SPATIOTEMPORAL MODELLING OF ENDEMIC-EPIDEMIC CHOLERA IN NIGERIA

Abstract

This study used a multivariate negative binomial model to capture the Spatiotemporal endemic-epidemic of infectious disease and explore the spatial and temporal patterns of cholera outbreaks in Nigeria. The model for the epidemic part measured spatial weights for the disease spread across the geographical neighboring regions and the endemic part accounted for temporal variation of disease incidence. Weekly count data on cholera from the Nigeria Department of Disease Control and Monitoring Epidemiology (NCDC SED) between January 1st and November 19th, 2018 was used to illustrate the model. In fitting the model, the study has shown that the model with seasonality and autoregressive components provided an adequate fit for the cholera count data and also perform better than the model without seasonality and autoregression for modelling the Spatiotemporal dependency structure of cholera disease

Keywords: disease; surveillance; epidemic proportion; negative binomial model; Spatiotemporal dependence; cholera

1.0 Background

Cholera is caused as an acute watery diarrhea disease by contaminated water with the toxigenic strains of Vibrio cholerae serogroups O1 or O139 or by the ingestion of food or Clemens *et al.*（2017). It is always characterized by Severe dehydration, sometimes fatal left untreated and watery diarrhoea, with or without vomiting (Microbiology Society, 2016). According to Microbiology Society, (2016) that the case fatality rate (CFR) from untreated cholera can be as high as 30–50%, but when there is quick administration of rehydration therapy can reduce it to as low as 1%. Ali *et al.* (2015) reported that the global estimates for cholera cases and deaths are about 2.9 million and 95,000 per year, and which 17 African countries reported over 150,000 cholera cases from all the outbreaks in 2017, NCDC (2017)

In Nigeria, cholera is endemic and seasonal, especially in the rainy season and more often in poorly sanitized areas. Cholera infection is closely associated with inadequate access to clean water and sanitation from densely populated areas to other neighborhoods WHO (2011). Historically, Nigeria has experienced multiple outbreaks of cholera characterized by high case fertility rate (CFR), including the 1991 epidemic with 59,478 cases and 7654 deaths.

This outbreak remains the highest in the country with a CFR of 12.9%. In March, 1999, another major cholera outbreak happened in Kano state, with instances spreading to two states namely: Edo and Adamawa states; and the outbreak led to 26,358 cases and 2085 deaths. The closing predominant cholera outbreak prior to 2018 became in 2014, at some point of which the wide variety of instances recorded cases surpassed over half of the quantity of cases recorded between 2012 and 2013 in addition to among 2015 and 2017. Dalhat *et al*., (2014) pronounced that, Nigeria recorded 787 cases and 1716 deaths (CFR 4.1%) throughout 18 states between January to December 2010. In line with international proof, however, the cholera burden in Nigeria is underestimated as reported by Mengel *et al.*, (2014).

There is increasing research on probabilistic models to fully understand the transmission and persistence of the disease. The susceptible infected removed (SIR) model and the chain binomial model (Andersson & Britton, 2000; Daley & Gani, 1999) were used for the spread of an infectious disease over time. These models are developed for the infection mechanism of a disease, based on data of a completely observed infection process. Morton and Finkenstädt (2005) proposed a stochastic discrete time variable of the SIR model for infectious diseases transmission within and between districts and susceptible individuals interact and carried out model fitting and inference using Markov chain Monte Carlo approach. In another approach, Kleinman *et al*. (2004) proposed a generalized linear mixed model for the spatiotemporal modelling of disease counts that follows a binomial distribution for the counts. Also, Knorr-Held & Richardson (2003) proposed a model for space-time meningococcal disease data dividing an 'endemic' pattern for periods of no outbreaks and a 'hyper endemic' pattern that allows for an auto regression on functions of counts of the same and neighboring regions. and the endemic pattern was built with respect to chronic disease models including structured time, space, and seasonal effects. Sebastiani *et al*. (2006) used

dynamic Bayesian networks to include four different data streams into a multivariate model for influenza surveillance. Böhning (2003). used an Empirical Bayes (EB) techniques for space-time disease surveillance and Mugglin *et al*. (2002) used log-linear Poisson model for space-time influenza data with assumption that the logarithm of the mean depends on a multivariate Gaussian autoregressive process among three levels, an endemic level, an epidemic level, and for the decline of the counts after the outbreak.

Meyer & Held (2014) proposed a power model for short-time human travel and for long-term predictions of infectious transmission disease in both space and time. Additionally, Meyer & Held (2014) reported that power models produce better predictions of final counts, epidemic curves, and regional final counts. Held *et al*. (2017) also admitted that power model predictions perform better than predictions from models with simpler spatial assumptions. Held *et al*. (2005) proposed the first multivariate time-series model framework for aggregated surveillance data and further developed in Paul *et al.* (2008), Paul & Held (2011), and Meyer & Held (2014) respectively.

The aim of this study is to adapt the model by Paul *et al.* (2008) for modelling the cholera in Nigeria and implement the model for the analysis of 2018 cholera count data. The objective was to explore spatiotemporal characteristics of cholera and to describe the epidemiology week of cholera outbreak in Nigeria.

2.0 Materials and methods

2.1 Data used

Secondary surveillance data covering weekly cholera counts from 1 January to 19 November 2018 was received from NCDCSED mainly tasked with coordinating surveillance and response efforts for cholera outbreaks in Anambra and Eboni in the southeast. Adamawa, Borno, Bauchi, Gombe, and Yobe in the northeast. Abuja, Kogi, Kwarra, Nasarawa, Niger, and Plateau in the north central area of Nigeria. Jigawa, Kaduna, Kano, Katsina, Kebbi,

Sokoto, and Zamfara are all in the northwest. Persons aged two years or older with acute watery diarrhea and severe dehydration, or those who died within a week after having acute watery diarrhea in the same area fall in the population of cholera case. Cases of cholera were included in the current study if they were under the age of two and met the case description. The confirmed cholera cases were those in which Vibrio cholerae O1 or O139 was isolated in the feces by the Nigerian Disease Control Center's microbiological investigation (2017). The original records were 44,198 cases, while a total number of 194 cases were duplicated. After removal of duplicated ones, a final number of records was 44,044. Records without an epidemiological week was only 8 cases and a final record used in this study was 43,996 cases and 836 deaths.

2.2 Methodology

A multivariate negative binomial model is used to model the 2018 cholera outbreak in Nigeria.

Since there was over dispersion of cholera in all affected states. Negative binomial distribution follows some strong assumptions about the data. If the variance is significantly larger than the expected value, called the spread, then a negative binomial model is appropriate, but the Poisson distribution is a good alternative model if the mean and variance of the random variables are assumed to be equal (Gardner *et al*. 1995).

Models

Let y_{rt} represents cholera counts observed in unit r at time t, $r = 1, \dots, 4$ geographical regions over $t = 1, \dots, 47$ weekly time points. In this study, single disease is $y_{1,t}$, cholera, observed in the four geographical regions and for the number of choleras counts in a single region, for example, January 2018 is. $y_{1,1}$ The counts are assumed to be distributed as negative binomial, $y_{rt}|y_{i.t-1} \sim \text{NegBin}(\mu_{rt}, \varphi)$ with conditional mean

$$\mu_{rt} = \lambda_{rt} y_{r,t-1} + \exp(\eta_{rt}) \qquad (1)$$

And the conditional variance of y_{rt} increases to; $\mu_{rt}(1+\varphi\mu_{rt})$ with additional unknown over dispersion parameter $\varphi > 0$.

Decomposed the disease incidence μ_{rt} into two parts: the 'epidemic' part which allows for capturing the occasional outbreaks is given as:

$$\tau_{rt} = \lambda_{rt} y_{r,t-1} \quad (2)$$

where, λ is an unknown autoregressive parameter.

And the endemic' part which describes the endemic seasonal patterns is given as:

$$\varsigma_{rt} = \exp(\eta_{rt}). \quad (3)$$

Equation (1) is further adjusted to capture the spread of a disease across the neighboring states. Also, incorporating the sum of the previous number of counts $y_{j,t-1}$ in other units j, $j \neq r$ as a potential explanatory variable for the disease incidence in unit r.and introducing additional weight in the epidemic part of Equation (2) so that;

$$\tau_{rt} = \lambda_{rt} y_{r,t-1} + \phi_r \sum_{j \neq r} \omega_{jr}\, y_{j,t-1} \quad (4)$$

where, $y_{j,t-1}$ are the counts observed in region j at time $t-q$ with lag $q \in \{1, 2, \ldots\}$, ω_{jr} are the chosen weights and the influence of $y_{j,t-1}$, $j \neq r$ on y_{rt} is quantified by the additional autoregressive parameters ϕ_r. Therefore, the relative population of each of the four geographical regions are measured to determine the weights ω_{jr}.

To examine the temporal variation of cholera counts, the endemic ς_{rt} includes an overall trend and a sinusoidal wave for weekly data frequency $w_h = 2\pi s/4H$, (because data was weekly). The ratio of the population fraction η_{rt} is included as a multiplicative offset. The endemic part of Equation (3) gives:

$$log(\varsigma_{rt}) = \eta_{rt} = \alpha_{rt} + \sum_{h=1}^{H} (\gamma_h \sin(w_h t) + \delta_h \cos(w_h t)) \quad (5)$$

where, H is the number of harmonics to be added, h are the Fourier frequencies and α_{rt} allows for different incidence levels in each of the regions.

3.0 Results

Spatial weights in terms of prevalence rates (number of cholera cases/total number of people (per 1000) in the four affected geographical regions in Nigeria, is given in Table 1. The weight for: Southeast is 0.02316, Northcentral is 0.05324, Northwest is 0.38476, and Northeast is 0.91920. These weights are indications that cholera was more prevalent in Northeast than the others and means that the population of Northeast region is at a higher risk than the populations of other regions.

Table 1: Weight matrix of cholera cases in four affected geographical regions, Nigeria, 2018

Geographical region	**Southeast**	**Northcentral**	**Northwest**	**Northeast**
Southeast	1	2.8323	5.8277	2.7780
Northcentral	0.3531	1	2.0576	0.9809
Northwest	0.1716	0.4856	1	0.4767
Northeast	0.3599	1.0195	2.0977	1

Using the weights ω_{jr} n Equation (4), a weight matrix of dimension 4 × 4 in Table 1 shown the cholera transmission from one region to other regions. For example, the spatial weights between Southeast to north-central, northwest, and northeast are 2.8323, 5.8277, and 2.7780, respectively. Two different negative binomial models, including the $H = 1$ seasonal term, were fitted in the endemic part to test whether the seasonal part and the autoregressive part were $\lambda_{rt} y_{r,t-1}$ added to the linear predictor. The results of the fitted models of Equations (4) and (5) are given n (Table 2) standard errors were given in parentheses.

Table 2: Results of the fitted Negative Binomial Models

Without seasonality part and autoregression component					
Distribution	$\hat{\lambda}$(SE)	$\hat{\varphi}$(SE)	$\widehat{\phi_r}$(SE)	Log-L	AIC
Negative binomial	- - - -	0.0664(0.3071)	0.9742(0.0429) 0.4444(0.0731) 0.8238(0.1060) 0.0453(0.0674)	-1384.71	1883.96
With both seasonality and autoregression					
Distribution	$\hat{\lambda}$(SE)	$\hat{\varphi}$(SE)	$\widehat{\phi_r}$(SE)	Log-L	AIC
Negative binomial	0.8903(0.0889) 0.1742(0.0186) 0.8903(0.0758) 0.8112(0.0857)	0.0816(0.3588)	0.0706(0.0100) 0.0351(0.0053) 0.1004(0.0665) 0.0305(0.0330)	-1353.04	1859.71

Table 2 shows that a model with seasonal and autoregressive components maximizes the log-likelihood function compared to a model without seasonal and autoregressive components. Maximum likelihood estimates for the model using the seasonal component and the autoregressive component λ are 0.8903 (0.0889), 0.1742 (0.0186), 0.8903 (0.0758), and 0.8112 (0.0857) in the four regions. These values indicate the presence of heterogeneity in the autoregressive component and can be easily interpreted as the epidemic rate of the outbreak of cholera disease. Akaike's Information Criterion (AIC) calculated for the two models confirmed whether it makes sense for these data to account and consider over dispersion. Models with both seasonal and autoregressive overcome other model with a small AIC (1859.71) and has to be part of the model since, it is more efficient than a purely parameter-driven model. And because it takes account the seasonality, over dispersion, and localized epidemics, that are common characteristics of infectious disease data.

3.1 Exploratory Analysis

An exploratory analysis of the spatiotemporal characteristics of the study population is shown in (Table 3). The key outcomes are attack rate and case fatality rate presented in (Table 4) and distribution of cholera cases by epidemiological week in (Table 5).

Table 3: Characteristics of the epidemic season by Week from Jan. 1st to Nov., 19th 2018

Epidemic Week	Final count	Consecutive Weeks (January)	Consecutive Weeks (Season)
Week1	91	1st Week	Dry
Week2	93	1st Week	Dry
Week3	52	1st Week	Dry
Week4	93	1st Week	Dry
Week5	101	1st Week	Dry
Week6	352	1st Week	Dry
Week7	253	1st Week	Dry
Week8	192	1st Week	Dry
Week9	173	1st Week	Dry
Week10	253	2nd Week	Dry
Week11	292	2nd Week	Dry
Week12	301	2nd Week	Dry
Week13	521	2nd Week	Rainy
Week14	542	2nd Week	Rainy
Week15	901	2nd Week	Rainy

Week16	1000	2nd Week	Rainy
Week17	1203	2nd Week	Rainy
Week18	1003	2nd Week	Rainy
Week19	1201	2nd Week	Rainy
Week20	1002	2nd Week	Rainy
Week21	1351	2nd Week	Rainy
Week22	1215	2nd Week	Rainy
Week23	1308	2nd Week	Rainy
Week24	1258	2nd Week	Rainy
Week25	1108	2nd Week	Rainy
Week26	1109	2nd Week	Rainy
Week27	805	2nd Week	Rainy
Week28	793	2nd Week	Rainy
Week29	1000	3rd Week	Rainy
Week30	1011	3rd Week	Rainy
Week31	1364	3rd Week	Rainy
Week32	1540	3rd Week	Rainy
Week33	1030	3rd Week	Rainy
Week34	1615	3rd Week	Rainy
Week35	2614	4th Week	Rainy
Week36	2764	4th Week	Rainy
Week37	3064	4th Week	Rainy
Week38	2300	4th Week	Rainy
Week39	1968	4th Week	Rainy
Week40	1558	4th Week	Rainy
Week41	1302	4th Week	Rainy
Week42	811	4th Week	Rainy
Week43	532	4th Week	Rainy
Week44	418	4th Week	Rainy
Week45	301	4th Week	Dry
Week46	102	4th Week	Dry
Week47	126	4th Week	Dry

The counts for each week vary in several ways: epidemic Week, final count, consecutive Weeks (began on Sunday and ended on Saturday) and consecutive Weeks (season) (Table 3). The data for week35, Week36 and Week37 (in red) represent the extreme nature of the cholera pandemic. Incidence peaks much higher, at 3064 counts, than at any other time in the data set which was about 94.48% of cholera cases and were reported during the rainy season as also reported in (Table 5). This means that the majority of cases were as a result of water flood. The data for Week5 represented the peak weak listed as 52 because the 2018 epidemic season is really in the first wave of the dry epidemic season.

Table 4: Distribution of cholera attack rates and case fatality rates by region, Nigeria, 2018

Geographical region	Projected 2018 population	Cases	Deaths	Attack rate/100,000 population	CFR (%)
Southeast	8,852,569.68	205	8	2.32	3.90
Northeast	24,593,161.29	22,606	251	91.92	1.11
Northcentral	25,072,869.86	1,335	62	5.33	4.64
Northwest	51,590,496.43	19,850	515	38.48	2.59
Total	**110,109,097.26**	**43,996**	**836**	**127.43**	**1.90**

Table 4 shows the distribution of cholera AR and CFR. The overall AR during the breakout period was 127.43 / 100,000. Specifically, the northeast (91.92 / 100,000 population) and northwest (38.48 / 100,000 population) are two other geographic areas, such as Northcentral and Southeast, which are residents of 5.33 / 100,000 and 2.32 / 100,000, respectively. CFRs are generally high in all affected geographic regions, with approximately 75% of these regions reporting high CFRs in excess of 1.90% at the national level. In particular, Northcentral recorded the highest CFR (4.64%). The northeast recorded the second highest CFR (3.90%) and the northwest recorded the CFR (2.59%).

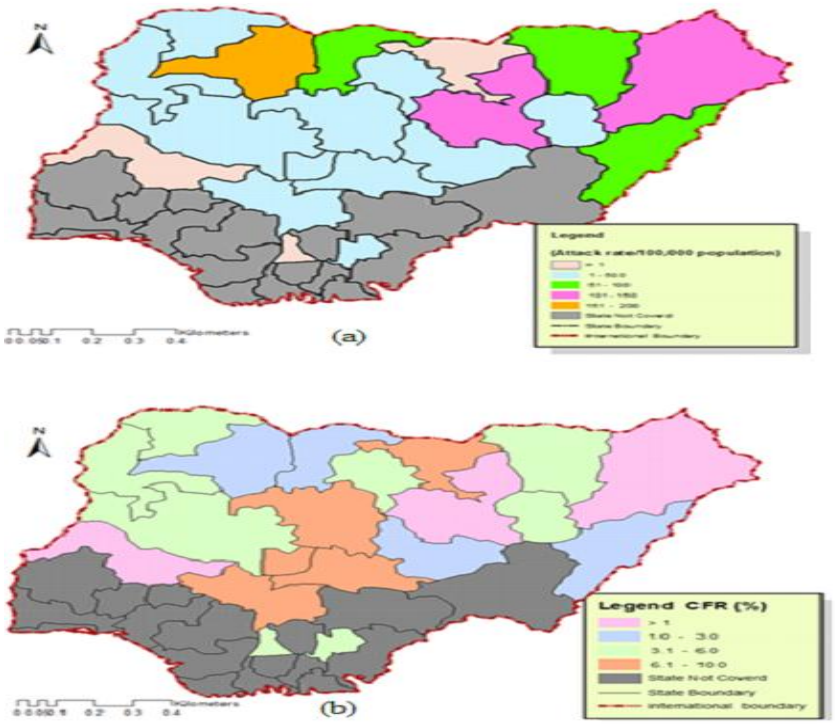

Figure 1: Spatial maps: (a) Attack Rates and (b) Case Fatality Rates.

The spatial distribution of cholera cases in terms of attack rates and case fatality rates across the 20 affected states is shown in Figure. 1. The modes of attack rates were found in category 6: 60 to 100(per 100,000) and category 5: 30 to 49.9(per 100,000) which were notably found in northeast and northwest regions. The spatial distribution of case fatality rates was more often in category 5: with 5.0% and above than categories 3 and 4: with (2.0 to 3.5%) and (3.5 to 5.0%) which were notably dispersed in northcentral, and northwest regions.

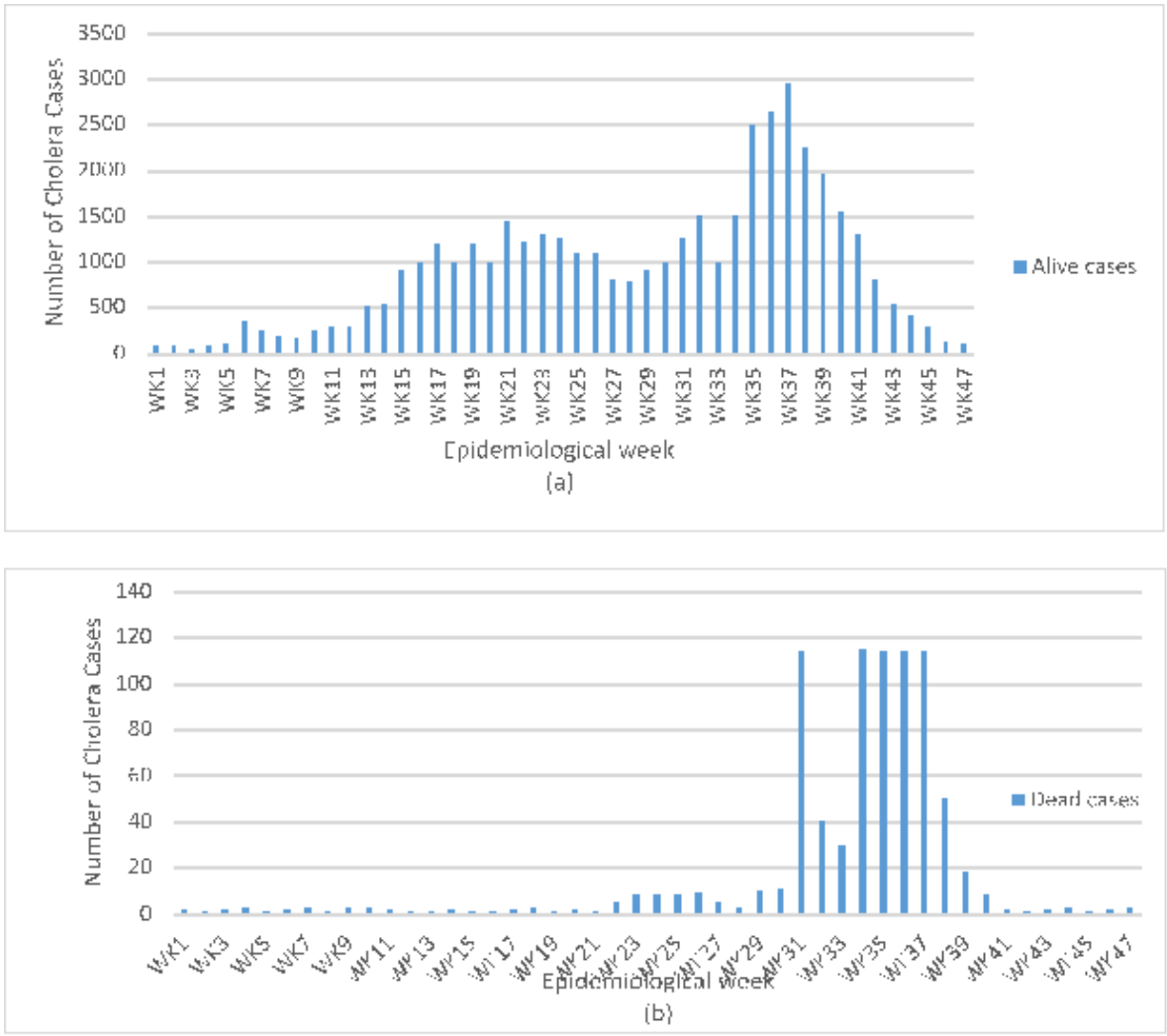

Figure 2: Plot by epidemic Week for (a) Alive and (b) Deaths

The epidemiological curve for cholera cases alive and fatalities by epidemic Week are shown in Figure 2. The bulk of cholera cases occurred in the second and fourth waves, with a peak at week 37; nevertheless, there was a preponderance of cholera deaths near the conclusion of the third wave and the start of the fourth wave, with occasional occurrences of death in between.

Table 5: Cholera Cases by Epidemiological Week in Nigeria, 2018.

Characteristic	**Epidemiological week**				
	Week 1–9 Cases (%)	Week 10–28 Cases (%)	Week 29–34 Cases (%)	Week 35–47 Cases (%)	**Total Cases (%)**

Age (years)					
< 5	386 (34.50)	4551 (25.96)	1422 (19.08)	3899 (21.79)	10258(23.32)
≥ 5	731 (65.33)	12,955 (73.91)	5744 (77.06)	12,947(72.35)	32377(75,59)
Missing	2(0.18)	22(0.13)	288(3.86)	1049(5.86)	1361 (3.09)
Sex					
Female	567 (50.67)	8782 (50.10)	3773 (50.62)	9200 (51.41)	22322(50.74)
Male	552 (49.33)	8746 (49.90)	3681 (49.38)	8695 (48.59)	21674(49.26)
Geographical region					
Southeast	3 (0.27)	188 (1.07)	14 (0.19)	0 (0.00)	205(0.47)
Northeast	874 (78.11)	12,372 (70.58)	807 (10.83)	8553 (47.80)	1335(3.03)
Northcentral	3 (0.27)	1083 (6.18)	158 (2.12)	91 (0.51)	19850(45.12)
Northwest	239 (21.36)	3885 (22.16)	6475 (86.87)	9251 (51.70)	22606(51.38)
Season					
Dry	0 (0.00)	997 (5.69)	7454 (100)	311 (1.74)	2427(5.52)
Rainy	1119 (100)	16,531 (94.31)	0 (0.00)	17,584(98.26)	41569(94.48)
Outbreak setting					
Rural	887 (79.27)	3073 (17.53)	4093 (54.91)	7448 (41.62)	15501(35.23)
Urban	199(17.79)	14382(82.05)	3318(44.51)	10119(56.54)	28018(63.68)
Missing	33(2.95)	73(0.42)	43(0.58)	328(1.83)	477(1.08)

Epidemiological Weekly Cholera Cases, Table 5 shows that very high number of cholera cases were consistently recorded during the 29-34 Weeks, which was about 77.06% of those aged 5 years and older. For cholera cases by sex, it shows that the distribution of cholera cases was about the same between men and women throughout the week. In terms of geographic region, the northeastern states accounted for more cases in (1-9) Weeks (78.11%) and (10-28) Weeks (70.58%), while the northeastern states accounted for higher cases in Weeks (29-34) (86.87%) and (35-47) Weeks (51.70%). About (94.48%) of cholera cases were reported during the rainy season. The epidemiological week during the outbreak of cholera also seemed to be heavily influenced by seasonality.

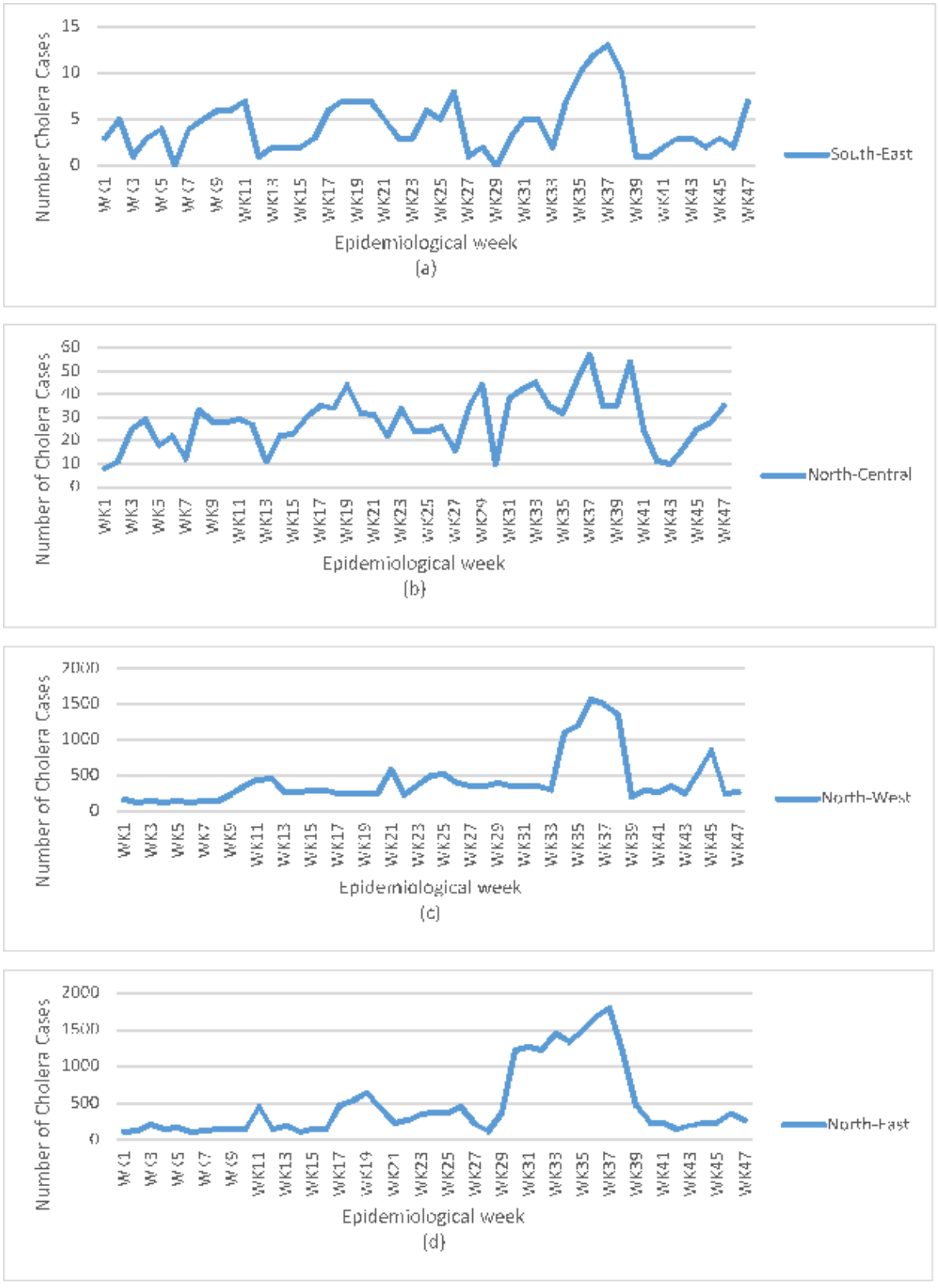

Figure 3: (a) Southeast (b) Northcentral (c) Northwest and (d) Northeast 2018 epidemic weekly plot.

The plotted time series from Weeks 1 to 47 (Figure 1) shows the overall seasonality of the data, with higher incidence between Weeks 35 to 37 toward the end of the 2nd quarter to the beginning of the third quarter when rainy season is expected to begins.

Conclusion

From the results of this study, the fitted negative binomial model shown that a negative binomial model with both seasonality and autoregressive components is more rational for cholera count data than without seasonality and autoregressive. The study therefore, concluded that it is best suitable for modeling the spatiotemporal dependence structure of infectious disease. The results of this study are consistent with the report by Paul *et al*. (2008) and Sifat & Israt (2011).

For the exploratory analysis of spatiotemporal characteristics, the analyses shown that there are three problems. First, there was a significant spike in cholera cases and deaths between Weeks 35 and 47, which coincided with the end of the rainy season across the country and increased the likelihood of water sources being contaminated by floods during these times. , Second, the majority of cases were reported in rural areas from Weeks 1 to 9, Week 29 to 34, and Week 35 to 47, since many people rely on contaminated water sources as water levels drop toward the conclusion of the rainy season. Finally, the CFR in this study is 1.9 percent, which is greater than the accepted guideline of 1%. (WHO, 2011; and WHO, 2017).

Recommendations

1. Regular monitoring by the technical working groups of the affected states is required to know the current epidemiology of cholera in the country.

2. Provide medical facilities to the affected Municipalities (LGA) Cholera Treatment Center (CTC) for rapid examination of suspected cholera cases.

3. The study recommend a further research on the spatiotemporal cholera model that will detect routes of transmission.

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