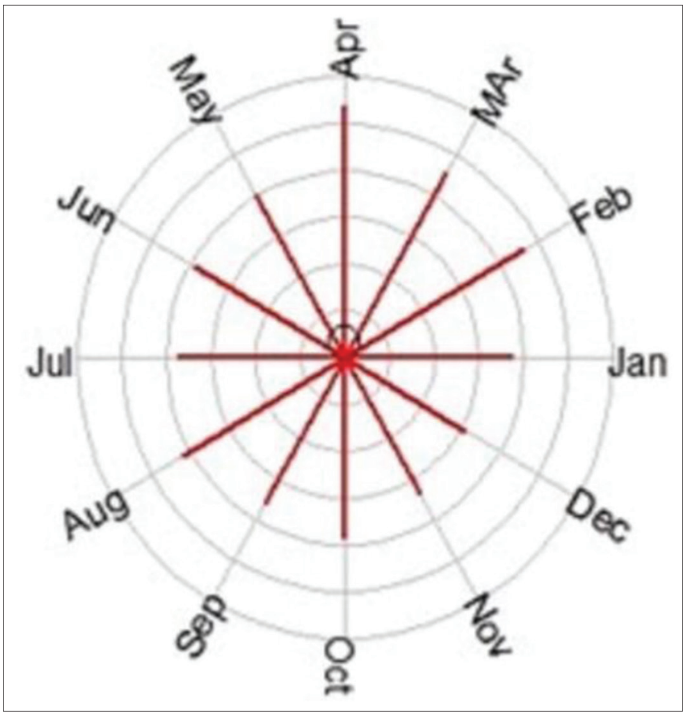

Figure 2: Radial plot of frequency of bacterial meningitis

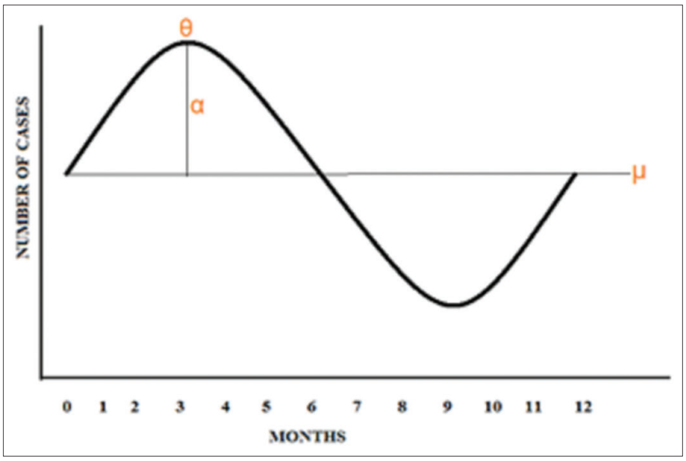

Figure 3: Simple sinusoidal harmonic curve

Table 3: Number of cases of bacterial meningitis (per 1 lakh in-patients) in different seasons during 5-year period (2014–2018)

Season	Year					Total
	2014	2015	2016	2017	2018	
Summer (February–May)	876	1177	1039	1138	466	4696
Monsoon (June–September)	922	622	862	967	510	3883
Winter (October–January)	834	852	828	615	480	3609
Total	2632	2651	2729	2720	1456	12188

The seasonal distribution of bacterial meningitis cases was observed using Edward's model.[13] The line diagram in Figure 4 obtained from Episheet[14] shows fitting of the weighted monthly counts to a sine curve. This assumes 1 yearly peak and one low with 6 months in between. The red line in the figure shows such a fitted sine curve from which it is deduced that April month has got maximum frequency of meningitis cases.

Wavelet Analysis

Wavelet analyses were conducted to explore the periodicity in the time series data. For this study, time series were decomposed using local polynomial regression in the time-frequency domain in the periodic band between 2 and 16 months. Wavelet coefficients are calculated using a mathematical function and represented on a time-frequency two-dimensional plot called the wavelet power spectrum. The resulting wavelet power spectrum was used to identify whether a 12-month periodic component (annual seasonality) was detected.

In Figure 5, the time series data for bacterial meningitis have been decomposed to understand the seasonality and trend of the disease. The recurrence of a particular pattern can be seen every year which proves that bacterial meningitis followed a typical course in its occurrence throughout a year. It is also observed that there is increasing trend in the beginning, that is, in the year 2014, and declining trend at the end, that is, in the year 2018, thereby suggesting cyclical trend in the hospital admissions of bacterial meningitis cases.

Wavelet Transform of Time Series Data for Bacterial Meningitis

In Figure 6, the time series shows a significant 4-month periodicity over the entire period. Shaded regions on either end delimit the cone of influence, where edge effects become important and spectral information is less robust. The wavelet power values increase from blue to red, and white contour lines indicate the significance level.

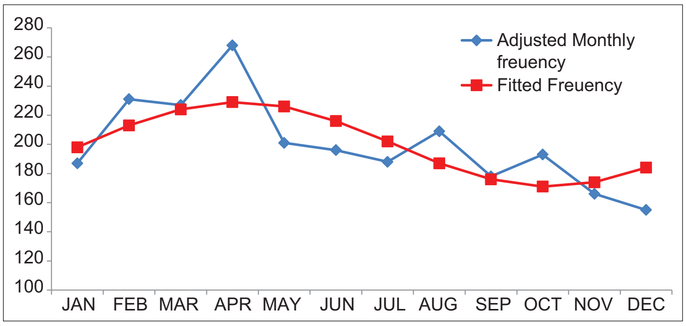

Figure 4: Observed and predicted (Edward's model) seasonal distribution of bacterial meningitis cases (2014–2018)

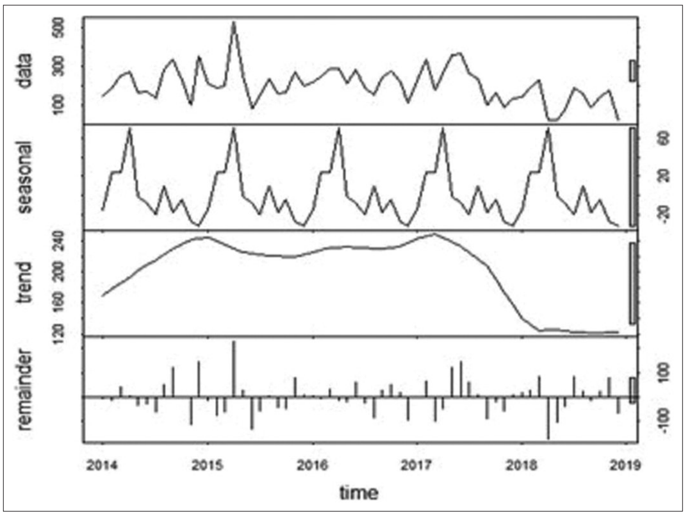

Figure 5: STL decomposition of time series data for bacterial meningitis

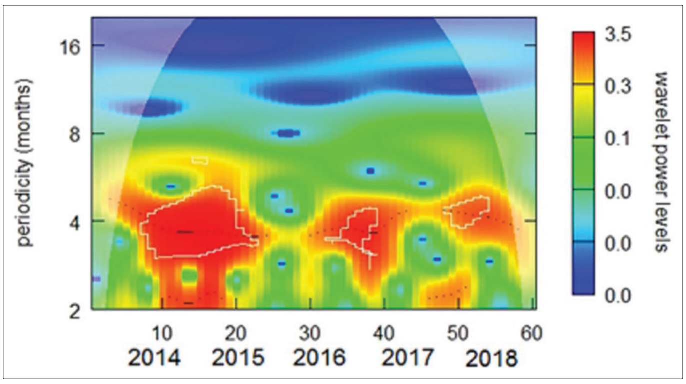

Figure 6: Spectrogram of bacterial meningitis cases

DISCUSSION

In the present study, a time series analysis of bacterial meningitis has been developed by compiling monthly data for a period of 5 years from January 2014 to December 2018. This resembles the laboratory-based retrospective analysis of bacterial meningitis conducted for 5 years in Gondar University Referral Hospital Laboratory by Tegene *et al.*[17] This can also be seen in a population-based and sentinel hospital surveillance of acute bacterial meningitis done among persons of all ages in Burkina Faso and Togo for a period of 5 years by Traore *et al.*[18]

According to the current study, the peaks for hospitalizations of bacterial meningitis cases were predominantly in March–May and the troughs in September–November. This is similar to the studies done by Paireau *et al*.,[19] Traore *et al*.,[18] and Maïnassara *et al*.[20] which all showed increase in the incidence of cases in the months near April. Whereas in a study conducted by Molyneux *et al*.,[21] rate of admissions of patients with bacterial meningitis was decreased in the months of hot dry season.

However, this study depicted that seasonality for aggregate years occurs as peak effect in summer. This mimics the results of many studies done on bacterial meningitis such as Paireau *et al*.,[19] Gedlu *et al*.,[22] Sinclair *et al*.,[23] Greenwood,[24] and Schwartz *et al*.[25] This seasonality could be due to changes in temperature, humidity, and dust. Dust may influence the spread of meningitis in number of ways. The most common proposed mechanism is that dust particle can irritate the person's throat making it more vulnerable to infections. Dust also forces people to stay indoors, where they may transmit the disease more early to each other. In addition, these climate conditions could facilitate the pathogen invasion by damaging the nasopharyngeal mucosa.

Magnitude of seasonal ratio between peak and trough months was between 1.2 and 1.7. This kind of value can be appreciated even in other diseases like pulmonary tuberculosis, as observed in the study by Akhtar and Mohammad,[26] where the peak-to-low ratio was 1.51 (95% CI 1.39–1.65) and the highest frequency of occurrence was in late April.

Hospitalizations for bacterial meningitis showed a cyclical trend over the years studied in the premises. Similar trend of epidemics can be seen even in the meningitis belt of Africa which has been substantiated by the studies done by Cuevas *et al*.[27] and Molesworth *et al*.[28]

Wavelet analysis of the study showed periodicity of 3–4 months for all years. Whereas in, Paireau *et al*.,[19] all 25 countries included in the analyses for *N. meningitidis* had a significant 12 months periodicity. In case of study by Tegene *et al*.,[17] 6 months periodicity seen for pneumococcal meningitis and that by Traore *et al*.,[18] 6 months periodicity for meningitis caused by both *N. meningitidis* and *S. pneumoniae*. The reason for not appreciating significant 12 months periodicity in the current study could be due to the overlapping of seasons in a tropical country like ours.

CONCLUSION

This study found evidence of seasonality for bacterial meningitis, thereby portraying the reflection between increased incidence of bacterial meningitis cases in the community and peak admissions in the hospital for the management of the same. The peaks for hospitalizations of bacterial meningitis were predominantly in summer season with maximum frequency in the month of April. This suggests the necessity of preparation in the health-care centers for the effective management of the cases and handling the burden of increased admissions during that particular period. Hospitalizations for bacterial meningitis showed a cyclical trend over the years studied.

Limitations

Since it is a retrospective study, the accuracy of diagnosis might be questionable, but bias is reduced by selecting only the cases with ICD coded documentary proof. There is a possibility that some cases may be treated in the outpatient department (OPD), but since bacterial meningitis is a serious condition, treatment of the cases on OPD basis without hospital admission is very rare. Variations in admission may not reflect the seasonal variations observed in the community; however, the aim of this study was not to calculate the seasonal incidence of meningitis in the community. No attempt is made to link the seasonality of bacterial meningitis with potential causes.

RECOMMENDATIONS

Hospital should be prepared for providing clinical services round the year; more resources may be required during the peak months of March–May. Further research should focus on the variation in number of hospital admissions of community-acquired acute bacterial meningitis.

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