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Exploring the Epidemiological Patterns and the Dynamics of Diphtheria Outbreak in Nigeria: A Compartment Model Approach

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ABSTRACT

Diphtheria, a highly contagious and vaccine-preventable disease caused by *Corynebacterium diphtheriae*, remains a global health concern despite effective vaccines. This study modeled diphtheria transmission dynamics in Nigeria using weekly case data from December 2022 to 2024 (53 weeks). A modified Kermack-McKendrick compartmental model and spatial autocorrelation index analyzed infection patterns across states. Results showed a transmission rate of 0.3, an average latent period of 5 days, and a 10-day contagious period. Approximately 5% of infected individuals required daily hospitalization, with a natural death/removal rate of 0.01. The average reproduction rate was 1.43, meaning one case could lead to 1.43 new infections. Moran's I revealed disease clustering, emphasizing the need for widespread vaccination, diphtheria antitoxin distribution, improved medical facilities, and regular public health campaigns for effective control.

Keywords: Disease Epidemiology, SEIHR Model, outbreak, Diphtheria, Nigeria.

INTRODUCTION

Diphtheria is an infectious disease caused mainly by a bacterium *Corynebacterium* diphtheria. It can also cause by *Corynebacterium ulcerans* (WHO,2023). Diphtheria is a serious and life-threatening disease which is highly contagious when in close contact with infected person(s), their belongings or respiratory droplets (coughing or sneezing) usually cause the disease to spread from person to person (Makeri, Peter & Pius, 2023). Although, diphtheria is preventable through immunization, but outbreaks do occur in countries with low vaccine coverage areas, resulting in significant morbidity and mortality in such countries. The bacterium releases a toxin that causes damage to the upper respiratory track of the respiratory system (via a buildup of grey tissue in the throat) and other body organs (WHO, 2024). This buildup, however, is accompanied by difficulty in breathing, heart rhythm challenge, swallowing problem and sometimes skin sores especially in a warm weather. These toxins, however, can have a serious effect on the heart and lungs of the subjects. Diphtheria infected persons can sometimes be asymptomatic with transmission taking place from infected to a susceptible individual, other can develop a mild disease and there may be a scenario for a severe disease situation which can sometimes lead to complications like airway obstruction, heart failure, nerve damage and sometimes deaths. Diphtheria can affect all age groups, however, individuals who are not immunized or under immunized are at risk of this disease. Likewise, young children who are unimmunized are vulnerable to this bacterium infection due to their low level of immunity (Castelo-Branco & Soveral, 2014). Additionally, living in a crowded and unhealthy environment with infected people can aid the spread of this disease. Symptoms of this disease include fever, sore throat, swelling of the neck (due to enlarging lymph nodes) and sometimes a barking cough and suffocation (WHO, 2024). Signs of diphtheria infection after exposure to an infected person starts from 2 to 5 days and the length of time for symptoms to show starts from 10 days after exposure (Clevelandclinic, 2024).

Diphtheria is a fatal disease with about 5-10% of the cases with higher mortality rate in young children especially those with incomplete and those without vaccination. However, in locations with poor access to adequate medical cares, facilities and diphtheria antitoxin (DAT), crude fatality rate can be as high as 40% (WHO, 2023). It is communicable for 2-6 weeks without antibiotics treatment and usually occur in spring or winter months.

In many parts of the world, diphtheria remains a serious public health concern despite the existence of effective vaccines. In 2017, there were about 8,819 cases of diphtheria reported worldwide. (Clarke *et al* 2019). The disease is prevalence mostly in places with no vaccination coverage or in places where incomplete vaccination is predominant. The global case counts range from countries with a higher case counts with about 66% case-patients were unvaccinated with higher proportion below 15 years of age to countries with a sporadic case counts with about 32% case-patients were unvaccinated and majority above 15 years of age which is in tandem with waning in vaccine immunity (Clarke *et al* 2019). The coverage of diphtheria–tetanus–pertussis (DTP) vaccine and booster dosses were suboptimal in most of these countries.

Among the previous records of diphtheria outbreaks in Nigeria, 2011 and 2022 outbreaks were notable (WHO, 2023). The most recent outbreak started in late 2022 through the year 2023 which left about 471 deaths from severe diphtheria cases from about 7,400 confirmed cases and about 12,000 suspected cases in 2023. Kano state was an epicenter of this outbreak which was recorded 19 Nigeria state. This outbreak in these state may be attributed to low vaccination and contact tracing (International Federation of Red Cross and Red Crescent Societies (IFRC), 2024).

The use of mathematical and statistical models to study epidemics is relics of old (Kermack and Mckenderic, 1927). For instance, one of the fundamental theories of epidemics 'susceptible-infected recovered (SIR)' compartment model was proposed back in in 1927. Ever since, other studies were documented in literature on the modelling infectious disease dynamics (Heesterbeek *et al*, 2015). These include application of SIR model to childhood infectious disease like measles reported in (Bartlet, 1957); incorporating temporal and spatial heterogeneity in infection patterns and demographic characteristics of households (Hagenlocher and Castro, 2015); individual based models and spatial simulations for veterinary outbreaks (Keeling 2005); emerging infections like SARS, contact tracing and modelling the spread of infections (Anderson *et al.,* 2004) appraisal epidemiology of diphtheria on a global scene (Clarke *et al* 2019; Makeri, Peter & Pius, 2023).

The spatial variability of occasional outbreaks of diphtheria especially in the northern part of Nigeria opens it up for further consideration and to understand the dynamics of diphtheria transmission, fosters early warning systems and create efficient control measures by the healthcare service providers and the public. Hence, adopting a mathematical model is a useful tool in achieving a diphtheria free society. Therefore, this study explored and modified the classical compartment SIR models by dividing the entire population into five compartments of Susceptible Exposed Infected Hospitalized and Recovered (SEIHR) to investigate the dynamics of diphtheria with a view to find efficient preventive measures to lower the disease's occurrence in near future in Nigeria.

MATERIALS AND METHODS

Data Source

The data collected for this study were reported diphtheria cases published on a weekly basis from the update released by the Nigerian Centre for Disease Control (NCDC), Abuja. It spans the period from 2022 to 2024 for the period of 53 weeks.

Ethical clearance

This study relies on statistics readily available to the public via NCDC website. The data used was exclusively information about the anonymous subjects which does not require ethical review and clearance.

Model Formulation and Diagram

This study modified the classical SEIR model with an extension of Hospitalized compartment. Therefore, the entire population at time t, $N(t)$ was compartmentalized into five categories. To form a SEIHR model given in (1).

Defining the following terms of the SEIHR model:

$S(t)$: Number of Susceptible individuals at time t

$$E(t)\text{: } Number\ of\ Exposed\ individual\ at\ t$$

$$I(t)\text{: } Number\ of\ Infected\ individuals\ at\ t$$

$$H(t)\text{: } Number\ of\ Hospitalized\ individuals\ at\ time\ t$$

$$R(t)\text{: } Number\ of\ recovered\ individuals\ at\ time\ t$$

Thus, the SEIHR is given by (1).

$$N(t) = S(t) + E(t) + I(t) + H(t) + R(t) \tag{1}$$

With the following parameters defined as follows:

$$\beta = Transmission\ rate$$

$$\alpha = Rate\ at\ which\ exposed\ individual\ become\ infected$$

$$\gamma = Recovery\ rate\ of\ infected\ individuals$$

$$\delta = Hospitalization\ rate$$

$$\mu = Recovery\ rate$$

$$\sigma = Natural\ birth/death\ rate$$

And the SEIHR model equation is stated in (2)

$$\frac{dS}{dt} = \sigma N - \beta SI - \sigma S$$

$$\frac{dE}{dt} = \beta SI - \alpha E - \sigma E$$

$$\frac{dI}{dt} = \alpha E - \gamma I - \delta I - \sigma I \tag{2}$$

$$\frac{dH}{dt} = \delta I - \mu H - \sigma H$$

$$\frac{dR}{dt} = \gamma I + \mu H - \sigma R$$

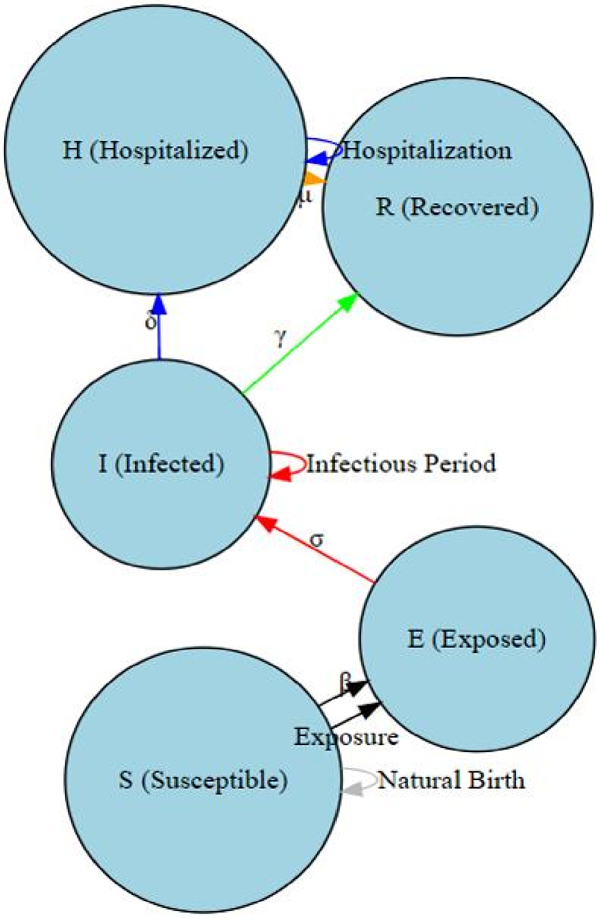


Figure 1: Model diagram.

Derivation of an Average Reproductive Rate (R_0)

The average reproductive number is an epidemiological parameter that describes the nature of a disease with regards to the contagious or transmissibility of infectious agents. It gives the number of secondary infections made by a single infected individual in contact with susceptible population for the entire infection period.

To derive R_0, break the step down into.

New infections matrix (F) which describes the rate of appearance of new infections.

Transition matrix (V) describes the rate of transfer out of the infected compartments.

New Infections Matrix (F)

The new infections occur primarily in the E (Exposed) compartment due to interactions between S (Susceptible) and I (Infected).

$$F = \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$$

Transition Matrix (V)

This matrix accounts for the progression between compartments due to recovery, hospitalization, and natural death.

$$V = \begin{pmatrix} \alpha E + \sigma E \\ -\alpha E + \gamma I + \delta I + \sigma I \end{pmatrix}$$

Jacobian Matrices

Now, to calculate R_0, evaluate the Jacobian matrices F and V at the disease-free equilibrium (DFE), where S=N, and E= I = 0.

Then, the matrices become

$$F = \begin{pmatrix} \beta & 0 \\ 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \alpha + \sigma & 0 \\ -\alpha & \gamma + \delta + \sigma \end{pmatrix}$$

The reproduction number R_0 is the spectral radius (dominant eigenvalue) of the matrix FV^{-1} in (3). where:

$$R_0 = \rho(FV^{-1})$$

The product FV^{-1} is

$$FV^{-1} = \begin{pmatrix} \frac{\beta}{\alpha+\sigma} & 0 \\ \frac{\beta\alpha}{(\alpha+\sigma)(\gamma+\delta+\sigma)} & 0 \end{pmatrix} \tag{3}$$

The dominant eigenvalue (largest eigenvalue) is

$$R_0 = \frac{\beta}{\alpha + \sigma}$$

When $R_0 > 1$, the disease will spread in the population. when $R_0 < 1$, the disease will eventually die out.

Moran I Statistics

An examination of spatial autocorrelation with distance lag via correlogram (covariance formation) employed Moran I Indices (Adu-Prah & Tetteh, 2015). Moran's I index is a statistical tool that measures local homogeneity (similarities) between two closed pixels. It calculates the extent of degree of association between observed values of the same random variable at different geographical locations as a function of distance apart or distance lag (Shi, He, & Zhang, 2018).

For any given distance lag d , Moran I autocorrelation coefficient is calculated as in (4).

$$I(d) = \frac{\dfrac{\sum\sum \omega_{ij}(d)(y_i - \overline{y})(y_j - \overline{y})}{\omega_T(d)}}{\dfrac{\sum (y_i - \overline{y})^2}{n}} \tag{4}$$

Where $\omega_{ij}(d)$ is the weight assigned to location i, j and the total weight is given as $\omega_T(d)$

RESULTS AND DISCUSSION

Results Based on SEIHR Model Analysis

Figure 1 gives the various plots based on the five compartments in SEIHR models. At the commencement of the outbreak, there were very high number of susceptible and expose population which gradually approaches horizontal axis in time. The infected population started rising at the beginning of outbreak which gradually increased up till around eight to ten weeks before gradual decreased in time and approaches horizontal axis as time increases. Hospitalized population started from origin and increased up to 20th week before diminishing returns sets in, this signified a reduction in infection cases. Recovered populations started from origin and followed an increasing trend from week zero to week 23 before they started flattened up till week 53 of this study period (Figure 2).

Parameter Estimates from SEIHR model

Table 1: Model Parameter Estimates.

Parameter	Estimate	Std. Error	z-value	p-value
β	0.31	0.02	17.86	< 0.001
α	0.20	0.03	6.26	< 0.001
γ	0.11	0.01	8.75	< 0.001
δ	0.05	0.00	240.04	< 0.001
σ	0.01	0.00	100000	< 0.001

The transmission rate β is 0.3, indicating moderate disease spread. (Table 1) This reflects a situation where containment measures may need to focus on reducing contact rates or improving isolation protocols to limit transmission. The progression rate (α) is 0.2, implying an average latent period of 5 days. This suggests that exposed individuals quickly become infectious, highlighting the importance of early detection and intervention during the incubation phase. The recovery rate γ is 0.1, indicating an average infectious period of 10 days. This suggests that infected individuals remain contagious for a significant duration, necessitating effective isolation and treatment to prevent further spread.

The hospitalization rate δ is 0.05, meaning that 5% of infected individuals require hospitalization daily. This could reflect either a relatively severe disease presentation in a subset of cases or a healthcare response prioritizing hospital care for infected individuals. The natural death or removal rate σ is 0.01, corresponding to an average time of 100 days for individuals to leave the system. This value accounts for deaths and other removals, aligning with background population dynamics and natural exits unrelated to the disease. These estimates provide insights into the dynamics of the disease and highlight areas for targeted public health interventions, such as reducing transmission rates or improving early detection and making diphtheria antitoxin (DAT) available for those infected with the disease.

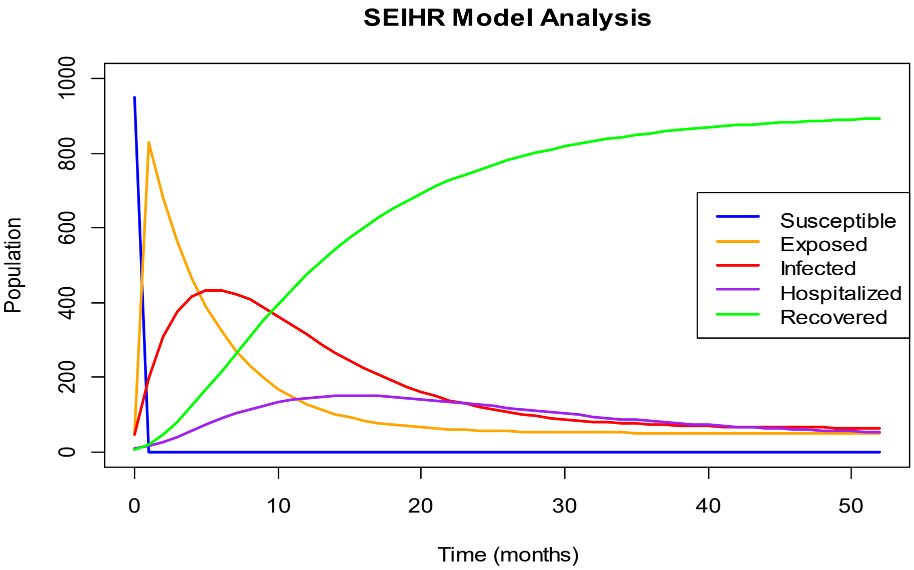


Figure 2: Combine SEIHR model Chart.

Average Reproduction Rate

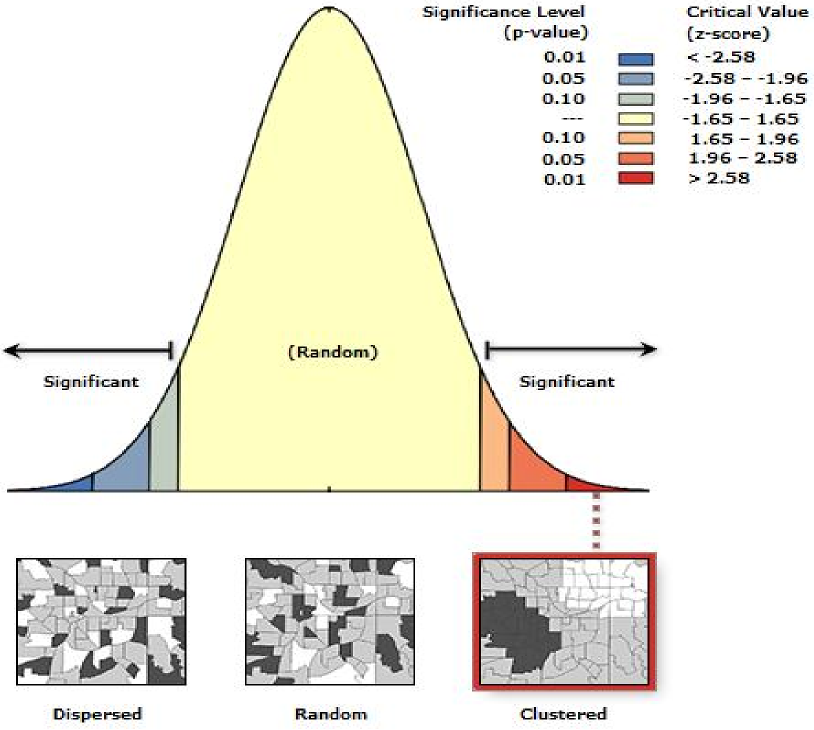
The computed average reproduction rate (R_0) is approximately 1.43. This implies on average; one infected individual is expected to cause 1.43 new infections in a fully susceptible population.

Also**,** since $R_0 > 1$, the disease has the potential to spread within the population, indicating that transmission is moderately sustained under current conditions.

Therefore, an R_0 of 1.43 suggests that diphtheria has the capacity to propagate under the given parameter estimates. Public health interventions should aim to reduce β (transmission rate) or increase ν (removal rate) and σ (progression to detectable stages) to control the disease effectively.

Spatial Autocorrelation Report

The Moran I index using distance decay method to generate the weight gave a spatial autocorrelation of 0.09 (Figure 3). The positive spatial autocorrelation in Moran I results reflected a direct association in incidence patterns neighboring states. This implies that there were similarities in disease dynamics across states. An increase in incidence patterns in a state causes an increase in the other states and the otherwise is true.



Given the z-score of 4.56055587275, there is a less than 1% likelihood that this clustered pattern could be the result of random chance.

Moran's Index:	0.085105
Expected Index:	-0.007299
Variance:	0.000411
z-score:	4.560556
p-value:	0.000005

Global Moran's I Summary

Input Feature Class:	Dipthera
Input Field:	ICOUNT
Conceptualization:	INVERSE_DISTANCE
Distance Method:	EUCLIDEAN
Row Standardization:	False
Distance Threshold:	21243.9218 Meters
Weights Matrix File:	None
Selection Set:	False

Figure 3: Moran I and Spatial Statistics.

DISCUSSION

Based on the analysis carried out, the various parameters of the SEIHR model revealed a sharp initial increase in the number of reported cases and hospitalizations for severe cases during the early weeks of the outbreak. This sharp rise aligns with the expected dynamics of infectious diseases, where an initially susceptible population is rapidly exposed to the pathogen, leading to a surge in cases. However, as interventions such as isolation, treatment, and public health measures are implemented, the number of cases often declines. This pattern highlights the critical role of early and robust epidemic response strategies. For instance, public awareness campaigns and rapid deployment of medical resources can significantly alter the trajectory of an outbreak. The observed trend is consistent with patterns seen during the COVID-19 pandemic, where aggressive public health measures successfully flattened the curve in many regions (Adeniran et al., 2020). The reduction in cases after the initial surge in this outbreak is likely attributable to improved access to diphtheria antitoxin (DAT) and the administration of booster vaccinations, as highlighted by WHO (2023). These measures underscore the importance of maintaining adequate stockpiles of essential medical supplies and vaccines, particularly in regions prone to outbreaks. Additionally, the role of vaccination in both preventing initial infections and limiting the spread within communities cannot be overstated. Booster doses are especially critical in mitigating the waning immunity that may occur in vaccinated populations over time.

Moran I statistics revealed significant spatial autocorrelation in the spread of diphtheria, with states bordering each other exhibiting similar patterns of infection and disease progression. This homogeneity likely stems from the high degree of human mobility across state borders and the absence of physical barriers in many areas. Such findings suggest that local containment measures alone may be insufficient during outbreaks of highly transmissible diseases like diphtheria. Instead, a coordinated regional approach is necessary, emphasizing cross-border collaboration and harmonized public health strategies. These results align with findings from (Balogun *et al*., 2022 & Makeri *et al*., 2023) who noted the challenges posed by unrestricted movement in controlling infectious diseases in Nigeria. However, the Moran I autocorrelation coefficient differed from values reported in phylogenetic studies of biological species, such as those observed by Paradis (2011), emphasizing that epidemiological patterns are influenced by distinct socio-environmental factors.

Results based on average reproductive number indicated the disease potential to increase. Intuitively, a value of R_0 above 1 signal danger, however, with availability of good medical facilities, presence of anti-tetanus vaccine and subjects' strict adherence to safety rules and protocols, the disease may be brought under control (WHO, 2023).

CONCLUSION

The study highlights the transmission dynamics of diphtheria in Nigeria and underscores the importance of effective public health interventions. It emphasizes the need for widespread vaccination, improved access to treatment, and robust public awareness campaigns. Additionally, the findings highlight the significance of coordinated control measures across states to manage and prevent the spread of the disease. These insights are vital for enhancing diphtheria prevention and control strategies in the country.

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