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Mathematical and Sensitivity Analysis on the Dynamics of Cholera Epidemic Model with Vaccination

Lawal Jibril
Department of Mathematical Sciences,
Federal University Gusau, Gusau, Nigeria

Samaila Musa
Department of Computer Science,
Federal University Gusau, Gusau, Nigeria

Abstract:- This paper provides a rigorous mathematical and sensitivity analysis on the cholera epidemic model with vaccination. The model consists of six system of nonlinearly differential equation. The basic properties of the model for positivity of solutions were investigated which the solution $S(t)$, $E(t)$, $I(t)$, $V(t)$, $R(t)$ and $P(t)$ are found to be nonnegative for $t \geq 0$. Existence and uniqueness of the model reveals that there exist a unique solution which is bounded and continuous in region D. The theoretical analysis of the model reveals that cholera will dies out whenever the threshold quantity R_0 is less than unity and it will persists in the community if otherwise The sensitivity analysis was performed around the baseline parameter value. The result shows that the contact rate in human β_1 with the value 0.6868, and the shedding rate ε with the value 0.5901 are the most sensitive parameter that influenced the threshold quantity R_0. Furthermore it was observed that any increase in the following parameter $\beta_2\ \eta\ \theta$ results in the increase of R_0. Similarly, increase in the following parameter $\rho\ \psi_1\ \alpha\ \gamma_2\ \phi\ \gamma_1$ decrease the threshold quantity R_0. The numerical simulation using an arbitrary set of parameter values were carried out and plotted in which the results for sensitivity analysis and threshold criterion were found to be in agreement with analytical results shown in Table 3 and Theorem 2.

Keywords:- *Cholera epidemic Model; differential equation; sensitivity analysis; threshold quantity; Vaccination.*

I. INTRODUCTION

Cholera is an acute intestinal infection caused by ingestion of food or water contaminated with the bacterium vibrio cholera. It is a disease of poverty, closely linked to poor sanitation, poor environmental infrastructure, and lack of health care services, increased population movement and lack of clean drinking water. Cholera has a short incubation period of a few hours to five days, and is characterized in the majority of cases by acute, profuse watery diarrhoea lasting from one to a few days. In its extreme form, cholera can be rapidly fatal [1, 2]. In October 2017, partners from the Global Task Force on Cholera Control launched a strategy for cholera control (GTFCC) named; Ending Cholera: A roadmap to 2030 partners endorsed a call to action on ending cholera, with strategies to reduce cholera deaths by 90% and to eliminate cholera by 2030 [3]. Recent studies have estimated that every year, there are roughly 1.3 to 4.0 million cases, and 21 000 to 143 000 deaths worldwide due to cholera [4].

Oral Cholera Vaccine (OCV) can play an important role in outbreak prevention and control, and in long term control of cholera [5]. Vaccination is the most effective method of preventing infectious diseases; widespread immunity due to vaccination is largely responsible for the worldwide eradication of smallpox and the elimination of diseases such as polio and tetanus from much of the world [6]. Currently there are three WHO pre-qualified oral cholera vaccines (OCV): Dukoral, Shanchol, and Euvichol. All the three vaccines require two doses for full protection [4]. The Cholera vaccines should always be used in conjunction with other cholera prevention and control strategies. However, vaccines serve only as additional control measures to prevent cholera and must not replace any other prevention and control measures recommended by WHO. These vaccines should be used in areas with endemic cholera, in humanitarian crises with high risk of cholera, and during cholera outbreaks [4, 5].

The modeling of infectious diseases is a tool that has been used to study the mechanisms by which diseases spread, to predict the future course of an outbreak, protect community, prevent transmissions and to evaluate strategies to control an epidemic. The 1920s saw the emergence of compartmental models, the Kermack–McKendrick epidemic model [7] describe the relationship between susceptible, infected and immune individuals in a population [4]. There has been many works on sensitivity analysis of the infectious diseases, for instance the recent work are of [9] they used there model to obtain the most sensitive parameter to R_0 is human birth rate β followed by condom efficacy and compliance, in the study of sensitivity analysis of Lassa fever model. [10] In their model on stability and sensitivity analysis of a deterministic epidemiological model with pseudo recovery. Their aim was to determine how changes in parameter affect the transmission and spread of the disease. The following parameter were used β, θ, α, μ and γ in their work. The recruitment rate μ, effective constant rate β, progression rate of the exposed to infectious class α, rate at which infectious become pseudo-recovered individuals γ and relapse of the pseudo due to partial treatment θ. They found that increasing the value of any of the parameter, β, θ, α increases the R_0 and the magnitude

of the infectious individuals in the community. Conversely, increasing the value of either μ or γ, decrease the R_0. Thus, decrease the magnitude of the infectious individuals in the community. [11] Carried out the sensitivity analysis to determine the model robustness to parameter values in their work to study optimal control strategy on human popilloma virus (HPV) model with backward bifurcation analysis. They obtain disease progression as the most sensitive parameter. They further observed that the parameter $\eta, \varphi, \gamma, \rho, \vartheta, \tau$ and κ increases the value of R_0, thus increases the endemicity of the disease. Conversely the parameter μ, δ, q, θ *and* ϕ decrease the value of the R_0 when they are increased. [12] Conducted sensitivity analysis and simulations including seasonal variation in the contact rate and shed rate in which they found that education, vaccination, and treatment reduced the value of R_0 and adopting interventions concurrently, significantly affected the effective reproduction number, they emphasized the benefits of good preventive measure and suggested that treatment and education may be most effective in an outbreak. [13] Conducted a sensitivity analysis and looked at the synchrony between the two populations. They found that if the disease went extinct in one patch, it was reintroduced by conflict from the disease endemic patch, they also found the endemic to be more severe in the patch with worse sanitation.

Recent studies on mathematical and sensitivity analysis of the cholera dynamics includes the work of [14] from their result it was observed that the effective contact rate and the low immunity rate were the key parameters that influenced the cholera dynamics in the community. In 2019, a new compartment model for a cholera carrier is developed by [15] on existence and sensitivity index of a cholera carrier epidemic model. They found that the following parameters $\beta_1, \beta_2, \beta_3$ and m affect the R_0. Thus any slight increases in the parameter value increases the chances for contracting cholera infection in the community.

In this work the model developed by [16] to study the solution of the cholera epidemic model using differential transform method was used. The study aimed to investigate mathematical and sensitivity analysis of the cholera epidemic model with vaccination. Thus, to understand the basic disease behaviour as well as to identify the key parameter values that affect the magnitude of transmission and spread of cholera in the community.

This paper is organized as follows: the model formulation is presented in section 2. Analysis of the cholera epidemic with vaccination model are presented in section 3. Numerical simulations and discussion of results are reported in section 4. Conclusions are presented in section 5 and references are presented in section 6.

II. MODEL FORMULATION

A. *Model Description and Formulationa*

The total human populations at a time t, denoted by $N(t)$ is subdivided into five compartments of Susceptible individuals, $S(t)$ Exposed individuals, $E(t)$ Infectious individuals, $I(t)$ Vaccinated individuals, $V(t)$ and Removed individuals, $R(t)$ so that $N(t) = S(t) + E(t) + I(t) + V(t) + R(t)$. And the contaminated source or bacterium v. cholerae population is given by $P(t)$.

The susceptible human population is formed through the recruitment of humans either by birth or migration into the population at a constant rate π. This population is decreased following appearance of the infection, which can be acquired by contact with an exposed or infectious individuals at a rate Γ (rate of infection) given by

$$\Gamma = \beta_1 (I + \eta V) + \frac{\beta_2 B}{1 + \tau B}$$

Where, the modification parameter associated with infection by vaccination compartment is $0 < \eta < 1$ accounts for the assumed reduction in transmissibility of exposed cholera carrier relative to vaccinated individuals.

$$\text{Hence, } \frac{dS}{dt} = \pi - \left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1 + \tau B} \right] S(t) - \mu S(t)$$

The population of the exposed is increased by infectious individuals at a rate Γ. The population of the exposed is decreased following the acute progression in individuals at a rate θ. Since 80% of the people infected with v. cholera strains exhibits no symptoms, we assume $(1-\rho)$ to be progression rate of susceptible to exposed class. The population of the exposed is decreased following the acute progression of exposed individuals at a rate θ.

Hence,

$$[\frac{dE}{dt} = (1-\rho) \left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1 + \tau B} \right] S(t) - (\mu + \theta) E(t)$$

The population of Infectious $I(t)$ is generated at the rate ρ. Since proportion of individuals who developed severe symptoms are assumed to be 20% with acute watery diarrhea leading to severe dehydration which resulted to death if untreated at a rate δ. Hence,

$$\frac{dI}{dt} = \rho \left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1 + \tau B} \right] S(t) + \theta E(t) - (\mu + \delta + \alpha + \gamma_1) I(t)$$

The population in the infectious is diminished due to vaccination administered at a rate α , then due to recovery (natural wane off) from mild infection at a rate γ_1 .

The population of vaccinated is generated following a vaccination administered at a rate α. The population is decreased following the recovery due to vaccine at a rate γ_2 and it further decreased following disease induced death as a result of failed vaccination in vaccinated individuals at a rate $\delta\psi$. Hence,

$$\frac{dV}{dt} = \alpha I(t) - (\mu + \psi\delta + \gamma_2)V(t)$$

The rate of change of the population of recovered individuals is increased by the successfully cure of the disease due to natural clearance and due to the vaccines administered in individuals at a rate γ_1 and γ_2 respectively. Hence,

$$\frac{dR}{dt} = \gamma_1 I(t) + \gamma_2 V(t) - \mu R(t)$$

The population of pathogen is generated following the shedding of the disease by an individuals in infectious population and as a result of vaccine failure on vaccinated individuals at a rate ε and $\psi_1\varepsilon$ respectively. Hence,

$$\frac{dP}{dt} = \varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi P(t)$$

With reference to [16], the formulation and assumptions above led to the following systems of ordinary differential equations. Thus, the model formulation is governed by the following system of nonlinear differential equations:

$$\frac{dS}{dt} = \pi - \left[\beta_1(I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right]S(t) - \mu S(t) \qquad (1)$$

$$\frac{dE}{dt} = (1-\rho)\left[\beta_1(I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right]S(t) - (\mu + \theta)E(t) \qquad (2)$$

$$\frac{dI}{dt} = \rho\left[\beta_1(I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right]S(t) + \theta E(t) - (\mu + \delta + \alpha + \gamma_1)I(t) \qquad (3)$$

$$\frac{dV}{dt} = \alpha I(t) - (\mu + \psi\delta + \gamma_2)V(t) \qquad (4)$$

$$\frac{dR}{dt} = \gamma_1 I(t) + \gamma_2 V(t) - \mu R(t) \qquad (5)$$

$$\frac{dP}{dt} = \varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi P(t) \qquad (6)$$

Subject to the initial conditions

$$\left.\begin{aligned} S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0 \\ V(0) = V_0,\ R(0) = R_0,\ P(0) = P_0 \end{aligned}\right\} \qquad (7)$$

B. Model Flow Diagram

With reference to [16] a flow diagram is shown in Figure 1 and also the description of states variables and parameters are described in Table 1.

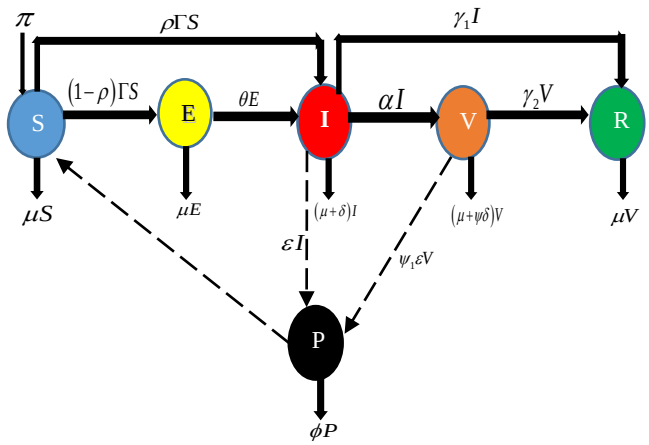

Fig. 1: A Flow Diagram of a Cholera Epidemic Model with Vaccination

C. Description of Model Variables and Parametres

Variable	*Description*
$S(t)$	Susceptible Individuals
$E(t)$	Exposed Individuals
$I(t)$	Infectious Individuals
$V(t)$	Vaccinated Individuals
$R(t)$	Removed Individuals
$P(t)$	Pathogens Population

Table 1: Description of Variables

Parameter	Description
π	Recruitment rate
β_1	Force of infection in human
ρ	Fast progression rate of susceptible $S(t)$ to infective class $I(t)$
β_2	Contact rate between environment to human
ψ	Modification parameter associated with reduced mortality of vaccinated individuals $V(t)$
ψ_1	Modification parameter associated with vaccine failure to reduce the shedding rate of vaccinated individuals $V(t)$
τ	Saturation constant
θ	Progression rate from $E(t)$ to $I(t)$ compartment.
α	Recovery rate for infectious individuals (Natural)
γ_1	Recovery rate for infectious individuals (Natural)
γ_2	Recovery rate for infectious individuals (Natural) vaccine recovery rate
ε	Shedding rate for infectious individuals
μ	Natural death rate
δ	Cholera induced death rate

Table 2: Description of Parameters

III. ANALYSIS OF THE CHOLERA EPIDEMIC MODEL WITH VACCINATION

This section aimed to explore the basic dynamical features of the cholera epidemic model $(1-6)$. Existence and uniqueness are tested at cholera free equilibrium state, basic reproduction number is computed and the sensitivity analysis on some parameters is carried out.

- *Solution of the model properties*

The model systems monitor the dynamics of human population and v. cholera in the pathogen population. Therefore, it is assumed that all the model variable and parameter to be nonnegative for all $t \geq 0$.

➢ *Theorem 1. (Positivity of Solution*

Given the nonnegative initial condition $(1-6)$, then the solution $S(t), E(t), I(t), V(t), R(t)$ and $P(t)$ are non-negative for $t \geq 0$.

Proof: From the model system $(1-6)$, the first equation gives

$$\frac{dS}{dt} = \pi - \left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right] S(t) - \mu S(t)$$

$$\frac{dS}{dt} \geq -\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P} + \mu\right] S(t) \quad (8)$$

$$\frac{dS}{S} \geq -\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P} + \mu\right] d(t)$$

$$\int \frac{dS}{S} \geq \int -\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P} + \mu\right] d(t)$$

$$S(t) \geq S(0)\ell^{-\left[\beta_1 (I+\eta V) + \frac{\beta_2 P}{1+\tau P} + \mu\right] t} \geq 0 \quad (9)$$

$$S(t) \geq 0 \quad (10)$$

From the model system $(1-6)$, the Second equation gives:

$$\frac{dE}{dt} = (1-\rho)\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right] S(t) - (\mu + \theta) E(t)$$

$$\frac{dE}{dt} \geq -(\mu + \theta) E(t)$$
$$\frac{dE}{E} \geq -(\mu + \theta) dt \quad (11)$$
$$\int \frac{dE}{E} \geq \int -(\mu + \theta) dt$$

$$E(t) \geq E(0)\ell^{-(\mu+\theta)t} \geq 0 \quad (12)$$

$$E(t) \geq 0 \quad (13)$$

From the model system $(1-6)$, the Second equation gives:

$$\frac{dI}{dt} = \rho\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right] S(t) + \theta E(t) - (\mu + \delta + \alpha + \gamma_1) I(t)$$

$$\frac{dI}{dt} \geq -(\mu + \delta + \alpha + \gamma_1) I(t)$$
$$\frac{dI}{I} \geq -(\mu + \delta + \alpha + \gamma_1) dt \quad (14)$$

$$\int \frac{dI}{I} \geq \int -(\mu + \delta + \alpha + \gamma_1) dt$$

$$I(t) \geq I(0)\ell^{-(\mu+\delta+\alpha+\gamma_1)t} \geq 0 \quad (15)$$

$$I(t) \geq 0 \quad (16)$$

Where, S_0, E_0 *and* I_0 are the susceptible, exposed and infectious population at time $t=0$ respectively. Similarly, we obtain from the remaining three equations of model $(1-6)$ that $V(t)$, $R(t)$ and $P(t)$.

- *Local Stability of the cholera Free equilibrium*

The Cholera free equilibrium of model $(1-6)$ is given by

$$p_0 = (S,E,I,V,R,P) = \left(\frac{\pi}{\mu},0,0,0,0,0\right) \tag{17}$$

The model has the associated next generation matrices given by

$$F = \begin{bmatrix} 0 & (1-\rho)\beta_1\frac{\pi}{\mu} & (1-\rho)\beta_1\eta\frac{\pi}{\mu} & (1-\rho)\beta_2\frac{\pi}{\mu} \\ 0 & \rho\beta_1\frac{\pi}{\mu} & \rho\beta_1\eta\frac{\pi}{\mu} & \rho\beta_2\frac{\pi}{\mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{18}$$

And,

$$V = \begin{bmatrix} Q_1 & 0 & 0 & 0 \\ -\theta & Q_2 & 0 & 0 \\ 0 & -\alpha & Q_3 & 0 \\ 0 & -\varepsilon & -\varepsilon\psi_1 & \phi \end{bmatrix} \tag{19}$$

On computation it follows that the reproduction number denoted by R_0 is given by

$$R_0 = \rho\left(FV^{-1}\right) = \frac{\pi A_1\left[\beta_1\phi(Q_3+\alpha\eta)+\beta_2\varepsilon(Q_2+\alpha\psi_1)\right]}{\mu\phi Q_1Q_2Q_3} \tag{20}$$

Where,

$$A_1 = \rho Q_1 + (1-\rho)\theta, \quad Q_1 = \mu+\theta, \quad Q_2 = \mu+\delta+\alpha+\gamma_1, \quad Q_3 = \mu+\psi\delta+\gamma_2 \tag{21}$$

➢ *Theorem 2. The cholera free equilibrium of model equation* $(1-6)$ is locally asymptotically stable (LAS) if $R_0<1$, and unstable if $R_0>1$.

The most important concept in epidemiology is the basic reproduction number (expected secondary infection). It measures the average number of new cases of cholera disease generated by a single cholera infected individual in a completely susceptible population.

- Existence of Endemic Equilibrium Point

The model equation $(1-6)$ has a unique endemic equilibrium point with $E, I>0$ given by

$$p^* = \left(S^*,E^*,I^*,V^*,R^*,P^*\right).$$

Proof: the model system $(1-6)$ is reduce to

$$\frac{dS}{dt} = \pi - \Gamma S(t) - \mu S(t) \tag{22}$$

$$\frac{dE}{dt} = (1-\rho)\Gamma S(t) - Q_1E(t) \tag{23}$$

$$\frac{dI}{dt} = \rho\Gamma S(t) + \theta E(t) - Q_2(t) \tag{24}$$

$$\frac{dV}{dt} = \alpha I(t) - Q_3V(t) \tag{25}$$

$$\frac{dR}{dt} = \gamma_1 I(t) + \gamma_2 V(t) - \mu R(t) \tag{26}$$

$$\frac{dP}{dt} = \varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi P(t) \tag{27}$$

Where,

$$Q_1 = (\mu+\theta), \quad Q_2 = (\mu+\delta+\alpha+\gamma_1), \quad Q_3 = \left(\mu+\psi\delta+\gamma_2\right)$$

Setting the *LHS* of equation (22 – 27) to zero we obtain the following results:

From model equation (22)

$$S = \frac{\pi}{\Gamma+\mu} \tag{28}$$

From model equation (23)

$$E = \frac{(1-\rho)\Gamma S}{Q_1} \tag{29}$$

On simplification we obtain

$$E = \frac{(1-\rho)\Gamma\pi}{Q(\Gamma+\mu)_1} = \frac{\Gamma\pi L_3}{Q(\Gamma+\mu)_1} \tag{30}$$

From model equation (24)

$$I = \frac{Q_1\rho\Gamma\pi+\theta\Gamma\pi(1-\rho)}{Q_1Q_2(\Gamma+\mu)} = \frac{\Gamma\pi L_2}{Q_1Q_2(\Gamma+\mu)} \tag{31}$$

From model equation (25)

$$V = \frac{\alpha I}{Q_3} = \frac{\alpha\Gamma\pi L_2}{Q_1Q_2Q_3(\Gamma+\mu)} \tag{32}$$

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From model equation (26)

$$R = \frac{\alpha I}{Q_3} = \frac{\alpha \Gamma \pi L_2}{Q_1 Q_2 Q_3 (\Gamma + \mu)} \quad (33)$$

From model equation (27)

$$P = \frac{\varepsilon I + \varepsilon \psi_1 V}{\phi} = \frac{\Gamma \pi L_1}{\phi Q_1 Q_2 Q_3 (\Gamma + \mu)} \quad (34)$$

Where,

$$L_1 = Q_3 \varepsilon L_2 + \alpha \varepsilon \psi_1 L_2, \quad L_2 = Q_1 \rho + \theta L_3, \quad L_3 = 1 - \rho \quad (35)$$

Our force of infection

$$\Gamma = \beta_1 (I + \eta V) + \frac{\beta_2 P}{1 + \tau P} \quad (36)$$

Substituting the value for S, E, I, V, B into equation (36) we have

$$\Gamma = \frac{\beta_1 \Gamma \pi L_2}{Q_1 Q_2 (\Gamma + \mu)} + \frac{\alpha \eta \Gamma \pi L_2}{Q_1 Q_2 Q_3 (\Gamma + \mu)} + \frac{\beta_2 \Gamma \pi L_1}{\phi Q_1 Q_2 Q_3 (\Gamma + \mu)} \quad (37)$$

$$\Gamma + \mu = \frac{\pi (\phi Q_3 \beta_1 L_2 + \phi \alpha \eta L_2 + \beta_2 L_1)}{\phi Q_1 Q_2 Q_3}$$

$$\Gamma = \frac{\pi (\phi Q_3 \beta_1 L_2 + \phi \alpha \eta L_2 + \beta_2 L_1)}{\phi Q_1 Q_2 Q_3} - \mu$$

$$\frac{\Gamma}{\mu} = \frac{\pi (\phi Q_3 \beta_1 L_2 + \phi \alpha \eta L_2 + \beta_2 L_1)}{\phi Q_1 Q_2 Q_3} - 1 \quad (38)$$

$$\Gamma = \frac{\mu (\phi Q_3 \beta_1 L_2 + \phi \alpha \eta L_2 + \beta_2 L_1)}{\mu \phi Q_1 Q_2 Q_3} - 1 \quad (39)$$

Further simplification and from equation (20) we obtain

$$\Gamma = \mu (R_0 - 1)$$

Therefore the EEP obtain in (29), (30), (31), (32) can be expressed in terms of R_0 as

$$S^* = \frac{\pi}{\mu R_0} \quad (40)$$

$$E^* = \frac{\mu (R_0 - 1)(1 - \rho)\pi}{\mu R_0 Q_1} \quad (41)$$

$$I^* = \frac{\mu (R_0 - 1)\pi L_2}{\mu R_0 Q_1 Q_2} \quad (42)$$

$$V^* = \frac{\mu \alpha (R_0 - 1)\pi L_2}{\mu R_0 Q_1 Q_2 Q_3} \quad (43)$$

$$R^* = \frac{\pi L_2 (R_0 - 1)[\gamma_1 Q_3 + \alpha \gamma_2]}{\mu R_0 Q_1 Q_2 Q_3} \quad (44)$$

$$P^* = \frac{\pi L_1 \mu (R_0 - 1)}{\mu R_0 \phi Q_1 Q_2 Q_3} \quad (45)$$

Where,

$$Q_1 = \mu + \theta \ , \ Q_2 = \mu + \delta + \alpha + \gamma_1 , Q_3 = \mu + \psi \delta + \gamma_2 ,$$
$$L_1 = Q_3 \varepsilon L_2 + \varepsilon \psi_1 \mu L_2 \ , \ L_2 = Q_1 \rho + \theta L_3 , L_3 = 1 - \rho \quad (46)$$

We summarize the following result from equation (41 – 45) in terms of R_0 .

- *Lemma 1:*
  The model equation (22 – 27) has a unique *EEP* if and only if $R_0 > 1$.

- *Existence and Uniqueness Results for Cholera Epidemic Model with vaccination*
  With reference to [17, 18]

  Given the systems of equation below:

$$\left.\begin{aligned} x_1' &= d_1 (t, x_1, x_2, ...x_n) \\ x_2' &= d_2 (t, x_1, x_2, ...x_n) \\ &: \\ x_n' &= d_{1n} (t, x_1, x_2, ...x_n) \end{aligned}\right\} (47)$$

  Then, system equation (47) is given in a compact form as

$$x_i' = d_i (t, x), \quad x_i (t_0) = x_0 ; \quad where, \ i = 1, 2, ...n$$

- Theorem 3
  Let D denote the region $|t - t_0| \le p$, $\|x - x_0\| \le q$ for $x = (x_1, x_2, ..., x_n)$, $x_0 = (x_{10}, x_{20}, ..., x_{2n})$ and suppose that $d(t, x)$ satisfies the Lipschitz condition $\|d(t, x_1) - d(t, x_2)\| \le k \|x_1 - x_2\|$. Whenever, (t, x_1) and (t, x_2) belong to, D, where k is a positive constant, then, there is a constant $\sigma > 0$ such that there exists a unique continuous vector solution $x(t)$ of the system in the interval $|t - t_0| \le \sigma$. If $\frac{\partial d_i}{\partial x_j}$, $i, j = 1, 2, ..., n$, is continuous and $m(x)$ is finite and bounded in, D then, the vector solution $x(t)$ exists and has a unique solution.

- *Remark:* The region of interest is $0 \le \xi \le R$ and a bounded solution of the form $0 \le R \le \infty$ is found in the region D, whose partial derivatives satisfy $\sigma \le \xi \le 0$, where ξ and σ are positive constants.

- *Theorem 4:*

Let D denote the region, $0 \le \xi \le R$. Then the model system (1 - 6) has a unique solution which is bounded and continuous in region, D.

Proof: Let

$$d_1 = \pi - \left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right] S(t) - \mu S(t) \tag{48}$$

$$d_2 = (1-\rho)\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right] S(t) - (\mu + \theta) E(t) \tag{49}$$

$$d_3 = \rho\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right] S(t) + \theta E(t) - (\mu + \delta + \alpha + \gamma_1) I(t) \tag{50}$$

$$d_4 = \alpha I(t) - (\mu + \psi\delta + \gamma_2) V(t) \tag{51}$$

$$d_5 = \gamma_1 I(t) + \gamma_2 V(t) - \mu R(t) \tag{52}$$

$$d_6 = \varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi P(t) \tag{53}$$

Where,

$Q_1 = \mu + \varepsilon - m$, $Q_2 = \mu + g\gamma + \mu_1$, $Q_3 = \mu_0 - b$

For convenience let

$$S(t) = S, E(t) = E, I(t) = I, V(t) = V, R(t) = R, P(t) = P \tag{54}$$

Then, the partial derivatives of the equations are as follows:

$$\left.\begin{aligned} &\left|\frac{\partial d_1}{\partial S}\right| = \left|-\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P} + \mu\right]\right| < \infty, \left|\frac{\partial d_1}{\partial E}\right| = 0, \left|\frac{\partial d_1}{\partial I}\right| = \left|-\beta_1 S\right| < \infty, \\ &\left|\frac{\partial d_1}{\partial V}\right| = \left|-\beta_1 \eta S\right| < \infty, \left|\frac{\partial d_1}{\partial R}\right| = 0, \left|\frac{\partial d_1}{\partial P}\right| = \left|\frac{\beta_2 S}{(1+\alpha P)^2}\right| < \infty \end{aligned}\right\} \tag{55}$$

$$\left.\begin{aligned} &\left|\frac{\partial d_2}{\partial S}\right| = \left|(1-\rho)\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right]\right| < \infty, \left|\frac{\partial d_2}{\partial E}\right| = \left|-(\mu + \theta)\right|, \left|\frac{\partial d_2}{\partial I}\right| = \left|(1-\rho)\beta_1 S\right| < \infty, \\ &\left|\frac{\partial d_2}{\partial V}\right| = \left|(1-\rho)\beta_1 \eta S\right| < \infty, \left|\frac{\partial d_2}{\partial R}\right| = 0, \left|\frac{\partial d_2}{\partial P}\right| = \left|\frac{(1-\rho)\beta_2 S}{(1+\alpha P)^2}\right| < \infty \end{aligned}\right\} \tag{56}$$

$$\left.\begin{aligned} &\left|\frac{\partial d_3}{\partial S}\right| = \left|\rho\left[\beta_1 (I + \eta V) + \frac{\beta_2 P}{1+\tau P}\right]\right| < \infty, \left|\frac{\partial d_3}{\partial E}\right| = |\theta| < \infty, \left|\frac{\partial d_3}{\partial I}\right| = \left|-(\mu + \delta + \alpha + \gamma_1)\right| < \infty, \\ &\left|\frac{\partial d_3}{\partial V}\right| = \left|\rho\beta_1 \eta S\right| < \infty, \left|\frac{\partial d_3}{\partial R}\right| = 0, \left|\frac{\partial d_3}{\partial P}\right| = \left|\frac{(1-\rho)\beta_2 S}{(1+\alpha P)^2}\right| < \infty \end{aligned}\right\} \tag{57}$$

$$\left|\frac{\partial d_4}{\partial S}\right| = 0, \left|\frac{\partial d_4}{\partial E}\right| = 0, \left|\frac{\partial d_4}{\partial I}\right| = |\alpha| < \infty, \left|\frac{\partial d_4}{\partial V}\right| = \left|-(\mu + \psi\delta + \gamma_2)\right| < \infty, \left|\frac{\partial d_4}{\partial R}\right| = 0, \left|\frac{\partial d_4}{\partial P}\right| = 0 \tag{58}$$

$$\left|\frac{\partial d_5}{\partial S}\right| = 0, \left|\frac{\partial d_5}{\partial E}\right| = 0, \left|\frac{\partial d_5}{\partial I}\right| = |\gamma_1| < \infty, \left|\frac{\partial d_5}{\partial V}\right| = |\gamma_2| < \infty, \left|\frac{\partial d_5}{\partial R}\right| = |-\mu| < \infty, \left|\frac{\partial d_5}{\partial P}\right| = 0 \tag{59}$$

$$\left|\frac{\partial d_6}{\partial S}\right| = 0, \left|\frac{\partial d_6}{\partial E}\right| = 0, \left|\frac{\partial d_6}{\partial I}\right| = |\varepsilon| < \infty, \left|\frac{\partial d_6}{\partial V}\right| = |\varepsilon\psi_1| < \infty, \left|\frac{\partial d_6}{\partial R}\right| = 0, \left|\frac{\partial d_6}{\partial P}\right| = |-\phi| < \infty \tag{60}$$

Thus, it was observed that all the partial derivatives obtained are continuous and bounded. Hence, it follows from Theorem 4 that in the region, D, there exist a unique solution to the model system $(1-6)$.

- *Sensitivity Analysis of Cholera Epidemic Model with Vaccination*

The key parameters in the model are identified in the analysis. The analysis measures the relative change in a variable with respect to the relative change in its parameters. This procedure enabled the identification of those parameters that are more sensitive to the increase or decrease of the basic reproduction number.

- *Proposition 1*

The sensitivity index of the quantity R_0 with respect to the parameter j_x is expressed as

$$\Upsilon_{j_x}^{R_0} = \frac{\partial R_0}{\partial j_x} \times \frac{j_x}{R_0}$$

- *Proof*

The sensitivity of R_0 is expressed as when the variable is a differentiable function of the parameter. Thus, for the model parameters $\beta_1\ \beta_2\ \eta\ \theta\ \varepsilon\ \rho\ \psi_1\ \alpha\ \gamma_2\ \phi\ \gamma_1$ we obtain the following results:

$$\Upsilon_{j_x}^{R_0} = \frac{\partial R_0}{\partial j_x} \times \frac{j_x}{R_0}$$

Thus, the computed indices are presented below:

$$\left.\begin{aligned}
\Upsilon_{\beta_1}^{R_0} &= \frac{\partial R_0}{\partial \beta_1}\times\frac{\beta_1}{R_0} = 0.6868231074\\
\Upsilon_{\beta_2}^{R_0} &= \frac{\partial R_0}{\partial \beta_2}\times\frac{\beta_2}{R_0} = 0.3599216760\\
\Upsilon_{\rho}^{R_0} &= \frac{\partial R_0}{\partial \rho}\times\frac{\rho}{R_0} = -0.1688298038\\
\Upsilon_{\varepsilon}^{R_0} &= \frac{\partial R_0}{\partial \varepsilon}\times\frac{\varepsilon}{R_0} = 0.5901193534
\end{aligned}\right\} \quad (61)$$

$$\left.\begin{aligned}
\Upsilon_{\eta}^{R_0} &= \frac{\partial R_0}{\partial \eta}\times\frac{\eta}{R_0} = 0.03122324620\\
\Upsilon_{\psi_1}^{R_0} &= \frac{\partial R_0}{\partial \psi_1}\times\frac{\psi_1}{R_0} = 0.01561162311\\
\Upsilon_{\gamma_1}^{R_0} &= \frac{\partial R_0}{\partial \gamma_1}\times\frac{\gamma_1}{R_0} = -\ 0.01553509788\\
\Upsilon_{\gamma_2}^{R_0} &= \frac{\partial R_0}{\partial \gamma_2}\times\frac{\gamma_2}{R_0} = -0.03838345451
\end{aligned}\right\} \quad (62)$$

$$\left.\begin{aligned}
\Upsilon_{\phi}^{R_0} &= \frac{\partial R_0}{\partial \phi}\times\frac{\phi}{R_0} = -0.5901193540\\
\Upsilon_{\alpha}^{R_0} &= \frac{\partial R_0}{\partial \alpha}\times\frac{\alpha}{R_0} = -0.04712444462\\
\Upsilon_{\theta}^{R_0} &= \frac{\partial R_0}{\partial \theta}\times\frac{\theta}{R_0} = 0.09980301103
\end{aligned}\right\} \quad (63)$$

- *Remarks:* This analysis is based on the parameters which are crucial to the disease prevalence and transmissions. The results is summarized in the table 3 below.

Parameter	Parameters value			
	Decription	Parameter Value	Reference	Sensitivity
β_1	Force of infection in human	0.05	[15]	+0.6868
ρ	Fast progression rate	0.5	[14]	-0. 1688
β_2	Force of infection in pathogen	0.05	[19]	+0.3599
ε	Shedding rate	0.01	[19]	+0.5901
ψ_1	Vaccine reduced failure	0.25	varied	+0.0156
γ_2	Vaccine recovery rate	0.05	[20]	-0.0384
η	Modification parameter	0.5	varied	+0.0312
ϕ	Vaccine failure in vaccinated	0.5	[9]	-0.5901
α	Vaccine rate	0.5	Estimate	-0.0471
γ_1	Natural recovery rate	0.2	Hartley	-0.0155
θ	Progression rate	0.3	[16]	+0.0998

Table 3: Numerical Values of the Sensitivity Indices and their Source

- *Interpretation of Sensitivity Index of the Model*

From Table 3, we obtain the most sensitive parameter to the least sensitive parameter by rearranging the these parameters in the order of their magnitude in descending order by ignoring the sign (absolute value) as follows: $\beta_1, \varepsilon, \phi, \beta_2, \rho, \theta, \alpha, \gamma_2, \eta, \psi_1$ and the least parameter is γ_1.

The sensitivity analysis results shows that the most sensitive parameter to the basic reproduction number $R_0 = 0.754838 < 1$ is the contact rate in human β_1, followed by shedding rate of infectious ε, followed by death rate of vibrio cholera ϕ, followed by concentration of vibrio cholera β_2, followed by exposure progression rate ρ and so on. From Table 2 it is evident that the results having negative values show that the relationship between the parameters and R_0 is inversely proportional. Thus, any increase in the parameters, ρ, ψ_1, γ_2, ϕ and γ_1 will cause a decrease in the same proportion in R_0. This implies a decrease in such parameters value will result in the increase of exactly the same proportion in R_0 since theyare inversely proportional to the R_0. For instance as sh own in Table 3 we obtain $R_0 = 0.754838 < 1$, therefore on varying the parameter value ϕ to 0.70 the value of R_0 decrease to 0.6648 and so on. Thus cholera eventually will disappear in the community with time. The positive sign in the sensitivity value, indicates that any increase in the parameter value had an impact to increase the basic reproduction number R_0, since the relationship is directly proportional. From Table 2 it is evident that, the parameters β_1 β_2 η θ and ε have positive impact which significantly increases the basic reproduction number R_0. For instance as shown in Table 3 and when $R_0 = 0.754838 < 1$, it was observed on varying parameter for β_1 to 0.06 the value of R_0 increases to 0.842764. On varying the parameter value of ε to 0.02 we obtain $R_0 = 1.07005 > 1$, thus, increase in each

parameter value will cause a significant increase in R_0 which eventually cholera will persists in the community. Based on the results obtain, it was observe that the contact rate in human β_1, shedding rate of infectious ε, and concentration of vibrio cholera β_2 were key parameters that influenced the triggering a cholera outbreak in the community. Hence, to curtail the spread of the disease, communities at risk are sensitize via intensive public health education in the following activities: basic hygiene, avoiding contaminated food and water, identification and supplied of sufficient vaccines and logistics.

IV. NUMERICAL SIMULATIONS AND DISCUSSIONS

A. Simulations

The numerical simulations of model system (1) using maple 18 software is carried out with initial conditions $S(0)=60, E(0)=40, I(0)=30, V(0)=29, R(0)=10, P(0)=5$ and the set of parameter values given in Table 3 whose sources are mainly from literatures as well as assumptions. The following results are obtained:

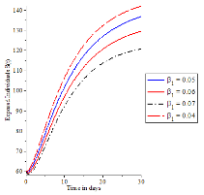
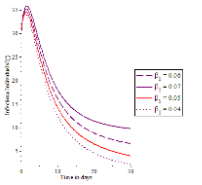


Fig. 1.


Fg. 3

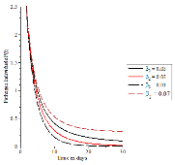


Fig.4

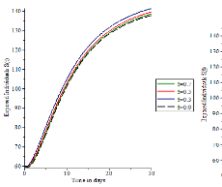


Fig. 5

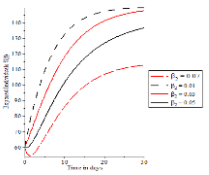


Fig. 6

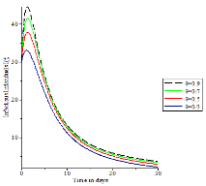


Fig. 7

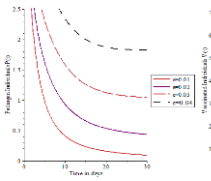


Fig. 8

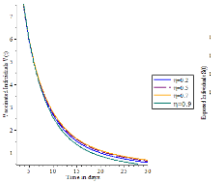


Fig. 9

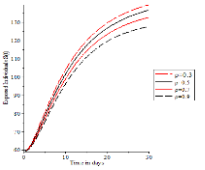


Fig. 10

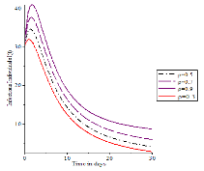


Fig. 11

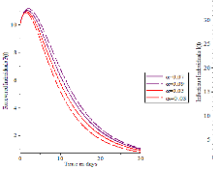


Fig. 12

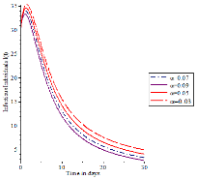


Fig. 13

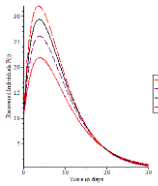


Fig. 14

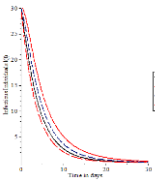


Fig. 15

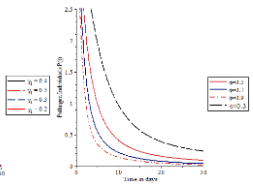


Fig. 16

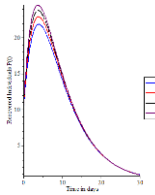


Fig. 17

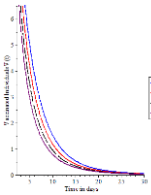


Fig. 18

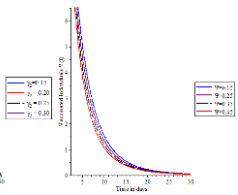


Fig. 19

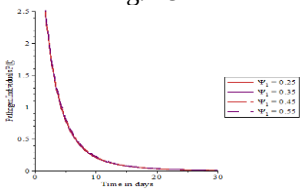


Fig. 20

Fig. 2 – 20. Simulations of the cholera model with vaccination using the parameters in Table 3, with $\pi=30$, $\psi=0.25$, $\tau=0$, $\mu=0.2$, $\delta=0.2$ for $R_0=0.754838<1$, which are in agreement with sensitivity index results obtained. Furthermore, on varying the value of parameter $\beta_1, \beta_2, \eta, \theta, \varepsilon, \rho, \psi_1, \alpha, \gamma_2, \phi$, and γ_1 in the populations of: exposed individuals $E(t)$, Infectious individuals $I(t)$, Vaccinated individuals $I(t)$, recovered individuals $R(t)$, and Pathogen populations $P(t)$ against time, t, with initial conditions, eventually population approach the Cholera-free equilibrium (in line with Theorem 4)

B. Discussions

The study explore the effects of the contact rate in human β_1 on the exposed population, $E(t)$. The results in Fig. 2 shows that an increase in the contact rate with poor sanitation or drinking contaminated water as a result of disaster or civil crisis results in the increase of the new cases of cholera in the population which increases the infectious population $I(t)$ as shown in Fig. 3. Thus, the community at risk shall be sensitize to drink and use safe water. Fig. 4 depict the effect of varying the parameter value of the force of transmission in pathogen population, $P(t)$. It evident that exposure to contaminated environment increases the risk of contracting cholera. The population of exposed class $E(t)$ decreases with increase in β_2 as shown in Fig. 5 so that of pathogen population $P(t)$ increases as shown in Fig. 4. Thus regular environmental sanitation is necessary to avoid further contamination of the environment. We study the effects of progression rate θ, from exposed population to infectious population and the results are as shown in Fig. 6. The results in Fig. 6 shows that an increase in θ results in the increase of the number of cholera infectious individuals $I(t)$ as shown in Fig. 7. Thus, if the cholera risk is not

properly addressed in the IDPs camps, surrounding area and within the conflict zone, then the risk of onward transmission will inevitably increase. The result In Fig. 8 the study depicts effects of shedding rate ε, in the pathogen population, $P(t)$. The result in Fig. 8 shows that an increase in shedding rate results in an increase in the pathogen population $P(t)$. Thus the basic hygiene shall be adequately practice for further compounding the prone diseases like cholera spreading. Fig. 9 depicts effect of varying of the modification of parameter η in the vaccinated population $V(t)$. The results in Fig, 9 shows that the parameter is less sensitive on R_0. Thus any increase in the parameter value the cholera population eventually reach a lower level. However available access to sufficient vaccines and logistics shall be made. Fig. 10 depict effect of progression rate ρ of exposed $E(t)$ to infectious population $I(t)$. The results in Fig. 10 shows that an increase in the rate of exposure results to an increase in the cholera infectious individuals $I(t)$ as shown in Fig. 11. Thus, available funding shall be used to support those communities neighboring the refugee camps. Fig. 12 depicts effect of vaccination rate α. The results in Fig. 12 show that increase in the parameter results in rapid progression of recovered individuals to the DFE. As shown in Fig. 12 it show that the infectious population eventually dies out as shown in Fig. 13, thus access to sufficient to vaccines shall be made available. Fig. 14 depict effect of recovery rate γ_1 for infectious individuals in the recovered population $R(t)$ and infectious individual's population $I(t)$ which the results are shown in Fig. 14. The result show that increase in the recovery rate of cholera infected individuals results in a decrease in the cholera infected individuals population $I(t)$ to increase as shown in Fig. 15. Fig. 16 depict the effect of death of vibrio cholera ϕ, we observed that in Fig. 16 the population of the vibrio cholera decrease in the rapidly to lower levels with time with in cresses in the parameter value of ϕ due to regular sanitation and basic hygiene in the community. Thus, environmental triggers of cholera outbreak shall be eliminated. The effects of vaccine recovery rate γ_2 is observed in Fig. 17 we observed that the population of recovered individual increase with increase in vaccine rate. In Fig. 18 we observed that vaccinated population $V(t)$ decreases with increase in vaccine coverage and increase a recovery population $R(t)$ with time as shown in Fig. 17. Thus, Fig. 17 and Fig. 18 depict positive impact of vaccination. In Fig. 19 the effect of modification parameter with mortality of vaccinated individuals ψ is observed. We found that increase in the parameter value results in the elimination of pathogen population $P(t)$. Thus, the disease will disappear in the community with time as shown in Fig. 19. The effects of modification parameter to reduce shedding rate ψ_1 was observed which it shown that pathogen population decreases rapidly to the lower level eventually over the time with increase in ψ_1 following the positive response of vaccination in the population. Thus, eventually cholera population will be eliminated with time as shown in Fig. 20. The simulations results reveals that to curtails the spread of cholera in the community, authorities shall enables conducive environment for good governance to bring an end to the refugees crisis, eradication of poverty, health security, and economic development so that total eradication of the disease would be achieved.

V. CONCLUSION

In this study, a deterministic of cholera epidemic model with vaccination is presented and analyzed rigorously to gain insight into the model existence and sensitivity analysis. The study comprises of six system of nonlinear ordinary differential equation. The model basic properties for positivity of solutions were investigated and it was shown that the solution $S(t), E(t), I(t), V(t), R(t), P(t)$ are nonnegative for $t \geq 0$. The model have two equilibrium namely, cholera free equilibrium and endemic equilibrium points. Thus, the cholera free equilibrium of model system is LAS if $R_0 < 1$ and unstable if $R_0 > 1$. The study investigate the existence and uniqueness of the model and the results show that there exist a unique solution which is bounded and continuous in D. the threshold parameter basic reproduction number R_0 was computed using next generation matrix approach and it reveals that when $R_0 \leq 1$ the cholera dies out and when $R_0 > 1$ cholera will persists in the population. The sensitivity index of the quantity R_0 with respect to the following parameter values β_1, β_2, η, θ, ε, ρ, ψ_1, α, γ_2, ϕ, and γ_1 were computed. The result showed that the contact rate in human β_1 with the value 0.6868 followed by the shedding rate ε with the value 0.5901 are found to be most sensitive parameter that influenced the R_0. Furthermore, results of sensitivity index show that any increase in the following parameter, β_1, β_2, η, θ, ε results in an increase in threshold quantity R_0. Similarly
an increases in the following parameters, ρ, ψ_1, α, γ_2, ϕ, and γ_1 results in the decrease in the threshold quantity R_0. The numerical simulations and illustrations on effect of the varying parameters value are presented and plotted which are found to be in good agreements with the analytical results as shown in Table 3 and Theorem 2. Hence, it is evident that local variation that influences the spread of cholera disease are contaminated water source, contaminated food during preparation and environmental sanitation. However, to curtail the spreads of cholera in the community; it is recommended that public health campaigns with emphasis to sanitation be conducted frequently, in the communities neighboring the overcrowded refugees and IDPs camps, as well as exposure to cholera at risk areas be avoided.

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