Using Shanchol Oral Vaccines To Prevent Cholera In children Under Five Years Of Age: A Deterministic Modeling Approach

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Abstract: Cholera epidemic remains a global threat to public health and a key indicator of lack of social development in most part of third world countries. Cases tend to be clustered by location as well as season, with most infections occurring in children ages 1-5 years. This research provides new mathematical deterministic compartmental models for preventive cholera transmission dynamics, using Shanchol Oral Vaccines for under five years age. These models were built on SIR and *vibrio cholera* (B) models .The transmission means; global impact and preventive mechanism of disease are discussed. We establish the Disease free and the endemic equilibrium states, and carried out the stability analysis of the Disease free equilibrium. It is shown that the model disease free equilibrium is locally and globally stable in as much we keep value of $T < 0$ and $D > 0$ (the state of complete eradication of cholera from entire population).

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1. Introduction

Cholera is an acute intestinal infection caused by ingestion of food or water contaminated with the bacteria *vibrio cholera 01 and 0139(Riyan 2004 AND WHO 2010)*. Every year there is an estimated 3-5 million cholera cases and 100,000-120,000 deaths due cholera .It has short incubation period, from less than one to five days, and produces an enterotoxin that causes a copious, painless, water diarrhea that can quickly lead to severe dehydration and death if treatment is not promptly. Vomiting also occurs in most patients. The short incubation period of two to five days, enhance the potentially explosive pattern of out breaks (Faruque 2008 and WHO 2010).Two serogroups of *v. cholera* - 01 and 0139 - causes out breaks (Alexander 2008). *v. cholera* 01 causes the majority of outbreak, while 0139 -first indentified in Bangladash in 1992 –is confined to South-East Asia. Non-01 and non-0139 v. cholera can cause mild diarrhea but dot not generate epidemics. The bacteria are transmitted via contaminated drinking water or food. Pathogenic *v. cholera* can survive refrigeration and freezing in food supplies. (Reildl et al 2002) The dosage of bacteria required to cause an infection in healthily volunteers via oral administration of living vibrios is greater than ~1000 organisms (Hartely 2006). After consuming an antacid, however, cholera development in most volunteers after consumption of only ~100 cholera *vibrios* experiments also show that *vibrios* consumed with food are more likely to cause infection than those from water alone (Finkelstein 1996). Cases tend to be clustered by location as well as season, with most infections occurring in children ages 1-5 years (WHO 2010).

Cholera transmission is closely linked to inadequate environmental management. Typical at-risk areas include peri-urban slums, where basic infrastructure is not available, as well as camps for internally displaced people or refugees, where minimum requirements of clean water and sanitation are not met. The consequences of a disaster – such as disruption of water and sanitation systems, or the displacement of populations to inadequate and overcrowded camps – can increase the risk of cholera transmission should the bacteria be present or introduced. Epidemics have never arisen from dead bodies. Cholera remains a global threat to public health and a key indicator of lack of social development. Recently, the re-emergence of cholera has been noted in parallel with the ever-increasing size of vulnerable populations living in unsanitary conditions (Emch 2008 and WHO2010).The number of cholera cases reported to WHO continues to rise. From 2004 to 2008, cases increased by 24% compared with the period from 2000 to 2004. For 2008 alone, a total of 190 130 cases were notified from 56 countries, including 5143 deaths. Many more cases were unaccounted for due to limitations in surveillance systems and fear of trade and travel sanctions. Cholera has long been, and continues to be, a world health issue. War and extreme

environmental event can contribute to the disease' ability to ravage communities to be a threat to much of the world (WHO 2010).

There are two types of safe and effective oral cholera vaccines currently available on the market. Both are whole-cell killed vaccines, one with a recombinant B-sub unit, the other without. Both have sustained protection of over 50% lasting for two years in endemic settings.

One vaccine (Dukoral) is WHO prequalified and licensed in over 60 countries. Dukoral has been shown to provide short-term protection of 85–90% against *V. cholerae* O1 among all age groups at 4–6 months following immunization. The other vaccine (Shanchol) is pending WHO prequalification and provides longer-term protection against *V. cholerae* O1 and O139 in children under five years of age. Both vaccines are administered in two doses given between seven days and six weeks apart. The vaccine with the B-subunit (Dukoral) is given in 150 ml of safe water. WHO recommends that immunization with currently available cholera vaccines be used in conjunction with the usually recommended control measures in areas where cholera is endemic as well as in areas at risk of outbreaks. Vaccines provide a short term effect while longer term activities like improving water and sanitation are put in place. When used, vaccination should target vulnerable populations living in high risk areas and should not disrupt the provision of other interventions to control or prevent cholera epidemics. The WHO 3-step decision making tool aims at guiding health authorities in deciding whether to use cholera vaccines in complex emergency settings.The use of the parenteral cholera vaccine has never been recommended by WHO due to its low protective efficacy and the high occurrence of severe adverse reactions(WHO 2010).

In this work, we study effect of shanchol oral vaccines in preventing under five years age from getting cholera using mathematical modeling technique. The model description, diagram and equation are presented in section. We obtained the equilibrium states in section three, while the stability analysis of the disease free equilibrium state was carried out in section four. The result was discussed in section five and concluding remarks presented in section six.

2. Model description

The population is partition into four compartment namely; S(t), I(t), R(t) and B(t) be the number susceptible, infected, removed individuals and toxigenic *v. cholera* in water at time t respectively. Let Λ be the recruitment rate into the susceptible class, which could include immigrants and/ or new born that are uninfected. We assume that μ_0 and μ_1 are the capital natural human death and cholera death rate. 'N' be the total population and ' a' be the capital exposure rate to contaminated water. $\lambda(B)$ the probability of any one exposed contaminated water and food to catch cholera, while γ the rate of recovering from cholera.'n_b' be the net growth of bacteria and ' e' is the capital contribution of the infected to the population of *v. cholera*. ' v ' is the vaccination within susceptible department, but it had no effect on the infection class.

Model diagram (Fig. 1)

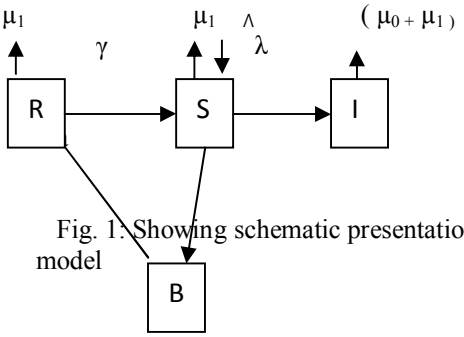

Fig. 1: Showing schematic presentation of the model

3.1 Model equation

$\frac{ds}{dt} = \Lambda - \mu_1 S - v S - a\lambda(B)S$ (1)

$\frac{dI}{dt} = a\lambda(B)S - (\mu_0 + \mu_1 + \gamma)I$ (2)

$\frac{dR}{dt} = \gamma I - \mu_1 R$ (3)

$\frac{dB}{dt} = B n_b + e\, I$ (4)

Equilibrium states of model: We now solve the model equations to obtain the equilibrium states .At the equilibrium state

$\frac{ds}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = \frac{dB}{dt} = 0$

Let S (t) = w, I (t) = x, R (t) = y, and B (t) = z

Then the system of equations become:

$\Lambda - \mu_1 w - vw - a\lambda wz = 0$ (5)

$a\lambda wz - (\mu_0 + \mu_1 + \gamma)x = 0$ (6)

$vw - \mu_1 y = 0$ (7)

$z n_b + e\, x = 0$ (8)

The disease free equilibrium state:

From equation (8), we have

$z = -\frac{ex}{n_b}$ (9)

substitute (8) into (6)

$a\lambda wz - (\mu_0 + \mu_1 + \gamma)x = 0$

$-a\lambda \frac{ex}{n_b} w - \gamma x - \mu_0 x - \mu_1 x = 0$

$(-a\lambda \frac{e}{n_b} w - \gamma - \mu_0 - \mu_1)\, x = 0$

Either x or $(-a\lambda \frac{e}{n_b} w - \gamma - \mu_0 - \mu_1) = 0$ (10)

$\Rightarrow$ x = 0 (11)

From equation (9)

$z = -\frac{ex}{n_b}$

but x = 0

$\Rightarrow z = 0$ (12)

From equation (5)

$\Lambda - \mu_1 w - vw - a\lambda wz = 0$

But z = 0

$\Rightarrow \Lambda - \mu_1 w - vw = 0$

$\Rightarrow w = \frac{\Lambda}{\mu_1 + v}$ (13)

From equation (7)

$vw - \mu_1 y = 0$

$\Rightarrow y = \frac{vw}{\mu_1}$

But $w = \frac{\Lambda}{\mu_1 + v}$

$\Rightarrow y = \frac{\Lambda}{(\mu_1 + v)\mu_1}$ (14)

From equation (10)

$-a\lambda\frac{e}{n_b}w - \gamma - \mu_0 - \mu_1 = 0$

$-a\lambda ew - \gamma n_b - \mu_0 n_b - \mu_1 n_b = 0$

$w = \frac{-n_b(\gamma + \mu_0 + \mu_1)}{a\lambda e} = 0$ (15)

From equation (7)

$vw - \mu_1 y = 0$

$y = \frac{vw}{\mu_1}$

$y = [\frac{-n_b(\gamma + \mu_0 + \mu_1)}{a\lambda e}]v \div \mu_1$

$y = \frac{-n_b v(\gamma + \mu_0 + \mu_1)}{a\lambda e \mu_1}$ (16)

from equation (5)

$\Lambda - \mu_1 w - vw - a\lambda wz = 0$

$z = \frac{\Lambda - \mu_1 w - vw - a\lambda w}{a\lambda w}$

but $w = \frac{-n_b(\gamma + \mu_0 + \mu_1)}{a\lambda e}$

$z = \frac{1}{a\lambda}[\frac{\Lambda}{w} - \mu_1 - v]$

$z = \frac{\Lambda a\lambda e + \gamma\mu_1 n_b + \mu_0\mu_1 n_b + \mu_1^2 n_b + vn_b\gamma + vn_b\mu_0 + vn_b\mu_1}{n_b(\gamma + \mu_0 + \mu_1)a\lambda}$

(17)

From equation (8)

$x = -\frac{zn_b}{e}$

$\Rightarrow x = \frac{\Lambda a\lambda e + \gamma\mu_1 n_b + \mu_0\mu_1 n_b + \mu_1^2 n_b + vn_b\gamma + vn_b\mu_0 + vn_b\mu_1}{a\lambda e(\gamma + \mu_0 + \mu_1)a\lambda}$

(18)

3.2 The equilibrium states are:

(i) The disease free equilibrium state which is given by:-

$(w, x, y, z) = \frac{\Lambda}{\mu_1 + v}, 0, \frac{\Lambda}{(\mu_1 + v)\mu_1}, 0$

(ii) The endemic equilibrium state which is given by:-

$w = \frac{-n_b(\gamma + \mu_0 + \mu_1)}{a\lambda e}$

$x = \frac{\Lambda a\lambda e + \gamma\mu_1 n_b + \mu_0\mu_1 n_b + \mu_1^2 n_b + vn_b\gamma + vn_b\mu_0 + vn_b\mu_1}{a\lambda e(\gamma + \mu_0 + \mu_1)a\lambda}$

$y = \frac{-n_b v(\gamma + \mu_0 + \mu_1)}{a\lambda e\mu_1}$

$z = \frac{\Lambda a\lambda e + \gamma\mu_1 n_b + \mu_0\mu_1 n_b + \mu_1^2 n_b + vn_b\gamma + v n_b\mu_0 + vn_b\mu_1}{n_b(\gamma + \mu_0 + \mu_1)a\lambda}$

3.3 Stabilty analysis of the disese free equilibrium atates

Having established the equilibrium states. We now investigate stability of Disease Free equilibrium states. To obtain this, we examine the behavior of the model population near the equilibrium state (Lenka 2007)

3.4 The characteristic equation: Recall that the system of equations at equilibrium state is:

$\Lambda - \mu_1 w - vw - a\lambda wz = 0$

$a\lambda wz - (\mu_0 + \mu_1 + \gamma)x = 0$

$vw - \mu_1 y = 0$

$zn_b + e\,x = 0$

We obtain the Jacobian matrix of this system of equations as presented by Benyah (2008)

$$\mathbf{J} = \begin{pmatrix} -\mu_1 - v - a\lambda z & 0 & 0 & -a\lambda w \\ a\lambda z & -(\mu_0 + \mu_1 + \gamma) & 0 & a\lambda w \\ v & 0 & -\mu_1 & 0 \\ 0 & e & o & n_b \end{pmatrix}$$

$$(w, x, y, z) = \left(\frac{\Lambda}{\mu_1 + v}, 0, \frac{\Lambda}{(\mu_1 + v)\mu_1}, 0\right)$$

$$J = \begin{pmatrix} -\mu_1 - v & 0 & 0 & \frac{-a\lambda\Lambda}{\mu_1 + v} \\ 0 & -(\mu_0 + \mu_1 + \gamma) & 0 & \frac{a\lambda\Lambda}{\mu_1 + v} \\ v & 0 & -\mu_1 & 0 \\ 0 & e & o & n_b \end{pmatrix}$$

We consider the characteristic equation $\mathrm{Det}(J - \lambda I) = 0$

$$J = \begin{pmatrix} -(\mu_1 + v + \lambda) & 0 & 0 & \frac{-a\lambda\Lambda}{\mu_1 + v} \\ 0 & -(\mu_0 + \mu_1 + \gamma + \lambda) & 0 & \frac{a\lambda\Lambda}{\mu_1 + v} \\ v & 0 & -(\mu_1 + \lambda) & 0 \\ 0 & e & o & n_b - \lambda \end{pmatrix}$$

To obtain the stability of the disease free equilibrium state, we use the principle of linearised stability (or so called decaying exponentials) Lenka (2007).
We now obtain trace (T) and the determinant (D).Then

$$T = -(\mu_1 + v + \lambda + \mu_0 + \mu_1 + \gamma + \lambda + \mu_1 + \lambda - n_b + \lambda) < 0$$

and its determinant is also given by

$$D = \frac{1}{\mu_1}\Big(\big(-\mu_1 - v - \lambda\big)\big(\mu_1 + \lambda\big)\big(\mu_1 \mu_0 n_b - \mu_1 \mu_0 \lambda + \mu_1^2 n_b - \mu_1^2 \lambda + \mu_1 \lambda n_b - \mu_1 \lambda^2 + e\, a\, \lambda\, \Lambda + e\, v\, \mu_1\big)\Big)$$

> 0

4.1 Discussions

From the stability analysis carried out in section four above, the roots of the characteristic equation have negative real parts. According to the principle of linearised stability; the disease free equalibrium state is locally asymptotically stable; Infact, the disease steady state is globally asymptotically stable (i.e, T < 0 and D > O)

4.2 Conclusions

In this study we presented a mathematical model of effect of shanchol oral vaccines in preventing under five years from getting cholera. We show that the disease free equilibrium is both locally asymptotically and globally stable for trace of J is less than zero and its determinant is greater than zero both models. Consequently, as long as we keep T< 0 and D> o, the disease –free state would be asymptotically stable. There will not be cholera in children under the five years age even in a naive region.

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