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Simulating the transmission dynamics and control of typhoid fever in Ibadan, Nigeria

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ABSTRACT: This study aims to assess transmission dynamics of typhoid and simulate effects of treatment, isolation and vaccination in reducing the burden of typhoid fever in Ibadan metropolis, Nigeria. Secondary data of the Integrated Disease Surveillance Response on reported typhoid fever cases for 2010 to 2017 period in Ibadan South-East Local Government Area, Oyo State, Nigeria were used to achieve the set-out objectives. The study adapted the Susceptible-Infected-Carrier-Recovered (SIIcR) model to simulate effects of the three preventive and control strategies on typhoid fever transmission. Typhoid fever cases were most rampant among the age groups 20 to 40 years (29.0% infected) and > 40 years (35% asymptomatic carriers and 45.0% death) and the least in age group 0 to 28 days (0.22% infected and no death case). A decreasing trend in typhoid fever cases (56 cases per year) was observed which was attributed to improved functional health facilities and their effective utilization. Significant seasonal variation in typhoid infections was found with the highest reported cases at the start of wet (April) and dry (November) seasons. The SIIcR model simulations suggested likelihood of typhoid fever epidemic within two weeks in the community if no prevention and intervention measures were put in place. Major reduction in the carriers' population significantly reduced the number of infected class and suggested disease-free population within a season of typhoid epidemic (100 days). Model simulations suggested that vaccination and isolation significantly reduced the effect of infected and asymptomatic carrier populations at $p<0.05$ on the transmission dynamics of typhoid fever.

Keywords: Isolation, SIIcR model, treatment, typhoid, vaccination.

INTRODUCTION

Typhoid fever (or enteric fever) is an infectious disease caused by a bacterium of the genus *Salmonella enterica serovar typhi* (*S. typhi*) and *Salmonella enterica serovar Paratyphi* (S. *Paratyphi*) that invade the body via the small intestines and colonize macrophages in the reticulum-endothelial system, from where it is shed into the bloodstream (Antillon et al., 2017; Dougan and Baker, 2014). It is a common disease in developing countries that is associated with environmental development (Khan et al., 2015), characterized by poor sanitation and hygiene and unsafe water supply (Mutua et al., 2017; Akinyemi et al., 2018). Symptoms of the disease typically include fatigue, weakness, prolonged (high) fever, frontal headache, malaise and marked loss of appetite sometimes accompanied by abdominal pains, nausea, and (in severe cases) intestinal perforation and neurological complications (Antillon et al., 2017). The incubation period is about 10 to 14 days and symptoms typically subside in 7 to 21 days (Khan et al., 2015). However, if it is not treated, it can cause the death of 5 to 30% of the infected persons (Abdullahi et al., 2013).

Human infection with *S. typhi* or S. *Paratyphi* is majorly through ingestion of food and water contaminated by faeces of an infected person, meat from infected animals and flies (such as *Musca domestica* flies) from infected animals (Joseph and Palmer, 1989; Maskaly, 2003). During acute infection, the bacteria in their natural habitat (i.e. human intestine) multiplies in mononuclear phagocytic cells before being released into the bloodstream of host and are carried to various organs (liver, spleen, kidneys) to form secondary foci (Bhan et al., 2005). A number of individuals called "asymptomatic carriers" continue to carry the bacteria in their body system after recovery from typhoid without exhibiting any symptoms. This class of population play an important role in the disease's transmission to others (Roumagnac et al., 2006) and their presence greatly hinders the eradication of typhoid fever using treatment (Naresh et al., 2008).

In sub-Saharan Africa, the incidence of typhoid fever was estimated to be 725 cases per 100,000 persons in 2010, even though there is lack of incidence studies conducted in West and Central Africa (Buckle et al., 2012). This infection constitutes serious sources of mortalities and morbidities and it is often encountered in the tropical countries like Nigeria (Ibekwe et al., 2008). Despite the fact that many advances have been made in recent times towards the fight against typhoid fever such as treatment with drugs, vaccination and environmental sanitation, the disease is still endemic in many developing countries and remain a substantial public health problem (Peter et al., 2017; Nyerere et al., 2018). Prevention of this disease is based primarily on ensuring access to proper sanitation infrastructure, safe water and food safety (Akinyemi et al., 2018; Stanaway et al., 2019). Similarly, antibiotics (such as chloramphenicol, co-trimaxazole, ciprofloxacin, tetracycline, ampicillin and trimethoprim-sulfamethaxaole) are used in the treatment of typhoid fever (Akinyemi et al., 2005). Infected patients are treated with the isolation method in hospital settings (WHO, 2009).

Considering the fact that that typhoid incidence and distribution among different age groups may vary both between and within countries (Sur et al., 2007), it is necessary to identify potential predictors of incidence that facilitate interpolation in developing countries, where the disease is suspected to remain endemic (Antillon et al., 2017).

Ibadan, the largest city in West Africa, is located in a highly endemic region where the problem of lack of good sanitation and poor water supply is prevalent (Jeminiwa et al., 2017). Significant parts of the huge population reside in places where there is no access to improved drinking water and sanitation, and live in congested slums where conditions are favourable for the transmission of typhoid fever and other enteric pathogens as speculated by Bhutta (2019). However, effects of carriers on the transmission dynamics of this disease in this city have not received adequate attention. Despite the advances in the use of mathematical models to predict the spread and control of infectious diseases for a long time (Yi et al., 2009; Sun and Hsieh, 2010; Pitzer et al., 2014; Date et al., 2015; Nthiiri et al., 2016; Mushayabasa, 2017), this advantage has not been fully exploited in developing countries where majority of the citizens are low-income earners. Thus, this present study investigates the transmission dynamics of typhoid fever in Ibadan, Nigeria. It adapted the Susceptible-Infected-Carrier-Recovered (SII_cR) model to simulate the impact of treatment, isolation and vaccination as preventive and control strategies to reduce the effect of infected and carriers on the burden of the disease in the city.

MATERIAL AND METHOD

Study area

Ibadan is located in Oyo State, Nigeria (Figure 1). It lies within longitude 7°2' E and 7°40' E and latitude 3°35' N and 4°10' N. The city covers a total area of about 3,082 km^2 (NPC, 2016). It lies about 120 km east of Benin republic in the forest zone close to the boundary between the forest and the savannah. The city ranges in elevation from 150 m in the valley area, to 275 m above sea level on the major north-south ridge which crosses the central part of the city (Agbola and Ojeleye, 2007). The population of Ibadan was put at about 3 million in 2006 and projected to be about 4 million by the end of 2019 (NPC, 2016). The annual mean rainfall is 1,420 mm while minimum and maximum temperature are 21.4 and 26.5°C respectively with relative humidity of 74.6% (Ojetade et al., 2013). The whole area is drained by four rivers with many tributaries with a channel length of 12.76 km and catchment area of 54.92 km^2. Major employments are retail trade, educational services, repair industries and public administration.

Data sources and methods

The Integrated Disease Surveillance Response (IDSR) on reported typhoid fever cases in Ibadan South-East Local Government Area (LGA) of Oyo State Nigeria from 2010 to 2017 were obtained from the Oyo State Ministry of Health, Ibadan. The study area has a large number of enlightened citizens and as such majority of inhabitants sought treatments at the city's referral health centre (Jeminiwa et al., 2017). The IDSR contains reported typhoid fever cases in all registered government recognized health facilities. The dataset contains information on the human population, number of health facilities, susceptible population and reported typhoid infection (infected, estimated carriers population, recovered and death) within the study area. Annual and seasonal changes in the observed typhoid fever cases during the study period were analysed and presented. The stochastic SII_cR model fully described in Chamuchi et al. (2014) was then adapted to simulate the observed transmission dynamics of typhoid fever within a season (100 days) of typhoid epidemic; a period long enough for the asymptomatic infected or carriers to show symptoms and for possible epidemic to take place (Kalajdzievska and Li, 2011; Mutua et al., 2017). The sensitivity of the model compartments to changes in the number of asymptomatic carriers was carried out to determine their impacts on the burden of typhoid fever in the study area. Similarly, the contributions of treatment, vaccination and isolation as preventive and control strategies for the spread of typhoid fever were simulated.

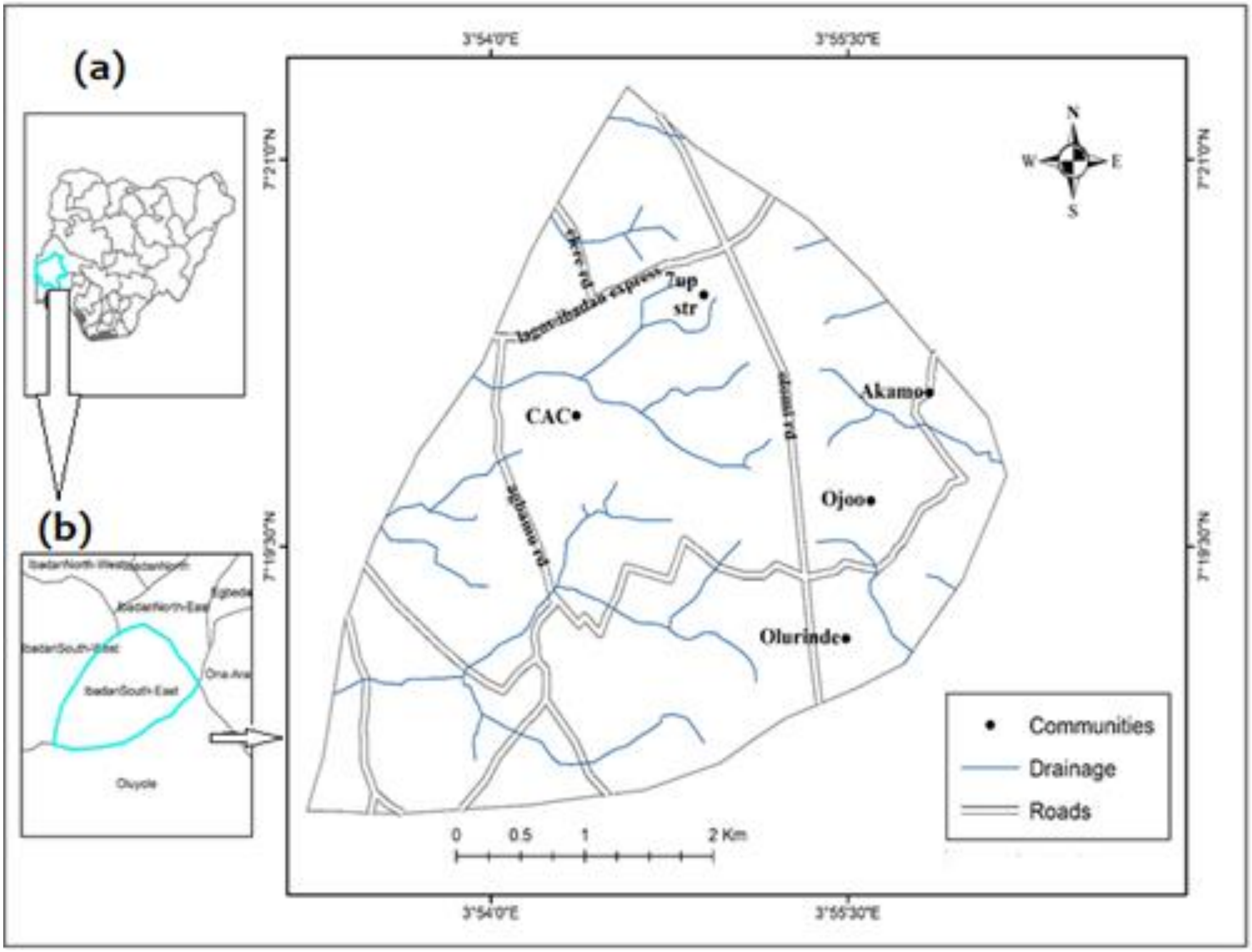

Figure 1. Map of the study area; (a) Nigeria and (b) Ibadan South-East Local Government Area.

Model description, formulation and simulations

The mathematical model of the type SII_cR (susceptible, infected, carriers and recovered) is a four compartmental model for infectious disease transmission. The model description and flow diagram as presented in Figure 2. The human population is partitioned into four distinct classes or compartments: susceptible (S), infected (I), asymptomatic carrier (I_c), and recovered (R). At any particular point in time (t), within a total population (N):

$$N(t) = S(t) + I(t) + I_C(t) + R(t) \qquad (1)$$

where S(t), I(t), I_c(t) and R(t) is the number of susceptible, infected, carriers and recovered cases within the human population with respect to time.

The disease is assumed to transmit horizontally either by direct contact (licking, touching, biting) or indirect contact (vectors or fomites) with no physical contact. Evolution from susceptible to infected depends on the total number of infected individuals encounters (number of contacts made by S per unit time, κ) and how contagious the particular disease is (disease transmission rate, β). Recovery after infection wipes out the disease from infected individuals, and the rate of recovery depends on the expected duration of the disease which is independent of other interactions between individuals. The model also assumes that the rate of transmission for carriers is greater than that of symptomatic infectious individuals. The stochastic differential equations that govern the model are (Chamuchi et al., 2014):

$$d(S)/dt = b - d_1 S - S(\beta I_c + \gamma I) - \theta S \qquad (2a)$$

$$d(I_c)/dt = pS(\beta I_c + \gamma I) - (d_2 + \alpha) I_c \qquad (2b)$$

$$d(I)/dt = (1-p)S(\beta I_c + \gamma I) - (d_3 + \pi)I + \alpha I_c \qquad (2c)$$

$$d(R)/dt = \pi I + \theta S - d_3 \qquad (2d)$$

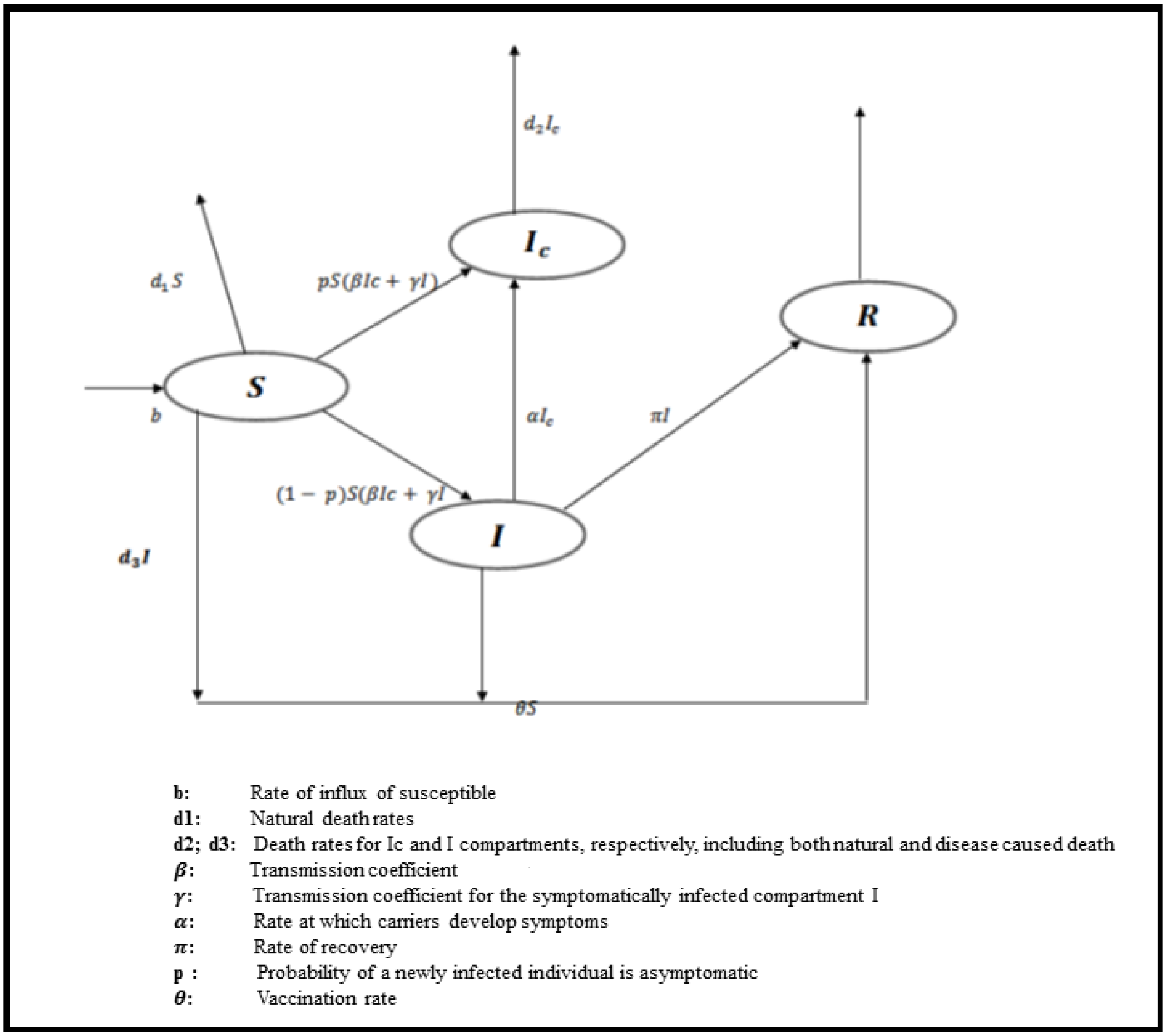

Figure 2. The flow diagram of SII_cR model for the transmission dynamics of typhoid fever adapted in this study (Chamuchi et al., 2014).

where, $S > 0$, $I > 0$, $I_c > 0$ and $R > 0$.

The basic reproduction number, R_0 for different infectious diseases have different theoretical formulations in the literature (Diekmann et al., 1990). In this study, we rely on the general definition as provided by Jones (2007) where R_0 is simply expressed as:

$$R_0 = \beta \times \kappa \times D \qquad (3)$$

where D is the average infectivity duration of the disease for an infected person and β is the disease transmission rate or coefficient.

The magnitude of R_0 helps to determine the amount of effort which is necessary either to prevent an epidemic or to eliminate an infection from a population. In general, if R_0 is greater than 1.0, the disease will continue to spread within a population (signaling disease outbreak or epidemic in a particular human population). However, if it is equal to 1.0 stable endemic equilibrium occurs, and if less the disease will eventually disappear from a population (indicating a disease-free population).

Table 1 gives the means and 95% credible intervals for the model parameters used in this study. The transmission dynamics of typhoid fever cases within 100 days was simulated using a daily discrete time steps in recursive form of Equation 2. Duration of 100 days is the longest presumed for the infected to show symptoms (migrate from I_c to I compartment) and for possible epidemic to take place as a result of introduction of at least an additional infected person to the total population (Kalajdzievska and Li, 2011; Mutua et al., 2017). The means of the observed monthly human populations of S (=340,640), I (= 1,460), Ic (= 2,919) and R (=1,455) in the study area were used as initial conditions in the model simulations. To investigate

Table 1 The values of model parameters used in the study.

Description	Symbol	Range of Values		
		Mean	Credible Interval	
			min	max
Rate at which carriers develop symptoms	α	0.59	0.48	0.66
Typhoid transmission coefficient for both the carrier, Ic and infected I compartments	β	0.08	0.055	0.085
Transmission coefficient for the symptomatically infected compartment I	γ	0.42	-	-
Rate of recovery	π	0.75	-	-
Probability of a newly infected individual is asymptomatic	p	0.33	-	-
Vaccination rate	θ	0.585	-	-
Rate of influx of susceptible (per month)	b	981	798	1104
Natural death rates	d_1	0.020	-	-
Death rates for Ic compartment including both natural and disease caused death	d_2	0.010	-	-
Death rates for I compartment including both natural and disease caused death	d_3	0.012	-	-
Average infectivity duration for an infected person	D	14 days	12	21
Number of contacts made by S per unit time	κ	10	6.3	15.2

the sensitivity of the model compartments to varying numbers of carriers, initial number of carriers as observed (I_c = 2,919) was changed to 1,027 (just below the observed), 29,309 (far above) and 211 people (far below) in the simulations and the model outputs were compared. The initial number of infected persons in the model as observed (I = 1,460) was also varied below and above the observations hypothetically (*i.e.* I = 966, 35902 and 97) to explain effects of treatment on the dynamic of the disease. Similarly, typhoid transmission coefficient, β (0.08, 0.0072, 0.1, 0.006) and the interaction rate of the susceptible class with the infected and carriers groups, κ (= 10.0, 0.9, 20.0, 0.75) were varied hypothetically such that $R_0 \approx 1$, >>> 1 and < 1) to be able to examine the effects of vaccination and isolation respectively on the spread of typhoid fever. Student t-test statistics were also performed to examine if these preventive and control strategies could significantly reduce the burden of typhoid fever in the study area.

RESULTS

Observed transmission dynamics of typhoid fever

Figure 3 gives a statistical summary of the sample population, density, functional health facilities and susceptible class as documented in IDSR on reported typhoid fever cases in Ibadan South-East LGA of Oyo State Nigeria from 2010 to 2017. The mean and standard deviation of the sample population were 314,456 and 65,544 people respectively. Results showed significant increasing annual trend in the human population (13,522 people per year) at p<0.05 and a growth rate of 3.4 (Figure 3a). The mean population density was 5,950 people km^{-2} which was found to be increasing significantly by 232 people km^{-2} $year^{-1}$ during the special observation period (Figure 3b). The number of functional health facilities (centres) increased by average of 2 per year to reach a maximum of 43 in the year 2017 (Figure 3c). However, the trend was not statistically significant compared with the population growth. The number of susceptible populations was also observed to increase significantly by 13,474 people $year^{-1}$ from the year 2010 to a maximum of 387,500 people in 2017 (Figure 3b). Furthermore, total number of observed infected persons, asymptomatic carriers, recovered and death are shown in Figure 4. The number of infected (I), carriers (I_c), recovered (R) and death compartments were relatively higher between 2011 and 2014 when the number of functional health facilities dropped. The least values of I (937 people), Ic (1,850), R (850) and death (1 person) were recorded in 2017. Figure 5 describes the percentage distribution of infected persons, asymptomatic carriers and death rates among different age groups. It revealed that, generally, typhoid fever cases (infected, asymptomatic carriers and death) were more prevalent in age-group 20 to 40 years and >40 years and least prevalent in age groups 0 to 28 days. Rate of infection were 29% (20 to 40 years), 23.3% (11 to 19 years), 22.5% (>40 years) and 0.22% (0 to 28 days). In addition, there were more deaths among the adults than the children. For example, cases of fatality were 45% among the age group >40 years and none among the children of age group 0 to 28 days. Figure 6 illustrates annual cycle of reported cases of typhoid Fever. Results revealed high and significant seasonal variation in typhoid infections in the study area. There were more cases of typhoid (carriers, infected and death) at the beginning of wet season (April) and dry (November) than at the peaks

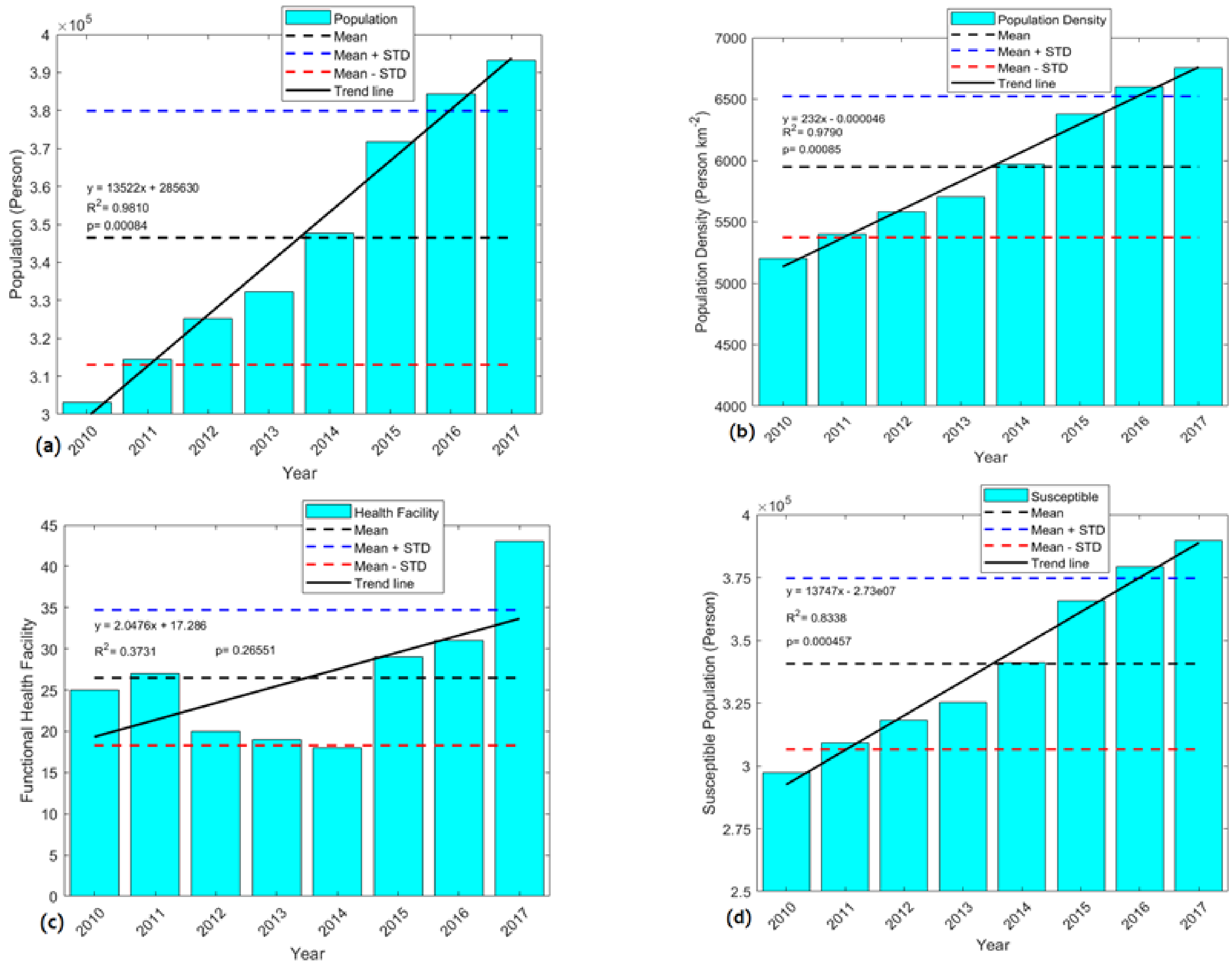

Figure 3. Total number of sample (a) population, (b) population density, (c) health facility and (d) susceptible class in Ibadan South-East LGA of Oyo State Nigeria from 2010 to 2017.

of both seasons.

Simulations and effects of carriers on transmission dynamics of typhoid fever

Figure 7 shows the simulated transmission dynamics of typhoid fever within a season (100 days) of typhoid epidemic due to the presence of infected and carrier individuals in the total population of 346,477 people. The estimated R_0 was 11.2. This is an indication that the disease will continue to spread within the population with a high possibility of an epidemic within days. Consequently, the simulations showed that the number of infected had a peak value of about 260,000 people on the 13th to 15th day (Figure 7). This was a sign of an epidemic ($R_0 > 1$) within 13 and 15 days of presence of a total of 1,463 infected and 2,919 carriers into the population. However, all recovered after 85 to 100 days. This reveals that an epidemic of typhoid fever could occur within two weeks in the community if no effective intervention such as preventive and control measures are put in place. Results of the sensitivity study with varying initial number of carriers in the population are illustrated in Figure 8. Although, increased in the number of carriers have positive impact on the number of infected compartment (slightly increased it), the impact was not significant (p=0.642). However, reduction in the number of carriers to a minimum possible significantly reduced number of infected compartment and suggested a disease-free population within the 100-day simulation period (Figure 8d). This result is affirmed by outcomes of t-test analysis in Table 2 which indicates significant changes in the number of infected and carriers' population at $p<0.05$ when the initial

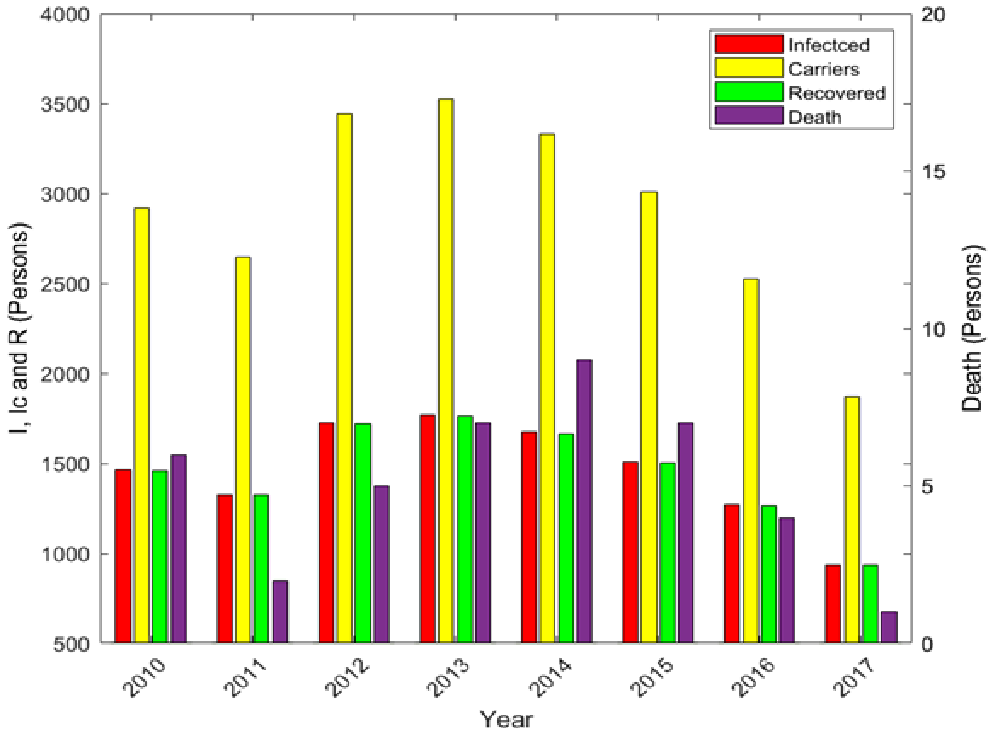

Figure 4 Annual total number of infected persons (I), asymptomatic carriers (I_c), recovered (R) and death in Ibadan South-East LGA of Oyo State Nigeria from 2010 to 2017. The vertical axis on the left is for I, I_c and R while the vertical axis on the right is for the death compartment.

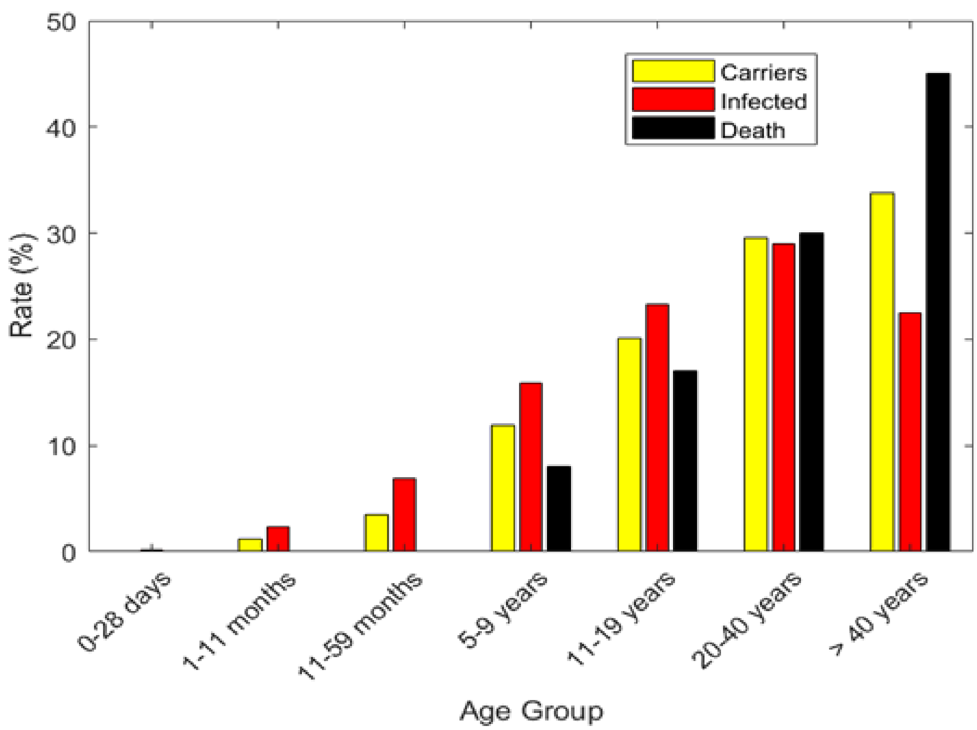

Figure 5. Percentage distribution of infected persons and death rates among different age groups in Ibadan South-East LGA of Oyo State Nigeria (2010-2017).

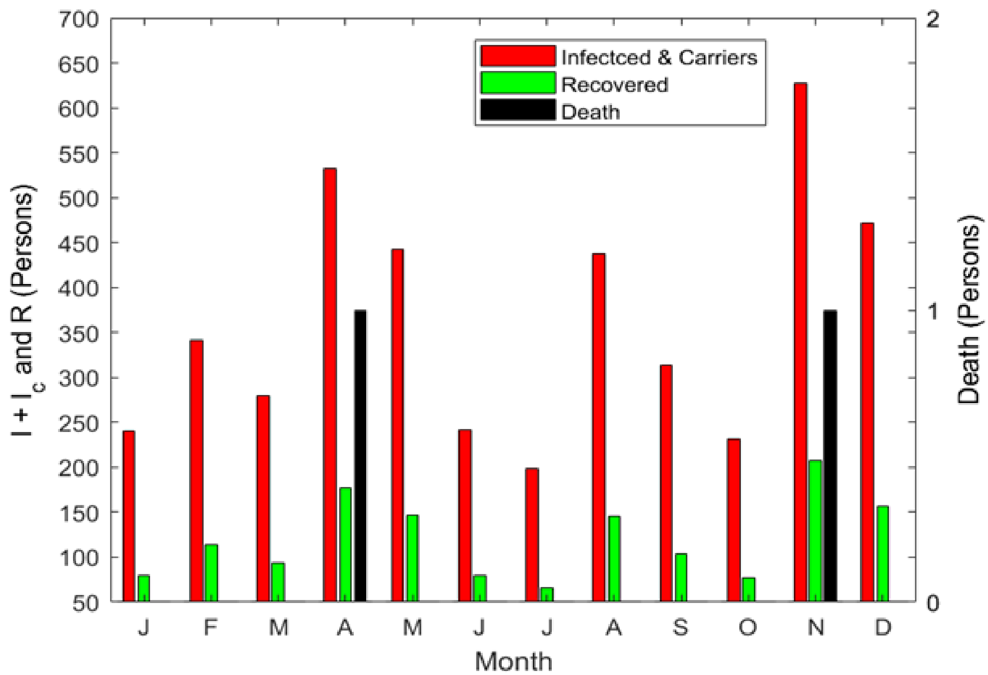

Figure 6. Monthly total number of infected persons plus asymptomatic carriers ($I+ I_c$), recovered and death in Ibadan South-East LGA of Oyo State Nigeria from 2010 to 2017. The vertical axis on the left is for ($I+ I_c$) and R while the vertical axis on the right is for the death compartment.

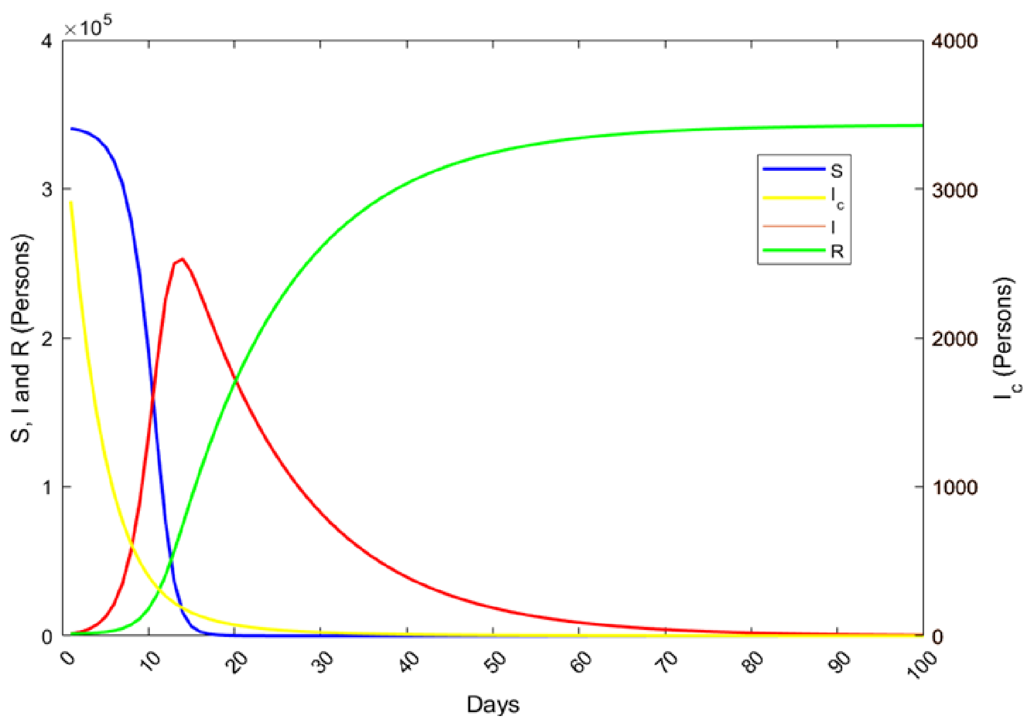

Figure 7. Simulated transmission dynamics of typhoid fever within a season of typhoid epidemic of 100 days in Ibadan South-East Local Government Area (LGA), Oyo State. The vertical axis on the left is for S, I and R while the vertical axis on the right is for the I_c compartment.

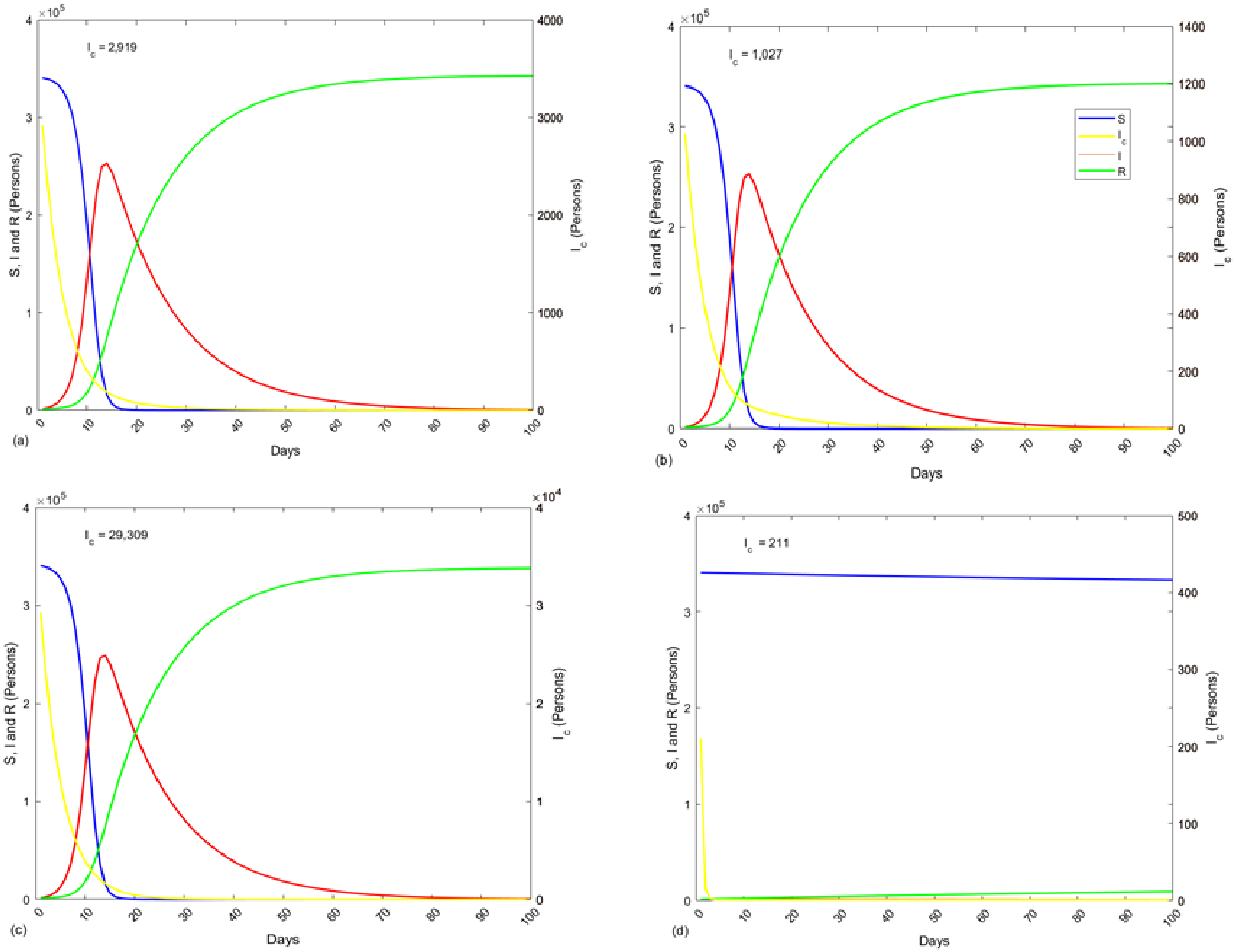

Figure 8. Simulated effects of changes in the number of carriers (Ic) on transmission dynamics of typhoid fever (susceptible, carriers, infected, recovered) in Ibadan South-East Local Government Area(LGA), Oyo State using initial number of carriers equals (a) 2,919 people as observed; (b) 1,027 people, below observed; (c) 29,309 people, far above observed; and (d) 211 people, far below observed. The vertical axis on the left is for S, I and R while the vertical axis on the right is for the I_c compartment.

value of asymptomatic carrier, Ic was varied.

Effects of preventive and control interventions

Simulated impacts of isolation as a control strategy on the typhoid transmission dynamics is illustrated in Figure 9. Reduction in the number of contacts made (interaction) by potential transmitters from κ =10 to κ = 0.9 through isolation (such that is $R_0 \approx 1$) significantly reduced the infected compartment and suggested a disease-free population (Figure 9b). On the other hand, increasing κ to 20 (such that $R_0 >> 1$) increased the peak of the epidemic and the time of occurrence was shorten to about 8 days (Figure 9c). Results of t-test in Table 3 confirmed the significance of the impacts of isolation on the infected and carrier population at $p<0.05$. Reducing the rate of interaction to 0.75 (such that $R_0<1$) indicated a more disease-free population within the 100-day period (Figure 9d). Results of the simulated effects of treatment as a control strategy are shown in Figure 10. Reduction in the number of infected individuals through treatment was found to lower the number of infected population (Figure 10b). Conversely, increase in the number of infected persons due to lack of treatment increased the number of infected, its peak and shorten the time of occurrence of the outbreak (Figure 10c). Results in Table 4 indicated that impact was not significant. Finally, Figure 11 shows the impact of vaccination as a preventive strategy on the infected population. Reduction in typhoid transmission coefficient β (such that is $R_0 \approx 1$) reduced the infected and

Table 2. Results of student t-test statistics on the changes in carrier and infected population due to variations in the number of carriers, Ic.

Pairs	Variables	Mean	STD	t-stat	df	p
Pair 1	Ici1 vs Ici2	106.843	62.326	3.1288	99	0.0023
Pair 2	Ici1 vs Ici3	813.837	121.900	-3.1288	99	0.0023
Pair 3	Ici1 vs Ici4	78.719	35.376	13.3344	99	0.0012

STD = Standard deviation, df = degree of freedom, p = p-probability. [Note that Ici1, Ici2, Ici3 and Ici4 are number of carriers and infected obtained when initial value of Ic = 2,919, 1,027, 29,309 and 211 respectively].

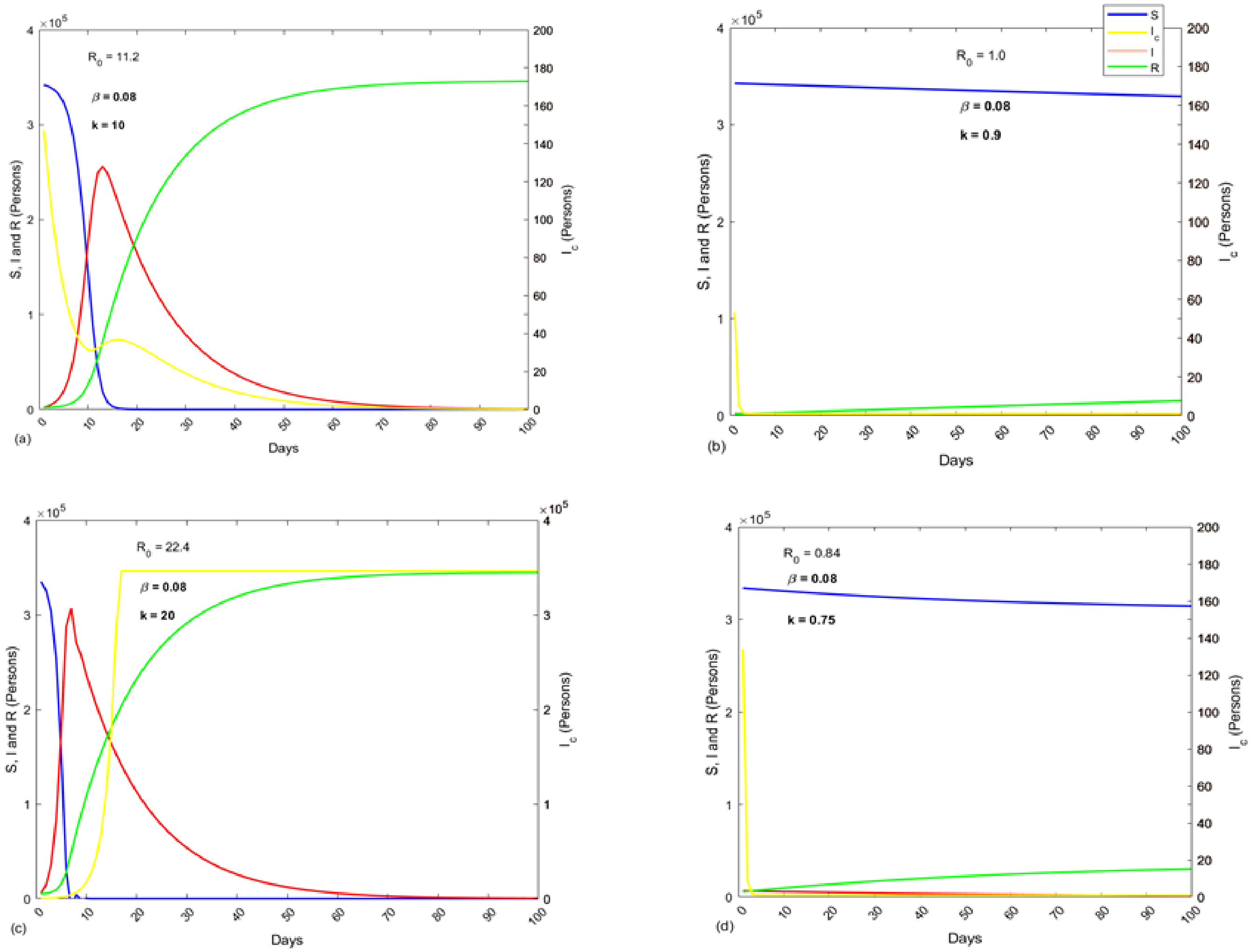

Figure 9. Effects of isolation (changes in the interaction rate, κ) on transmission dynamics of typhoid fever (susceptible, carriers, infected, recovered) in Ibadan South-East Local Government Area(LGA), Oyo State using κ equals (a) 10, as observed where R_0 = 11.2; (b) 0.9, below observation such that $R_0 \approx 1$; (c) 20, far above observation such that is $R_0 >> 11.2$; and (d) 0.75, far below observation such that is $R_0 < 1$. The vertical axis on the left is for S, I and R while the vertical axis on the right is for the I_c compartment.

carrier compartments to pave way for a disease-free population (Figure 11b). On the other hand, decreasing the immunity by increasing the disease's transmission rate (such that R_0>>1) increased the peak of the epidemic and the time of occurrence was shorten to about 10 days (Figure 11c). Results of t-test in Table 5 confirmed the significance of the impacts of vaccination (higher immunity less disease's transmission rate) on the infected population at p<0.05. Reducing β to 0.005 (such that R_0<1) showed that the disease eventually disappeared from the

Table 3 Results of student t-test statistics on the changes in carrier and infected population due to variations in number of contacts made per unit time, κ.

Pairs	Variables	Mean	STD	t-stat	df	p
Pair 1	Ici1 vs Ici2	8.594	21.729	6.4133	99	0.000
Pair 2	Ici1 vs Ici3	149371.100	114460.000	-26.0964	99	0.000
Pair 3	Ici1 vs Ici4	8.993	20.271	6.4813	99	0.000

STD = Standard deviation, df = degree of freedom, p = p-probability. [Note that Ici1, Ici2, Ici3 and Ici4 are numbers of carriers and infected obtained when κ = 10.0, 0.9, 20.0 and 0.75 respectively].

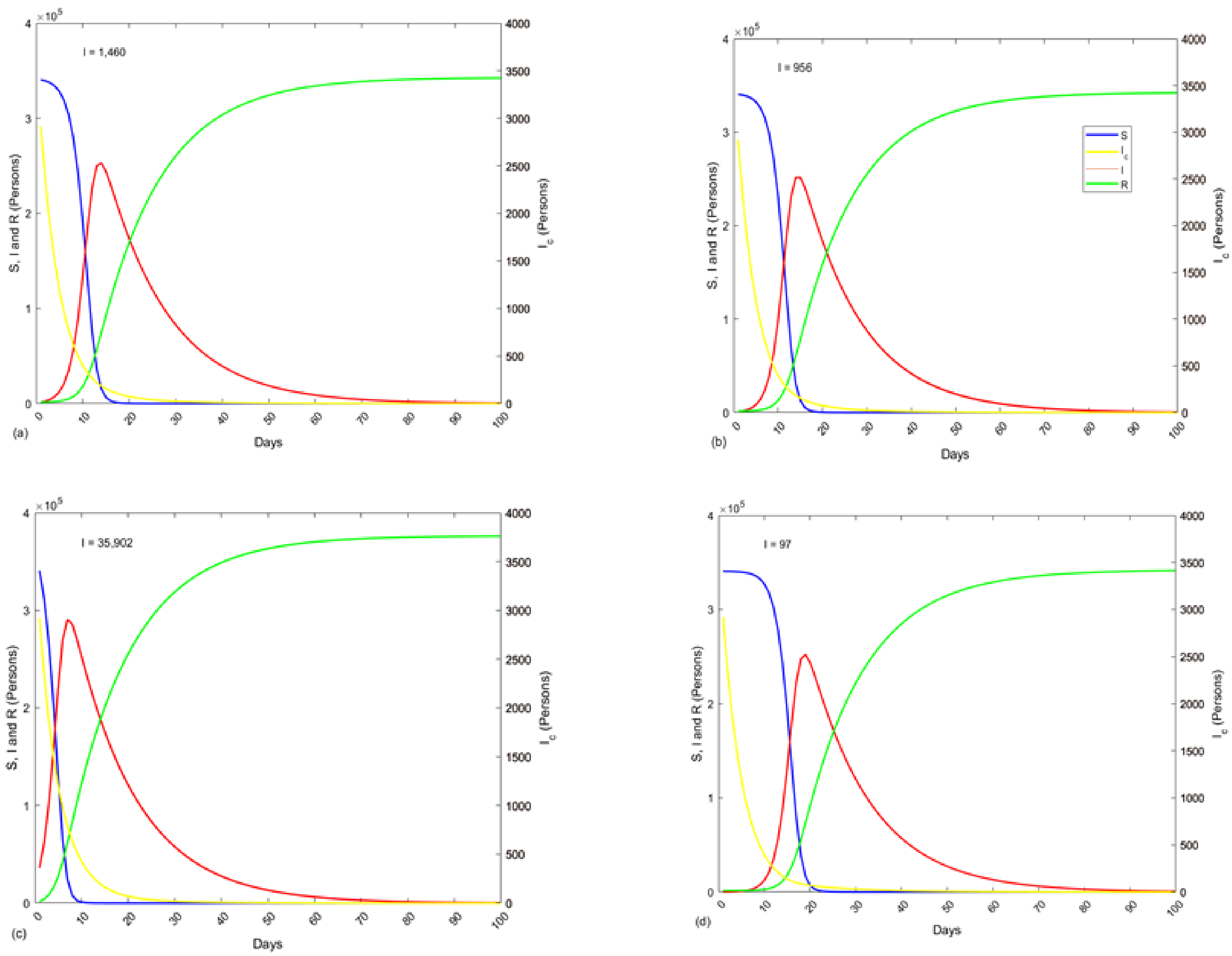

Figure 10. Effects of treatments (changes in number of infected persons, I) on transmission dynamics of typhoid fever (susceptible, carriers, infected, recovered) in Ibadan South-East Local Government Area(LGA), Oyo State using I equals (a) 1,460, as observed; (b) 966, below observation; (c) 35902, far above observation; and (d) 97, far below observation. The vertical axis on the left is for S, I and R while the vertical axis on the right is for the I_c compartment.

population after 90 days (Figure 11d). In all, isolation and vaccination as preventive and control strategies had significant impacts on reducing cumulative typhoid cases in the study area.

DISCUSSION

There was a significant increase in the population density (232 people km^{-2} $year^{-1}$) during the study period. This

Table 4 Results of student t-test statistics on the changes in carrier and infected populations due to variations in the number of infected individuals, I.

Pairs	Variables	Mean	STD	t-stat	df	p
Pair 1	Ici1 vs Ici2	154.153	0.8343	-0.3330	99	0.7399
Pair 2	Ici1 vs Ici3	154.379	6.4284	-0.7467	99	0.4570
Pair 3	Ici1 vs Ici4	154.247	5.0054	-0.4321	99	0.6666

STD = Standard deviation, df = degree of freedom, p = p-probability. [Note that Ici1, Ici2, Ici3 and Ici4 are numbers of carriers and infected obtained when initial value of I = 1460, 966, 35902 and 97 respectively].

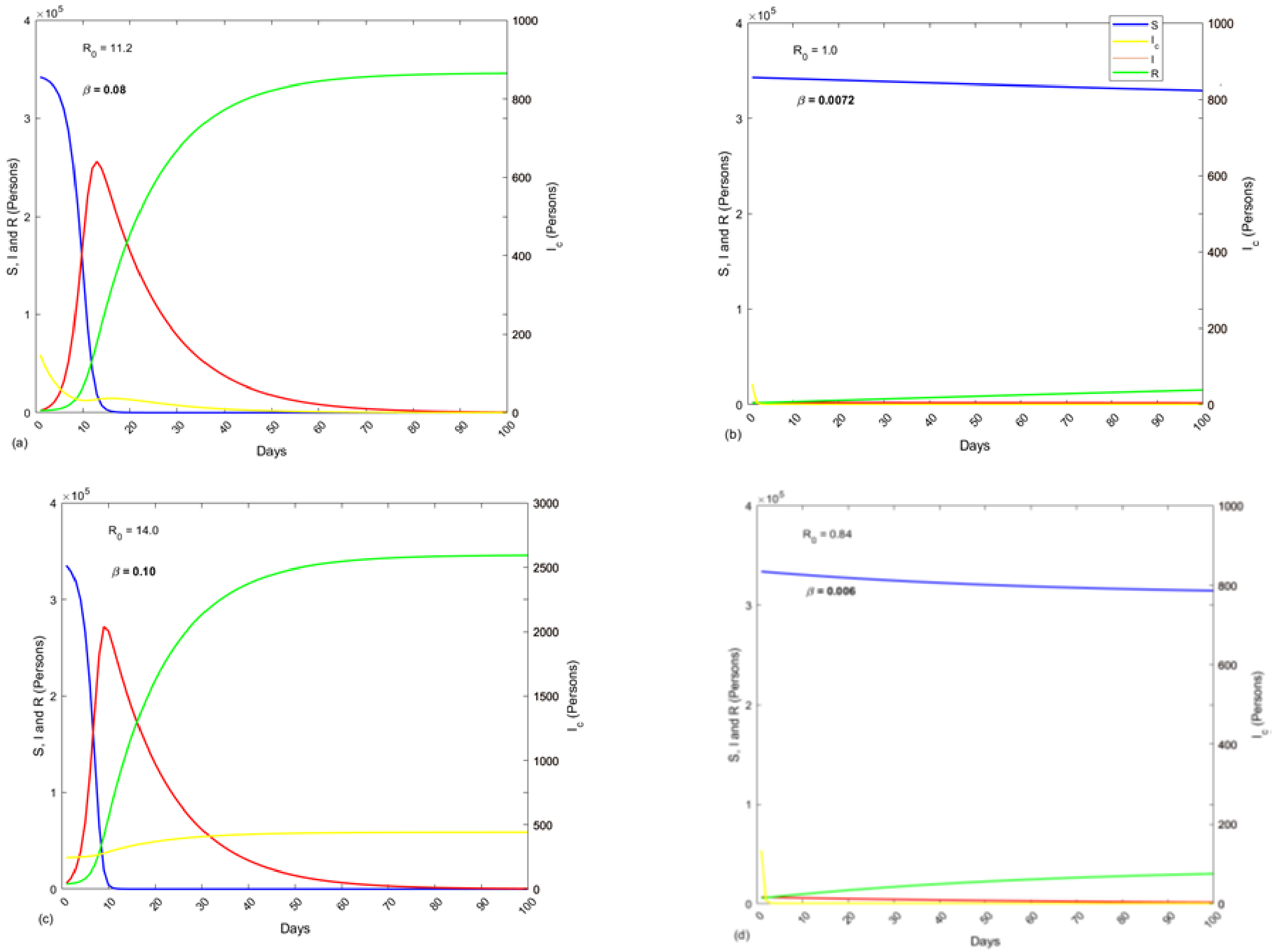

Figure 11. Effects of vaccination (changes in typhoid transmission rate, β*)* on transmission dynamics of typhoid fever (susceptible, carriers, infected, recovered) in Ibadan South-East Local Government Area (LGA), Oyo State using β equals (a) 0.08, as observed where $R_0 = 11.2$; (b) 0.0072, below observation such that $R_0 \approx 1$; (c) 0.10, far above observation such that $R_0 >> 11.2$; and (d) 0.006, far below observation such that $R_0 < 1$. The vertical axis on the left is for S, I and R while the vertical axis <<on the right is for the I_c compartment.

pattern of population distribution is a common trend in Africa where birth rates are not controlled by law due to their heterogeneous cultural and religious background. Similarly, the number of susceptible people increased by 13,474 people year^{-1}. Ameh and Opara (2004) subscribed to the fact that increased population could engender rise in the cases of infectious diseases particularly in Africa where there is inadequate infrastructural development and poor sanitation and personal hygiene. Interestingly, there was a decreasing trend (56 people year^{-1}) in the reported

Table 5 Results of student t-test statistics on the changes in carrier and infected populations due to variations in typhoid transmission coefficient, β.

Pairs	Variables	Mean	STD	t-stat	df	p
Pair 1	Ici1 vs Ici2	9.423	19.298	6.3628	99	0.000
Pair 2	Ici1 vs Ici3	209.293	81.472	-47.558	99	0.000
Pair 3	Ici1 vs Ici4	8.979	20.410	6.4511	99	0.000

STD = Standard deviation, df = degree of freedom, p = p-probability. [Note that Ici1, Ici2, Ici3 and Ici4 are number of carriers obtained when β = 0.08, 0.0072, 0.1 and 0.006 respectively].

typhoid fever cases during the study period. This is traceable to the improved functional health facilities and their utilization particularly between 2015 and 2017. A drop in the number of these facilities between 2011 and 2014 could be attributed to inadequate funding by the government and poor maintenance culture. It has been reported that adequate health infrastructure aids quick and effective treatment which has the greatest influence on reducing cumulative typhoid cases (Kalajdzievska and Li, 2011).

The results also revealed that typhoid fever cases (infected, carriers and death) were more prevalent among age-groups 20 to 40 years and >40 years which occupy economically and epidemiologically strategic positions in the society. This could be attributed to the fact that these age groups are predominantly youths and market traders whose restlessness in a struggle to make ends meet increases their chance of interacting more with the infected and asymptomatic carriers in the community. Results from the survey of the area revealed that majority of the markets have no means of proper waste disposal and no modern toilets. Therefore, human faeces and urine disposed into streams and gutters might have found their way into ground water and rivers which the community depends solely on for their domestic uses. Majority of the inhabitants inhabits dilapidated and old buildings with no modern toilet system and poor sanitation practices. All these are found to increase the chances of transmission of this disease among the adults. This corroborates the findings of Miriam (2005) who reported that living or interacting in areas exposed to typhoid fever is a risk factor. In addition, adults might be more vulnerable to the disease due to the continual use of antibiotics as a treatment. It has been widely reported that overuse of antibiotics could contribute to the development and spread of antibiotic-resistant *S. typhi* among adults (Akinyemi et al., 2018). The findings are in agreements with those reported in Ogunleye et al. (2013) where incidence rate of enteric fever was higher among subject aged above 20 years. This pattern in observed age distribution poses a serious health concern as these groups of individuals occupies epidemiologically and economically strategic positions in the society.

Evidences from the results showed high seasonal variations in typhoid infection (infected, carriers and death) with highest magnitudes at the beginning of wet (April) and dry (November) seasons. Higher incidences at the start of wet season could be attributed to the facts that accumulated faeces contaminated with *S. typhi* deposited during dry season are being washed down into streams and rivers which are used for domestic and agricultural purpose. This is so because hygienic disposal of excreta with *S. typhi* can survive in water for days (Choo et al., 1999). Similarly, shortage of drinking water occasioned by the onset of dry season could trigger cases of typhoid fever as large number of residents will be scouting for safe water.

Model simulations for a season of typhoid epidemic suggested that an outbreak of typhoid fever could occur within two weeks within the community if no effective preventive and intervention measures were put in place. In agreement with the literature, higher R_0 increase typhoid infections and possibility of epidemic in the community (Mutua et al., 2017). However, reduction in the number of carriers significantly reduced number of infected compartment ($0.0012 \leq p \geq 0.0023$) and suggested a disease-free population within the 100-day simulation period. In agreement with Naresh et al. (2008), the results suggested that infectious population is responsive to changes in the levels of carriers. This is so because carrier population is believed to increase with rise in cumulative density of habitat characteristics (such as plant and vegetation in residential areas, open drainage, garbage dumps, water storage tanks, ponds, etc.) which provide a very conducive environment for breeding, growth and survival of carriers such as *M. domestica* flies leading to the increased spread of typhoid fever (González-Guzmán, 1989; Shukla et al., 2014). Furthermore, isolation of the infected and carrier individuals by reducing the rate of interactions of the susceptible class with the infected and carriers' groups significantly reduced the infected compartment and suggested a disease-free population. This result is in agreement with the findings of Takahashi et al. (2010) where it was reported that isolating the infected population upon diagnosis will have a great influence on reducing the cumulative typhoid cases. Peter et al. (2017) in their independent study also reported that the spread of typhoid disease largely depends on the contact rates with infected individuals within a population and the disease burden can control by effectively controlling the infected population; for example, through isolation of the infected individuals. Reduction in the number of infected individuals through treatment was found to lower the number of infected populations. However, these changes were found to be insignificant (0.4570 ≤ p ≥ 0.7399). This could be as a result of the significant contribution of the carriers whose presence are constantly been felt in the community. In agreement with Roumagnac et al. (2006) and Naresh et al. (2008), the presence of asymptomatic carriers (and their increasing number) in the population played an important role in the disease transmission and could greatly hinders the eradication of typhoid fever using treatment. The impact of vaccination as a preventive strategy on the infected population by decreasing the disease's transmission rate (or increasing the immunity of the susceptible class to typhoid infection) was found to be significant. The results confirm the findings of Kalajdzievska and Li (2011) and Stanaway et al. (2019) that vaccination rate has a great influence on the magnitude of the reproduction number. Omame et al. (2015) specifically reported that increased vaccination rate will lead to typhoid disease extinction while low vaccination rate as well as improper treatment for carriers will produce an epidemic. The findings confirm previous assertion that combination of prevention and treatment is the best cost-effective strategy to eradicate typhoid disease (Edward and Nyerere, 2015; Tilahun et al., 2017).

Conclusion

The study revealed significant increase in the population density and number of susceptible people during the study period. However, there was a general increase in the number of functional health facilities which resulted in a decreasing trend in the reported typhoid fever cases. Typhoid fever cases (infected and death) were more prevalent among age-groups 20 to 40 years and >40 years which occupy economically and epidemiologically strategic positions in the society. The reason was adduced to inadequate safe water supply, low income, poor sanitation and personal hygiene among the majority market traders and spread of antibiotic-resistant *S. typhi* due to overuse of antibiotics. There were remarkable seasonal variations in reported cases of typhoid fever (infected, carriers and death) and model simulations suggested that an outbreak of typhoid fever could occur within two weeks within the community if no effective intervention such as preventive and control measures are in place. Finally, the choice of vaccination and isolation as preventive and control strategies on the typhoid transmission dynamics could significantly reduce the burden of typhoid fever in the study area.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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