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Effects of Carriers on the Transmission dynamics of Non- Typhoidal Salmonella Epidemics

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Abstract: **The impact of control strategies to effectively control the burden of the effect of carriers on the salmonella diarrhea is investigated in this paper. This model studies the dynamics of diarrhea by formulating and analyzing the impact of carriers. According to the pathogenesis of salmonella, the model had been designed as an SIR system comprising of a non-constant population. The disease-free state and basic reproduction number (R_0) have been computed for this system. In epidemics, there are always two cases: $R_0<1$ (diseases free state) and $R_0>1$ (epidemic existing state).**

Keywords: **Carriers, Salmonella, Salmonellosis, Diarrhea, Mathematical Modeling, Epidemics, Epidemic Modeling, Basic Reproduction Number.**

I. INTRODUCTION

An infectious disease is one that can be spread or transmitted from one host to another. Diarrhea is an infectious disease. There are individuals who are able to transmit their illness but do not exhibit any symptoms. These individuals are called "carriers" and they play an important role in the transmission of the disease. The focus of this study is on infectious diseases carriers. In the context of global health, the repeated threats presented by infectious diseases cannot be disregarded. It has been recorded that in 2008, infectious diseases accounted for about 16% of death worldwide. Infectious diseases are also known as transmissible diseases and as the name suggests, these diseases can be transmitted throughout a certain population. Considering a closed population, the introduction of an infective individual or an external vector can result in the spread of an infectious disease within the population [13]. Example of external vectors including water, air ,body fluids or biological vectors which carry infectious agents such as protozoa, bacteria or virus. Among many other communicable diseases, water related diseases occupy a significant position as water is a essential to life an many diseases can easily be transmitted through water. Direct or indirect ingestion of contaminated water containing pathogenic microorganisms can cause the spread of numerous infectious diseases.

Diarrhea -Global and National Burden

Diarrhea is one of the most common infectious diseases that is transmitted through contaminated water. The WHO (World Health Organization) estimates that there are about 1.7 billion diarrhea cases per year around world-wide [14]. Diarrhea is listed as the second leading cause of mortality in children causing around 700000 child deaths per year, with children under five at higher risk of getting severe diarrhea [14]. According to the health statistics of the country, there are about 15000 cases of diarrhea reported in 2012. Together with this, there were an approximate of about 200 deaths recorded due to diarrhea. There are many type of each pathogen that can cause diarrhea as a diseases or can cause other diseases that result in diarrhea. Salmonella is a bacteria genus that is closely related to diarrhea. A specific serotype, salmonella enteritis, causes salmonella enteritis, causes salmonellosis which is a communicable intestinal infection. Common

symptoms of salmonellosis include diarrhea, fever and abdominal cramps. Extremes of age and immunosuppressive condition act as high risk factors and thus small children and elderly people are more prone to diseases like salmonellosis [2]. Although the fecal-oral route plays a vital role in the transmission of the bacteria, there are certain foodstuffs that are considered to cause a large number of infections. On a global level, salmonella is the second most common pathogen causing diarrhea. Salmonella occupies a noteworthy rank in the cause and spread of diarrhea. Based on research work, it was concluded that salmonella is one of the most common bacteria pathogens that causes diarrhea [12]. Thus, a system that incorporates the dynamics and transmission of salmonella diarrhea will prove to be of great advantage in combating diarrheal outbreaks in the country. It is envisaged that the system will act as a tool that will provide appropriate information as output results that can be used by the public health sectors to build up prevention strategies which will be employed in controlling bacterial transmission and hence diseases outbreaks.

Overview of the Model

Epidemic modeling is a distinctive approach to understand the disease dynamics. With the increasing threats of infectious diseases throughout the world, models depicting the respective transmission are becoming more important. These models are simply tools that are used to predict the infections mechanisms and future outbreaks of diseases. Although many treatment models are employed across the globe to combat epidemic such as the diarrhea, many individuals fail to receive or respond to these methods. Thus, the epidemic models focus more on the prevention mechanisms. Various studies carried out in to prove the importance of prevention. One of the most common and strong treatments of diarrhea is the oral rehydration salt (ORS) therapy. A research work showed that a certain part of the population did not have the ORS. Out of the people who had ORS at their residence, only 74 % of them had the knowledge about the preparation and usage. Therefore, while ORS was found out to be widely available, the expected result of successfully defeating the diseases was not gained [11]. In such situations, prevention is highly recommended which can be obtained by exploiting the proposed model herewith. In the present study, a proposed model is portrayed which diseases and is predictive in nature. Any probability of a future diseases outbreak will be alerted using this model thus it will help in developing a prevention strategy. On completion, the structure will be incorporated into a system of active maps of the country such that the future prevention will be shown on the maps using graphics highlighting on the expected areas and time periods of infections. This feature will be greatly useful to the public diarrheal outbreaks. A communication platform will also be included in the model which will present an automated alert service to the general public. Using this communication interface, all the information about the diseases can be passed on to a major portion of the public. It is anticipated that once they receive alerts, the public will also take the necessary steps to protect themselves such that the disease is avoided in every way. The initial stage of building the dynamics of salmonella diarrhea has been elaborated in this paper. The model presented herewith signifies as the base on which the future enhancements will be done to achieve the whole system.

Prevention method will be greatly enhanced by the above model which will prove to be very advantageous for the society. The population having a lower social-economic level is most likely to catch a disease like diarrhea. Individuals in such populations are generally not aware of the treatment methods and if at all the treatment is given, they may not respond to it due to the unavailability of adequate facilities [11]. In such a situation, prevention will help in reducing the untimely death of millions across the globe. On the other hand, diseases such as salmonellosis cause heavy economic burdens under the veil of simple treatment. It has been estimated that approximately $ 2.8 billion is spent annually in the United States for salmonella infections [10].the model described here is highly cost effective and does not require any profound knowledge for operation. If such an undemanding model is exploited for the prevention of these diseases, it is exceptionally clear that countries worldwide will economically too.

II. BACKGROUND

2.1 Other Models:

Epidemic models have been implemented in various forms with regard to infectious diseases. Among them, continuous epidemic model are most common. In 1927, Karmack and Mckendrick introduced a compartmental epidemic model consisting of three compartments- the Susceptible-Infected-Recovered (SIR) model [4]. In its simplest form, the SIR model can be shown as follows:

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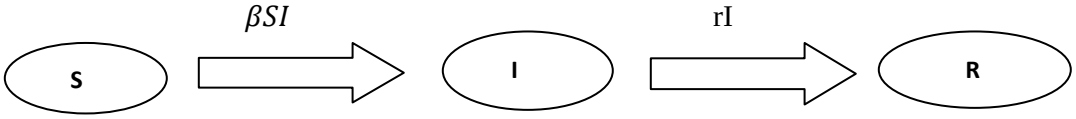

Ordinary differential equations and some defined parameters are used to define the SIR model as shown below in equation (1) to (3). In the model, β represent the infectivity parameter and r is the rate of recovery. This implies that no randomness is involved in the model [4].

$$\frac{dS}{dt} = -\beta SI \qquad (1)$$

$$\frac{dI}{dt} = \beta SI - rI \qquad (2)$$

$$\frac{dR}{dt} = rI \qquad (3)$$

The SIR model has been largely used in epidemic modeling and is generally found to act as the basis for other models. Using the above traditional model as a foundation, other continuous models have been built for epidemiology. The Biomedical modeling as a foundation, other continuous models have been built for epidemiology. The SIR model has also been used to develop other type of models for epidemics .for example, the University of New South Wales, Australia, has used the basic SIR model and created an agent based model for Hepatitis C Virus which gives rise to liver diseases. This model uses inputs such as age, sex and immigrant status and delivers outputs such as infections, cure and death rates related to the disease. Discrete modeling usually is also widely used in epidemics as data needed for modeling epidemics is usually collected at discrete times [1]. Modeling in the discrete mode involves the calculation of the population size for the next time interval. This characteristic of diseases models discloses the predictive ability of the model and thus proves to be very advantageous. SARS (severe Acute Respiratory Syndrome) in China has been modeled using discrete modeling. Three more compartments are added to the basic SIR model namely the exposed, quarantined and diagnosed individuals. In this model, the basic reproduction number was used to formulate the asymptotic behavior of diseases and prove the importance of quarantine for such diseases [15]. Some diseases can be modeled successfully using only two compartments from the basic SIR model- the susceptible and infected classes. Gonorrhea and malaria are such examples. The dynamical behavior of these diseases can be determined using discrete SI and SIS models [9]. An additional research on these diseases included the effects of seasonality in the model. This work uses the fact that seasonal factors directly affect the pathogens related to such diseases [6].

2.2. Disease Epidemiology and Pathogenesis

As the levels of infectious diseases are increasing at remarkable rates around the globe, several efforts are being executed for their eradication. Epidemic modeling is one such effort that can be used to plan the methods of prevention of infectious disease. Prevention of diseases lessens the possibility of outbreaks and thus reduces economic requirements too. Infectious diseases can be classified into many subsets including water- borne, Vector-borne and food borne. Water-borne diseases are infectious disease spread mainly and through water and they have a significant impact on health, globally. One of the most widespread water related disease is diarrhea and it continues to en dander the population at large. Diarrhea is caused by bacteria, virus or other parasitic organisms and is predominantly transmitted through contaminated food and water. In order to reduce the spread of the transmission of this disease, it is necessary to recognize the diseases characteristic and pathogenesis as this forms the basis of the methods that can be implemented to fight the diffusion of the pathogens. Diarrhea is an infectious disease that is characterized by the passage of three or more liquid stools per day. Other symptoms of diarrhea include that is abdominal pain, fever and dehydration [2]. Dehydration is the most severe of all the symptoms as it results in the loss of many necessary salts and chemicals along with water. The condition of dehydration can eventually turn out to be extremely harsh causing death, especially in small children. Diarrhea can present in an individual as a disease on its own or a symptoms of another disease. In both cases there are many pathogens that can transmit diarrhea. Out of many other bacteria, salmonella is one of the most common causes of diarrhea. Salmonella infections can cause typhoid or can be non–typhoidal. Diarrhea appears as a major symptom in non – typhoidal salmonella infections. Although sometimes overlooked, non-typhi serotypes of salmonella cause a higher proportion of infections in developed countries [2]. The global burden of non-typhoidal salmonelosis is estimated to be approximately 93 million cases annually. As the main transmission method of salmonella happens to be foodstuffs, 80

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million of the above cases are food borne. In humans, salmonella is widely acquired by the ingestion of contaminated food material. Out of all foods, eggs and poultry are found to be often highly infected with salmonella. Apart from contaminated food, indirect transmission by unhygienic hand washing habits and contaminated surfaces can also occur. The bacteria can also br caught through pet reptiles and rodents [7]. The infective dose of the bacteria is quite high ranging to about 100000 bacilli [2] but this dose does not reduce the danger of the pathogen due to its easy transmission.

Symptoms begins to appear after about 24 hours following ingestion of contaminated food or water [8] and may manifest in different forms like gastroenteritis and enteric fever [7]. Out of these, gastroenteritis is associated with diarrhea which may last for about a week [7]. In general, an oral rehydration therapy is carried out for treatment of gastroenteritis to replace the lost fluids and electrolytes. Antibiotics may be used in severe cases or for immune suppressed individuals. Symptoms subside after a few days but the patient may remain contagious for even months. Almost any person is susceptible to salmonella and can become infected by the ingestion of contaminated food. Upon treatment, the infected individual may completely recover which means that the total bacterial population is flushed out of the body, or may become an asymptomatic carrier. An asymptomatic carrier does not show any symptoms but since the bacteria are still in the body, they are shed into the environment perpetuating the spread of the disease. Both types of infected people gradually become recovered with exception cases of severity. As salmonellosis become more severe, it results in further complications in the body such as septic arthritis and pneumonia [8]. At this point, minor symptoms such As diarrhea normally fade away. Because this research is mainly based on the eradication of diarrhea, the extreme severe cases of salmonellosis have not been included. After a certain time period of recovery, a person becomes re-susceptible to the bacteria as the immune system gradually declines. The above mentioned practical stages of infection have been implemented into a model and manipulated to show the dynamics of the diseases.

III. THE MODEL

3.1. Description

The model considered herewith is a redesigned version of the fundamental SIR model based on the properties of salmonella infections. There are four compartments included in the system, which can be described as follows:

1. Susceptible (S) – this represent the individuals of the whole human population that can catch the disease.
2. Symptomatic Infected (IS) – these are the individuals who have been infected by the bacteria and show clinical manifestations of the disease. They are capable of transmitting the disease to other susceptible individuals.
3. Asymptomatic Infected (IA) – the people in this group have externally recovered from the disease but continue to carry the bacteria. They do not show any symptoms and are capable of infecting the susceptible class.
4. Recovered (R) – this class consists of the individual who have been completely recovered from the disease meaning they neither show symptoms nor do they carry the bacteria. These individuals gradually lose their immunity and become susceptible after a certain period of time.

A schematic illustration of the model is given below. All the associated parameters are described in Table 1.

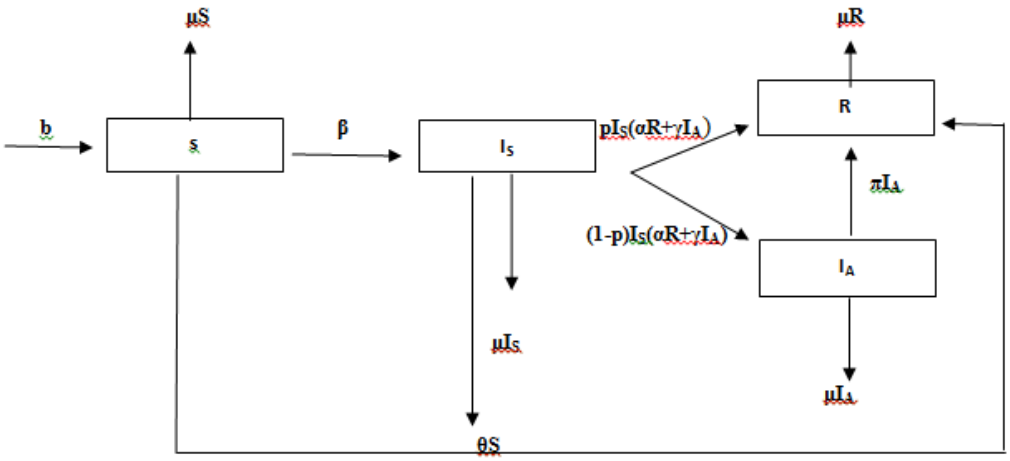

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Table1. Parameter Description

B	Rate of influx of susceptible
μ	Natural death rates
β	Transmission coefficient for I_S
α	Rate of recovery from I_S
γ	Transmission coefficient for the asymptomatically infected compartment I_A
π	Rate of recovery from I_A
θ	Vaccination rate
P	Probability of recovery

The susceptible population, as the name suggests, is non-resistant to the disease and gets in contact with the pathogen through the infected population. Both the infected classes contribute to the pathogen population and hence transmit the disease. Resolution of the symptoms could mean that one has become bacteria carrier or he has recovered. The asymptomatic carrier also recovers progressively as the pathogen clears from his body. For some time, the body maintains an immunity levels and the individual remains in the recovered class but gradually, this immunity level can drop rendering the recovered population to become susceptible to the disease again.

In the above described system, the following assumptions are made:

1. The shedding rate of bacteria by the infected population consists of both direct and indirect shedding
2. All individuals are born as susceptible
3. Salmonella persists in the environment for several days, hence the pathogen death rate is assumed to be zero.

Using the above mentioned parameters and assumptions, the extended compartment model can be defined using the following equations:

$$\frac{dS}{dt} = b - \mu S - \beta S I_S - \theta S \qquad (1)$$

$$\frac{dI_S}{dt} = \beta S I_S - I_S(\alpha R + \gamma I_A) - \mu I_s \qquad (2)$$

$$\frac{dI_A}{dt} = (1 - P) I_s(\alpha R + \gamma I_A) - \mu I_A - \pi I_A \qquad (3)$$

$$\frac{dR}{dt} = P I_S(\alpha R + \gamma I_A) + \pi I_A + \theta S - \mu R \qquad (4)$$

Parameter Calculation:

For the analysis of the above model, the first step is to calculate the diseases free equilibrium. The diseases free equilibrium (DFE) is the state at which there are no infections at all in the population. If the population has to be free of the disease and pathogens, it directly implies that the infectious states need to be assumed to be zero, i.e. $I_A = I_S = 0$. Since the infectious population has been assumed to be zero, it entails that there will be no recovered population either .therefore R=0. At this state, the only nonzero class is the susceptible class. At the DFE, all classes are denoted with an asterisk. In order to get the asymptotic state, the non zero components on the right hand side of equation (1) will be equal to zero.

$$b - \mu S^* - \beta S^* I^*_S - \theta S^* = 0$$

$$b - \mu S^* - \theta S^* = 0$$

$$-(\mu + \theta) S^* = -b$$

$$S^* = \frac{b}{(\mu + \theta)} \qquad (5)$$

Thus, the DFE can be described as follows:

DFE $=\left(\frac{b}{(\mu+\theta)}, 0, 0\right)$

After calculation of the DFE, the evaluation of the basic reproduction number (R_0) follows. R_0 can be calculated using the next generation matrix, G [10].The next generation matrix is computed using the infected state(s) and is defined as follows:

$G = FV^{-1}$

Where F is the Jacobian matrix of the new infections matrix(f) and V is the jacobian matrix of the other changes matrix (v) in the infected stare (s).calculations here are done at the DFE state.R_0 is defined as the highest eigen value of the next generation matrix. For the system above, there are two infectious states , the symptomatic infected and the asymptomatic infected. Using these two states, the two matrices f and v can be expressed as follows:

$$f = \begin{bmatrix} \beta S I_S \\ (1-P) I_S (\alpha R + \gamma I_A) \end{bmatrix} \quad \text{and}$$

$$v = \begin{bmatrix} (\mu + \alpha R + \gamma I_A) I_S \\ (\mu + \pi) I_A \end{bmatrix}$$

If calculated at DFE, $S^* = \frac{b}{(\mu+\theta)}$

$$\text{Therefore, } f = \begin{bmatrix} \frac{\beta b I_S}{(\mu+\theta)} \\ (1-P) I_S (\alpha R + \gamma I_A) \end{bmatrix}$$

$$v = \begin{bmatrix} (\mu + \alpha R + \gamma I_A) I_S \\ (\mu + \pi) I_A \end{bmatrix}$$

Calculating the jacobian matrices:

$$F = \begin{bmatrix} \frac{\beta b}{\mu+\theta} & 0 \\ (1-p)(\alpha R + \gamma I_A) & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} (\mu + \alpha R + \gamma I_A) & 0 \\ 0 & (\mu + \pi) \end{bmatrix}$$

Using the above matrices the next generation matrix, G is evaluated:

Since we know that $V^{-1} = \frac{adj\, V}{|V|}$ so,

$$adj\, V = \begin{bmatrix} (\mu + \pi) & 0 \\ 0 & (\mu + \alpha R + \gamma I_A) \end{bmatrix}$$

And,

$$|V| = (\mu + \alpha R + \gamma I_A)(\mu + \pi)$$

Therefore

$$V^{-1} = \frac{\begin{bmatrix} (\mu+\pi) & 0 \\ 0 & (\mu+\alpha R+\gamma I_A) \end{bmatrix}}{(\mu+\alpha R+\gamma I_A)(\mu+\pi)}$$

Now since $G = FV^{-1}$

$$= \begin{bmatrix} \frac{\beta b}{(\mu+\theta)} & 0 \\ (1-p)(\alpha R + \gamma I_A) & 0 \end{bmatrix} \frac{\begin{bmatrix} (\mu+\pi) & 0 \\ 0 & (\mu+\alpha R+\gamma I_A) \end{bmatrix}}{(\mu+\alpha R+\gamma I_A)(\mu+\pi)}$$

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$$= \begin{bmatrix} \frac{\beta b}{(\mu+\theta)(\mu+\alpha R+\gamma I_A)} & 0 \\ \frac{(1-p)(\alpha R+\gamma I_A)}{(\mu+\alpha R+\gamma I_A)} & 0 \end{bmatrix}$$

$$G = \begin{bmatrix} \frac{\beta b}{(\mu+\theta)(\mu+\alpha R+\gamma I_A)} & 0 \\ \frac{(1-P)(\alpha R+\gamma I_A)}{(\mu+\alpha R+\gamma I_A)} & 0 \end{bmatrix}$$

By calculating the largest eigen value of the next generation matrix, the basic reproduction number of this model is worked out as:

$$R0 = \frac{\beta b}{(\mu+\theta)(\alpha R+\mu+\gamma I_A)}$$

And since $R=I_A=0$

So $\mathbf{R_0} = \frac{\boldsymbol{\beta b}}{(\boldsymbol{\mu+\theta})\boldsymbol{\mu}}$

IV. NUMERICAL ANALYSIS AND DISCUSSION

The infectivity rate, β, is used to govern the value of the basic reproduction number. Two circumstances have to be considered: $R_0<1$ and $R_0>1$. For this, first the value of the infectivity rate will be worked out for $R_0=1$. Using this value as a base, the infectivity rate will be altered such that the above two situations are obtained.

For $R_0=1$;

$$\frac{\boldsymbol{\beta b}}{\boldsymbol{\mu(\mu+\theta}} = \mathbf{1}$$

$$\boldsymbol{\beta} = \frac{\boldsymbol{\mu(\mu+\theta)}}{\boldsymbol{b}}$$

Using b=10, μ=.15 and θ=.0625

β=.0031875

So if β<.0031875 then $R_0<1$ and if β>.0031875 then $R_0>1$

V. CONCLUSION

A mathematical model for investigating the effects of carriers on the transmission dynamics of non typhoidal salmonella is developed and analyzed. Analysis of system was done by evaluating the basic reproduction number. It was proved that as long as the value of R_0 is kept minimal, the disease can be eradicated from the population. The model shows that the higher values of R_0 , the more likely an epidemic will spread at higher rates . R_0 can be kept low by employing various policies such as increasing knowledge of public in terms of prevention and treatment, increasing hygiene conditions at work places and better water treatment facilities.

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