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Construction of Stochastic Co-Dynamics Modelling for the Transmission of Healthcare Associated Infections

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Abstract

In this paper, we proposed a multidimensional stochastic co-infection model that describes the transmission of the hospital-acquired and community-acquired methicillin-resistant Staphylococcus aureus. Stochasticity is incorporated to accommodate the random effect as epidemiological phenomenons are random due to environmental and other factors. The existence and uniqueness of a solution for the model are studied.

AMS subject classification:
Keywords: MRSA infection, stochastic co-infection model, transition probability, Brownian motion.

1. Introduction

It has been known that there was only one methicillin-resistant Staphylococcus aureus (MRSA) strain that existed in hospital, called hospital-acquired MRSA (HA-MRSA), which predominantly infected elderly and debilitated patients [10]. Recently, however, studies confirmed the emergence of new strain of MRSA strain in the community called community-acquired MRSA (HA-MRSA) which by far genetically different from HA-MRSA [2]. Biologists and epidemiologists need to understand the transmission dynamics

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of the multidrug-resistant infections such as MRSA strains, that are prevalent and virulent resulting in high morbidity, mortality and healthcare costs [3]. [10] have been proposed a deterministic model to describe the transmission dynamics of the co-colonization of both strains (HA- and CA-MRSA). Furthermore, there have been numerous studies which dealt with multidrug-resistant infections in general including MRSA [4, 6, 12, 8].

However, it is observable that the population dynamics in real life is influenced by many unknown random variations such as changing behaviours, social cycles, environmental effects, public interventions, seasonal effects. A study by [11] developed both deterministic and stochastic models to assess the effect of environmental contamination and presence of volunteers on the dynamics of hospital infection in China. They found that the stochastic model gives the best fit for the data due to the existence of high randomization in the data. The inclusion of random components into well chosen differential equations lead to the emergence of new probabilistic puzzles and distinct challenges. In studying any random dynamical system, Itô stochastic differential equation has to be studied and developed. There are three main procedures to follow in developing a stochastic differential equation models that have to be applied in many areas including population biology, engineering, chemistry and financial mathematics [1]. The first procedure is developing a discrete stochastic model considering the changes in the system component over a small interval of time say Δt. The differential equation will be obtained as the time interval approaches to zero. The second procedure (used here) is determining all the independent random changes occurring in the system. The number of Weiner processes may exceed the number of the components in the system. In the third procedure, direct formulation of a stochastic differential equation is applied. Specific functional forms are assumed for the elements of the drift and diffusion matrix.

A general stochastic equation model can be described by

$$\frac{dX_t}{dt} = f(t, X_t) + g(t, X_t)W_t$$

X_t satisfies the stochastic differential equation

$$dX_t = f(t, X_t)dt + g(t, X_t)dB_t$$

or in integral form

$$X_t = X_0 + \int_0^t f(s, X_s)ds + \int_0^t g(s, X_s)dB_s$$

Stochastic epidemic models can really describe the spread of antimicrobial-resistant infections by considering the random nature of the population processes.

2. Formulation of Stochastic Model for Co-Infection of HA-MRSA and CA-MRSA Strains

For an extension, we initially considered the model developed by [5] to include the infection, and co-infection of patients with HA-MRSA and CA-MRSA strains, and the random effects or stochasticity. Here the model we developed represents the co-infection transmission of HA-MRSA and CA-MRSA strains. The patients in hospital are divided into six distinct compartments: susceptible patients (P_s), colonized patients with HA-MRSA strain (P_{ch}), colonized patients with CA-MRSA strain (P_{cc}), infected patients with HA-MRSA strain (P_{ih}), infected patients with CA-MRSA strain (P_{ic}) and patients co-infected with HA-MRSA and HA-MRSA strains (P_b). Here, N represents the total hospitalized patients. The daily admitting fraction of patients of HA-MRSA colonized, HA-MRSA infected, CA-MRSA colonized, CA-MRSA infected, and co-infected are π_{ch}, π_{ih}, π_{cc}, π_{ic}, and π_b, respectively, which summed up to total number of W admissions per a day to a hospital. The average length of hospital stay of susceptible, HA-MRSA colonized and CA-MRSA colonized patients are $1/\varepsilon_s$, $1/\varepsilon_{ch}$ and $1/\varepsilon_{cc}$, respectively (where ε_s, ε_{ch} and ε_{cc} are exit rate of susceptible, HA-MRSA and CA-MRSA colonized patients, respectively). The hand-hygiene compliance efficacy of healthcare workers is μ (in %). The rate of colonization transmission to patients from healthcare workers contaminated by HA-MRSA colonized patients, HA-MRSA infected patients, CA-MRSA colonized patients and CA-MRSA infected patients denoted by β_{ch}, β_{ih}, β_{cc}, β_{ic} and β_{ch}, respectively. λ_h, λ_{ihc}, λ_c and λ_{ich} indicate the rates of infection of colonized HA-MRSA patients, infected HA-MRSA patients to co-infection, colonized CA-MRSA patients and infected CA-MRSA patients to co-infection, respectively. The infection cure rates (back to colonization) of CA-MRSA and HA-MRSA infected patients are accommodated by ζ_h and ζ_c, respectively. α_h, α_c and α_b are decolonization rates of HA-MRSA colonized, CA-MRSA colonized and co-infected patients, respectively. The death rates of HA-MRSA infected, CA-MRSA infected and co-infected patients are σ_h, σ_c and σ_b, respectively. And the colonization rates of susceptible patients to the colonized HA-MRSA compartment are $\frac{(1-\mu)\,\beta_{ch}}{N}$ and $\frac{(1-\mu)\,\beta_{ih}}{N}$, and to that of colonized CA-MRSA compartment are $\frac{(1-\mu)\,\beta_{cc}}{N}$ and $\frac{(1-\mu)\,\beta_{ic}}{N}$.

We model the co-infection of patients with HA- and CA-MRSA strains with the random variables $(P_s(t), P_{ch}(t), P_{cc}(t), P_{ih}(t), P_{ic}(t), P_b(t))$ for $t \geq 0$. Let the values of $P_s(t), P_{ch}(t), P_{cc}(t), P_{ih}(t), P_{ic}(t), P_b(t)$ at time t be $P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b$, respectively. Let $\mathbf{X}(t) = (P_s(t), P_{ch}(t), P_{cc}(t), P_{ih}(t), P_{ic}(t), P_b(t))^t$ denote the stochastic processes of our six components problem and $\Delta\mathbf{X} = \mathbf{X}(t+\Delta t) - \mathbf{X}(t)$. So the state of the Markov chain (MC) at time t is denoted by $\{P_s(t) = P_s, P_{ch}(t) = P_{ch}, P_{cc}(t) = P_{cc}, P_{ih}(t) = P_{ih}, P_{ic}(t) = P_{ic}, P_b(t) = P_b\}$, $t \geq 0$ and P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b ϵ $\{0, 1, \text{âŁ¦}, N\}$. According to the diagram shown in Figure 1, we have $j = 23$ possible changes that occur to at least one of the six components in a small interval of time, Δt. Consequently, the probability of more than one increment or decrements to occur during that interval is of order $(\Delta t)^2$, which can be neglected. Therefore, the probabilities during a small time interval, Δt of transiting from one state to another are given in Table 1.

To construct the stochastic equation model, we need to compute the expectation and the covariance of the change of the processes [1]. Suppose the probability of the j^{th} change be p_j (given in Table 1). Suppose also that the j^{th} change alerts the i^{th} component by the amount $(\Delta\mathbf{X})_{ji}$, for $i = 1, 2, \ldots, 6$.

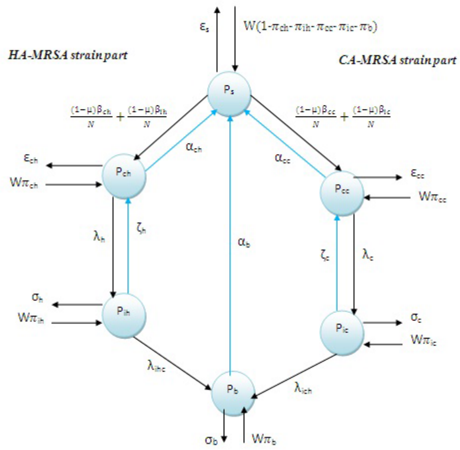

Figure 1: Flow diagram for the co-infection with HA-MRSA and CA-MRSA strains

Table 1: Possible changes of the processes and their corresponding probabilities

Transition States	Changes $(\Delta\mathbf{X})_j$	Probabilities (p_j)
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s - 1, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b)^t$	$(-1\,0\,0\,0\,0\,0)^t$	$\varepsilon_s P_s \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s + 1, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b)^t$	$(1\,0\,0\,0\,0\,0)^t$	$W(1 - \pi_{ch} - \pi_{ih} - \pi_{cc} - \pi_{ic} - \pi_b)\Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s - 1, P_{ch} + 1, P_{cc}, P_{ih}, P_{ic}, P_b)^t$	$(-1\,1\,0\,0\,0\,0)^t$	$\left(\frac{(1-\mu)}{N}\beta_{ch} + \frac{(1-\mu)}{N}\beta_{ih}\right) P_s \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s - 1, P_{ch}, P_{cc} + 1, P_{ih}, P_{ic}, P_b)^t$	$(-1\,0\,1\,0\,0\,0)^t$	$\left(\frac{(1-\mu)}{N}\beta_{cc} + \frac{(1-\mu)}{N}\beta_{ic}\right) P_s \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s + 1, P_{ch} - 1, P_{cc}, P_{ih}, P_{ic}, P_b)^t$	$(1\ -1\,0\,0\,0\,0)^t$	$\alpha_{ch} P_{ch} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s + 1, P_{ch}, P_{cc} - 1, P_{ih}, P_{ic}, P_b)^t$	$(1\,0\ -1\,0\,0\,0)^t$	$\alpha_{cc} P_{cc} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s + 1, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b - 1)^t$	$(1\,0\,0\,0\,0\ -1)^t$	$\alpha_b P_b \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch} - 1, P_{cc}, P_{ih}, P_{ic}, P_b)^t$	$(0\ -1\,0\,0\,0\,0)^t$	$\varepsilon_{ch} P_{ch} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch} + 1, P_{cc}, P_{ih}, P_{ic}, P_b)^t$	$(0\,1\,0\,0\,0\,0)^t$	$W\pi_{ch} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch} - 1, P_{cc}, P_{ih} + 1, P_{ic}, P_b)^t$	$(0\ -1\,0\,1\,0\,0)^t$	$\lambda_h P_{ch} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch} + 1, P_{cc}, P_{ih} - 1, P_{ic}, P_b)^t$	$(0\,1\,0\ -1\,0\,0)^t$	$\zeta_h P_{ih} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc} - 1, P_{ih}, P_{ic}, P_b)^t$	$(0\,0\ -1\,0\,0\,0)^t$	$\varepsilon_{cc} P_{cc} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc} + 1, P_{ih}, P_{ic}, P_b)^t$	$(0\,0\,1\,0\,0\,0)^t$	$W\pi_{cc} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc} - 1, P_{ih}, P_{ic} + 1, P_b)^t$	$(0\,0\ -1\,0\,1\,0)^t$	$\lambda_c P_{cc} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc} + 1, P_{ih}, P_{ic} - 1, P_b)^t$	$(0\,0\,1\,0\ -1\,0)^t$	$\zeta_c P_{ic} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih} - 1, P_{ic}, P_b)^t$	$(0\,0\,0\ -1\,0\,0)^t$	$\sigma_h P_{ih} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih} + 1, P_{ic}, P_b)^t$	$(0\,0\,0\,1\,0\,0)^t$	$W\pi_{ih} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih} - 1, P_{ic}, P_b + 1)^t$	$(0\,0\,0\ -1\,0\,1)^t$	$\lambda_{ihc} P_{ih} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic} - 1, P_b)^t$	$(0\,0\,0\,0\ -1\,0)^t$	$\sigma_c P_{ic} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic} + 1, P_b)^t$	$(0\,0\,0\,0\,1\,0)^t$	$W\pi_{ic} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic} - 1, P_b + 1)^t$	$(0\,0\,0\,0\ -1\,1)^t$	$\lambda_{ich} P_{ic} \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b - 1)^t$	$(0\,0\,0\,0\,0\ -1)^t$	$\sigma_b P_b \Delta t$
$(P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b) \to (P_s, P_{ch}, P_{cc}, P_{ih}, P_{ic}, P_b + 1)^t$	$(0\,0\,0\,0\,0\,1)^t$	$W\pi_b \Delta t$

Now, generally we can define the stochastic model as:

$$\begin{cases} d\mathbf{X}(t) = \mathbf{f}\big(t, \mathbf{X}(t)\big)dt + G\big(t, \mathbf{X}(t)\big)d\mathbf{W}(t) \\ \mathbf{X}(0) = \mathbf{X}_0 \end{cases} \tag{2.1}$$

where $\mathbf{W}$(t) is a vector of 23 independent wiener processes on the complete probability space $\big(\Omega, \mathcal{F}, (\mathcal{F}_t), \mathbb{P}\big)$. It is obligatory to find the drift vector and the diffusion matrix to create a sensible relation between the left and right hand sides of equation (2.1). The drift vector $\big(\mathbf{f}(\mathrm{t}, \mathbf{X}(\mathrm{t}))\big)$ and diffusion matrix $\big(\mathrm{G}(\mathrm{t}, \mathbf{X}(\mathrm{t}))\big)$ of equation (2.1) are computed as follows [13] by neglecting higher order terms of Δt. Before doing the expectations, we let

$$f_i\big(t, \mathbf{X}(t)\big) = \sum_{j=1}^{23} p_j (\Delta\mathbf{X})_{ji} \tag{2.1}$$

for $i = 1, 2, \ldots, 6$. Notice that equation (2.1) can be used to define the deterministic model with a system of ordinary differential equations as:

$$d\mathbf{X}(t) = \mathbf{f}\big(t, \mathbf{X}(t)\big)dt \tag{2.2}$$

where $\mathbf{f} = (f_1, f_2, \ldots, f_6)^t$. Euler's method is used to approximate equation (2.2) for small time interval, Δt as shown below.

$$X_{n+1,i} = X_{n,i} + f_i\big(t_n, \mathbf{X}(t_n)\big)\Delta t \tag{2.3}$$

where $t_n = n\Delta t$ and $X_{n,i} \approx X_i(t_n)$ for $i = 1, 2, \ldots, 6$ and $n = 0, 1, \ldots, N$. It is possible to formulate an accurate stochastic model by considering small but fixed interval of time, Δt. To do this, we take a random change, say $\mathbf{c}_j$ to order $o\big((\Delta t)\big)^2$ defined as:

$$\mathbf{c}_j = \begin{cases} \big((\Delta\mathbf{X})_{j1}, (\Delta\mathbf{X})_{j2}, \ldots, (\Delta\mathbf{X})_{j6}\big)^t & \text{with probability } p_j \\ (0, 0, \ldots, 0)^t & \text{with probability } 1 - p_j \end{cases} \tag{2.4}$$

By assuming small time interval Δt, $(\mathbf{c}_j)_i$ has mean $(\Delta\mathbf{X})_{ji} p_j$ and variance $(\Delta\mathbf{X})^2_{ji} p_j$ approximately. Thus, the stochastic model for $\mathbf{X}_n + 1$ given $\mathbf{X}_n$ is

$$\mathbf{X}_{n+1} = \mathbf{X}_n + \sum_{j=1}^{23} \mathbf{c}_j \tag{2.5}$$

for $n = 0, 1, \ldots, N$. Equation (2.5) can be written in component form:

$$X_{n+1,i} = X_{n,i} + \sum_{j=1}^{23} (\mathbf{c}_j)_i \tag{2.6}$$

Using Euler-Maruyama approximation, equation (2.6) for small but fixed interval of time Δt can be approximated by

$$X_{n+1,i} = X_{n,i} + f_i(t_n, \mathbf{X}_n)\Delta t + \sum_{j=1}^{23} (\Delta\mathbf{X})_{ji} p_j^{\frac{1}{2}} \tag{2.7}$$

for $n = 0, 1, \ldots, N$. where f_i defined as in equation (2.1).

Now we compute the expectation and variance of the change of the process to find the drift and diffusion coefficients in equation (2.1) as follows.

$$E\left(\Delta \mathrm{x}\right) = \sum_{j=1}^{23} (\Delta \mathrm{x})_j p_j = \begin{bmatrix} -1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \varepsilon_s P_s \Delta t + \cdots + \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} W\pi_b \Delta t$$

$$= \begin{bmatrix} -\varepsilon_s P_s + a - b - c + \alpha_{ch} P_{ch} + \alpha_{cc} P_{cc} + \alpha_b P_b \\ b - (\alpha_{ch} + \varepsilon_{ch} + \lambda_h) P_{ch} + W\pi_{ch} + \zeta_h P_{ih} \\ c - (\alpha_{cc} + \varepsilon_{cc} + \lambda_c) P_{cc} + W\pi_{cc} + \zeta_c P_{ic} \\ \lambda_h P_{ch} - (\zeta_h + \sigma_h + \lambda_{ihc}) P_{ih} + W\pi_{ih} \\ \lambda_c P_{cc} - (\zeta_c + \sigma_c + \lambda_{ich}) P_{ic} + W\pi_{ic} \\ -(\alpha_b + \sigma_b) P_b + \lambda_{ihc} P_{ih} + \lambda_{ich} P_{ic} + W\pi_b \end{bmatrix} \Delta t$$

and

$$Var\left(\Delta \mathrm{x}\right) \approx E\left(\Delta \mathbf{X} \left(\Delta \mathbf{X}\right)^t\right)$$

$$= \sum_{j=1}^{23} (\Delta \mathbf{X})_j (\Delta \mathbf{X})^t_j p_j = \begin{bmatrix} -1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \begin{bmatrix} -1 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \varepsilon_s P_s \Delta t$$

$$+ \cdots + \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} W\pi_b \Delta t$$

$$= \begin{bmatrix} \varepsilon_s P_s + a + b + c + d & -b - \alpha_{ch} P_{ch} & -c - \alpha_{cc} P_{cc} & 0 & 0 & -\alpha_b P_b \\ -b - \alpha_{ch} P_{ch} & b + e + W\pi_{ch} + \zeta_h P_{ih} & 0 & -\lambda_h P_{ch} - \zeta_h P_{ih} & 0 & 0 \\ -c - \alpha_{cc} P_{cc} & 0 & c + f + W\pi_{cc} + \zeta_c P_{ic} & 0 & -\lambda_c P_{cc} - \zeta_c P_{ic} & 0 \\ 0 & -\lambda_h P_{ch} - \zeta_h P_{ih} & 0 & \lambda_h P_{ch} + g + W\pi_{ih} & 0 & -\lambda_{ihc} P_{ih} \\ 0 & 0 & -\lambda_c P_{cc} - \zeta_c P_{ic} & 0 & \lambda_c P_{cc} + h + W\pi_{ic} & -\lambda_{ich} P_{ic} \\ -\alpha_b P_b & 0 & 0 & -\lambda_{ihc} P_{ih} & -\lambda_{ich} P_{ic} & k + l + W\pi_b \end{bmatrix} \Delta t$$

where

$a = W(1 - \pi_{ch} - \pi_{ih} - \pi_{cc} - \pi_{ic} - \pi_b)$, $b = \big(\frac{(1-\mu)}{N}\beta_{ch} + \frac{(1-\mu)}{N}\beta_{ih}\big)P_s$, $c = \big(\frac{(1-\mu)}{N}\beta_{cc} + \frac{(1-\mu)}{N}\beta_{ic}\big)P_s$, $d = \alpha_{ch}P_{ch} + \alpha_{cc}P_{cc} + \alpha_b P_b$, $e = (\alpha_{ch} + \varepsilon_{ch} + \lambda_h)P_{ch}$,

$f=(\alpha_{cc}+\varepsilon_{cc}+\lambda_c)P_{cc}, g=(\zeta_h+\sigma_h+\lambda_{ihc})P_{ih}, h=(\zeta_c+\sigma_c+\lambda_{ich})P_{ic}, k=(\alpha_b+\sigma_b)P_b$, $l=\lambda_{ihc}P_{ih}+\lambda_{ich}P_{ic}$ Therefore, using the transition probabilities (p_j) given in Table 1, the drift vector and the diffusion matrix in equation (2.1), respectively are

$$\mathbf{f}\big(t,\mathbf{X}(t)\big)=\frac{E\,(\Delta\mathbf{X})}{\Delta t}=\frac{1}{\Delta t}\begin{bmatrix}-p_1+p_2-p_3-p_4+p_5+p_6+p_7\\ p_3-p_5-p_8-p_{10}+p_9+p_{11}\\ p_4-p_6-p_{12}-p_{14}+p_{13}+p_{15}\\ p_{10}-p_{11}-p_{16}-p_{18}+p_{17}\\ p_{14}-p_{15}-p_{19}-p_{21}+p_{20}\\ -p_7-p_{221}+p_{18}+p_{21}+p_{23}\end{bmatrix} \tag{2.9}$$

and

$$G\big(t,\mathbf{X}(t)\big)=\left(\frac{Var\,(\Delta\mathbf{X})}{\Delta t}\right)^{1/2}$$

But in practice it is difficult to find the square root of the co-variance of the change $\big((Var\,(\Delta\mathbf{X})\,)^{1/2}\big)$. Since the $Var\,(\Delta\mathbf{X})$ is symmetric, we can find $G\big(t,\mathbf{X}(t)\big)$ such that $G\big(t,\mathbf{X}(t)\big)\big(G(t,\mathbf{X}(t))\big)^t=\dfrac{Var\,(\Delta\mathbf{X})}{\Delta t}$, in Cholesky decomposition form. Thus, the $(ij)^{th}$ entry of 6×23 matrix $G\big(t,\mathbf{X}(t)\big)$ is given by $g_{ij}=\big(\Delta X_j\big)_i\,\big(p_j\big)^{1/2}$. For simplicity, we take p_j given from Table 1. So, $G\big(t,\mathbf{X}(t)\big)$ is given as

$$G\big(t,\mathbf{X}(t)\big)=\frac{1}{\sqrt{\Delta t}}\begin{bmatrix}A & B\end{bmatrix}_{6\times 23} \tag{2.10}$$

where A and B are given below.

$$A=\begin{bmatrix}-\sqrt{p_1} & \sqrt{p_2} & -\sqrt{p_3} & -\sqrt{p_4} & \sqrt{p_5} & \sqrt{p_6} & \sqrt{p_7} & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & \sqrt{p_3} & 0 & -\sqrt{p_5} & 0 & 0 & -\sqrt{p_8} & \sqrt{p_9} & -\sqrt{p_{10}} & \sqrt{p_{11}} & 0\\ 0 & 0 & 0 & \sqrt{p_4} & 0 & -\sqrt{p_6} & 0 & 0 & 0 & 0 & 0 & -\sqrt{p_{12}}\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \sqrt{p_{10}} & -\sqrt{p_{11}} & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & -\sqrt{p_7} & 0 & 0 & 0 & 0 & 0\end{bmatrix}$$

$$B=\begin{bmatrix}0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ \sqrt{p_{13}} & -\sqrt{p_{14}} & \sqrt{p_{15}} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & -\sqrt{p_{16}} & \sqrt{p_{17}} & -\sqrt{p_{18}} & 0 & 0 & 0 & 0 & 0\\ 0 & \sqrt{p_{14}} & -\sqrt{p_{15}} & 0 & 0 & 0 & -\sqrt{p_{19}} & \sqrt{p_{20}} & -\sqrt{p_{21}} & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & \sqrt{p_{18}} & 0 & 0 & \sqrt{p_{21}} & -\sqrt{p_{22}} & \sqrt{p_{23}}\end{bmatrix}$$

Hence, our simplified and specific co-infection model is

$$
\begin{aligned}
dP_s(t) &= \frac{1}{\Delta t}\big(-p_1+p_2-p_3-p_4+p_5+p_6+p_7\big)dt \\
&\quad + \frac{1}{\sqrt{\Delta t}}\big(-\sqrt{p_1}dW_1(t)+\sqrt{p_2}dW_2(t)-\sqrt{p_3}dW_3(t)-\sqrt{p_4}dW_4(t)+\sqrt{p_5}dW_5(t)+\sqrt{p_6}dW_6(t)+\sqrt{p_7}dW_7(t)\big) \\
dP_{ch}(t) &= \frac{1}{\Delta t}\big(p_3-p_5-p_8+p_9-p_{10}+p_{11}\big)dt+\frac{1}{\sqrt{\Delta t}}\big(\sqrt{p_3}dW_3(t)-\sqrt{p_5}dW_5(t)-\sqrt{p_8}dW_8(t)+\sqrt{p_9}dW_9(t) \\
&\quad -\sqrt{p_{10}}dW_{10}(t)+\sqrt{p_{11}}dW_{11}(t)\big) \\
dP_{cc}(t) &= \frac{1}{\Delta t}\big(p_4-p_6-p_{12}+p_{13}-p_{14}+p_{15}\big)dt+\frac{1}{\sqrt{\Delta t}}\big(\sqrt{p_4}dW_4(t)-\sqrt{p_6}dW_6(t)-\sqrt{p_{12}}dW_{12}(t)+\sqrt{p_{13}}dW_{13}(t) \\
&\quad -\sqrt{p_{14}}dW_{14}(t)+\sqrt{p_{15}}dW_{15}(t)\big) \\
dP_{ih}(t) &= \frac{1}{\Delta t}\big(p_{10}-p_{11}-p_{16}+p_{17}-p_{18}\big)dt+\frac{1}{\sqrt{\Delta t}}\big(\sqrt{p_{10}}dW_{10}(t)-\sqrt{p_{11}}dW_{11}(t)-\sqrt{p_{16}}dW_{16}(t)+\sqrt{p_{17}}dW_{17}(t) \\
&\quad -\sqrt{p_{18}}dW_{18}(t)\big) \\
dP_{ic}(t) &= \frac{1}{\Delta t}\big(p_{14}-p_{15}-p_{19}+p_{20}-p_{21}\big)dt+\frac{1}{\sqrt{\Delta t}}\big(\sqrt{p_{14}}dW_{14}(t)-\sqrt{p_{15}}dW_{15}(t)-\sqrt{p_{19}}dW_{19}(t)+\sqrt{p_{20}}dW_{20}(t) \\
&\quad -\sqrt{p_{21}}dW_{17}(t)\big) \\
dP_b(t) &= \frac{1}{\Delta t}\big(-p_7+p_{18}+p_{21}-p_{22}+p_{23}\big)dt+\frac{1}{\sqrt{\Delta t}}\big(-\sqrt{p_7}dW_7(t)+\sqrt{p_{18}}dW_{18}(t)+\sqrt{p_{21}}dW_{21}(t)-\sqrt{p_{22}}dW_{22}(t) \\
&\quad +\sqrt{p_{23}}dW_{23}(t)\big)
\end{aligned}
$$

In matrix notation with initial values it can be stated as

$$
\begin{cases} d\mathbf{X}(t)=\mathbf{f}\big(t,\mathbf{X}(t)\big)dt+G\big(t,\mathbf{X}(t)\big)d\mathbf{W}(t) \\ \mathbf{X}(0)=\mathbf{X}_0 \end{cases} \tag{2.11}
$$

3. Existence and Uniqueness of Solutions of Stochastic Model for Co-Infection of HA-MRSA and CA-MRSA Strains

In this section we try to verify the existence and uniqueness of solution for the stochastic equation model given by equation (2.11). Before trying to see the theorem, we defined some notations and preliminaries. $\mathbb{R}^n$ is a n-dimensional Euclidean space with $|.|$ representing the norm in $\mathbb{R}^n$. M^t denotes the transpose of any vector or matrix M. Now we can define the theorem and find the solution for equation (2.11), and checking its uniqueness.

Theorem 3.1. (Stochastic equation model stated by equation (2.11)**)** For any given initial value $\mathbf{X}(0) = (P_s(0), P_{ch}(0), P_{cc}(0), P_{ih}(0), P_{ic}(0), P_b(0))^t = \mathbf{X}_0 \in \mathbb{R}^6_+$, there exist a unique positive solution $(P_s(t), P_{ch}(t), P_{cc}(t), P_{ih}(t), P_{ic}(t), P_b(t))$ of equation (2.11) such that the following two conditions hold.

- $c1)$ lipschitz condition: $max\{|f(t,x)-f(t,y)|, |g(t,x)-g(t,y)|\} \le c|x-y|$ for all $x, y \in \mathbb{R}^6_+$, $t \in [0,T]$ and for any constant c.
- $c2)$ linear growth condition: $max\{|f(t,x)|, |g(t,x)|\} \le h\,(1+|x|)$ for all $(t,x) \in \mathbb{R}^6_+ \times [0,T]$ and for any constant c.

Before start proving, let us state some helpful definitions and lemmas.

Definition 3.2. Suppose $f(t,\kappa)$ be a real-valued integrable function on the interval $[0,T]$, where $0 = t_0 < t_1 < t_2 < \cdots < t_{n-1} < t_n = T$. Then we define the integral

$\int_0^T f(t, \kappa)dt$ as

$$\lim_{n\to\infty} \sum_{i=1}^{n} f(t_{i-1}, \kappa)(t_i - t_{i-1}) \quad \text{for} \quad \kappa \in \Omega.$$

Definition 3.3. Suppose $G(t, \kappa)$ be a real-valued integrable function on the interval $[0, T]$, where $0 = t_0 < t_1 < t_2 < \cdots < t_{n-1} < t_n = T$, and let $W(t, \kappa)$ be stochastic/Wiener process. Then we define the integral $\int_0^T G(t, \kappa)dW(t, \kappa)$ as

$$\lim_{n\to\infty} \sum_{i=1}^{n} G(t_{i-1}, \kappa)(W(t_i, \kappa) - W(t_{i-1}, \kappa)) \quad \text{for} \quad \kappa \in \Omega.$$

Definition 3.4. Suppose $W(t, \kappa)$ is lispschitz continuous with respect to t for each sample κ. Then there exists a finite number $A(\kappa)$ such that

$$|W(t_i, \kappa) - W(t_{i-1}, \kappa)| \leq A(\kappa)|t_i - t_{i-1}|.$$

Lemma 3.5. Let $f(t, \kappa)$ be a d-dimensional integrable function on the interval $[0, T]$. Then,

$$\Big|\int_0^T f(t, \kappa)dt\Big| \leq \int_0^T \big|f(t, \kappa)\big|dt$$

Proof. Applying definition 3.2 we can get that

$$\begin{aligned}\Big|\int_0^T f(t, \kappa)dt\Big| &= \Big|\lim_{n\to\infty} \sum_{i=1}^{n} \sum_{k=1}^{d} f_k(t_i, \kappa)(t_i - t_{i-1})\Big| \\ &\leq \lim_{n\to\infty} \sum_{i=1}^{n} \sum_{k=1}^{d} \big|f_k(t_i, \kappa)(t_i - t_{i-1})\big| \\ &= \int_0^T \big|f(t, \kappa)\big|dt\end{aligned}$$

Hence, the lemma is proved as desired. ■

Lemma 3.6. Let $W(t, \kappa)$ be a m-dimensional stochastic process, and let $G(t, \kappa)$ be an $d \times m$ integrable diffusion matrix on the interval $[0, T]$. Then,

$$\Big|\int_0^T G(t, \kappa)dW(t, \kappa)\Big| \leq A(\kappa) \int_0^T \big|G(t)\big|dt$$

where $A(\kappa)$ is the lipschitz constant of the sample path W(t).

Proof. It follows from definitions 3.2, 3.3 and 3.4 that

$$
\begin{aligned}
\Big|\int_0^T G(t,\kappa)dW(t,\kappa)\Big| &= \Big|\lim_{n\to\infty}\sum_{i=1}^{n}\sum_{k=1}^{d}\sum_{j=1}^{m} G_{kj}(t_{i-1},\kappa)\big(W_j(t_i,\kappa)-W_j(t_{i-1},\kappa)\big)\Big| \\
&\le \lim_{n\to\infty}\sum_{i=1}^{n}\sum_{k=1}^{d}\sum_{j=1}^{m}\Big|G_{kj}(t_{i-1},\kappa)\big(W_j(t_i,\kappa) \quad - W_j(t_{i-1},\kappa)\big)\Big| \\
&\le A(\kappa)\lim_{n\to\infty}\sum_{i=1}^{n}\sum_{k=1}^{d}\sum_{j=1}^{m}\Big|G_{kj}(t_{i-1},\kappa)(t_i-t_{i-1})\Big| \\
&= A(\kappa)\int_0^T \Big|G(t,\kappa)\Big|dt
\end{aligned}
$$

This completes the proof as required. ■

Proof of Theorem 2.1: First let us proof the existence of solution. As given in equation (2.11) and the theorem, we assume the initial value as

$$\mathbf{X}(0) = (P_s(0), P_{ch}(0), P_{cc}(0), P_{ih}(0), P_{ic}(0), P_b(0))^t = \mathbf{X}_0 \in \mathbb{R}^6_+$$

We can define the Picard's iterations for positive integer $n \geq 0$ and for $t \in [0, T]$

$$X_{n+1}(t) = X_0 + \int_0^t f(s, X_n(s))ds + \int_0^t g(s, X_n(s))dW(s)$$

If we denote the difference say $X_{n+1}(t) - X_n(t)$ by $\phi_{n+1}(t)$, then we have

$$
\begin{aligned}
\phi_{n+1}(t) = &\int_0^t \big(f(s, X_n(s)) - f(s, X_{n-1}(s))\big)ds \\
&+ \int_0^t \big(G(s, X_n(s)) - G(s, X_{n-1}(s))\big)dW(s)
\end{aligned}
$$

Lipschitz Condition (c1) above implies

$$
\begin{cases} |f(s, X_n(s)) - f(s, X_{n-1}(s))| = c|\phi_n(s)| \quad \text{and} \\ |G(s, X_n(s)) - G(s, X_{n-1}(s))| = c|\phi_n(s)| \end{cases} \tag{3.1}
$$

Take $n = 1$. So the first difference is

$$\phi_1(t) = \int_0^t f(s, X_0(s))ds + \int_0^t G(s, X_0(s))dW(s)$$

Applying lemma 3.5 and 3.6 it follows that

$$\begin{aligned}
\max_{0\le r\le t}\left|\phi_1(r)\right| &= \max_{0\le r\le t}\Big|\int_0^r f(s,X_0(s))ds + \max_{0\le r\le t}\int_0^r G(s,X_0(s))dW(s)\Big| \\
&\le \max_{0\le r\le t}\Big|\int_0^r f(s,X_0(s))ds\Big| + \max_{0\le r\le t}\Big|\int_0^r G(s,X_0(s))dW(s)\Big| \\
&\le \max_{0\le r\le t}\int_0^t |f(s,X_0(s))|ds + A\max_{0\le r\le t}\int_0^r |G(s,X_0(s))|ds \\
&\le \int_0^t |f(s,X_0(s))|ds + A\int_0^t |G(s,X_0(s))|ds
\end{aligned}$$

Using the linear growth condition (and equation (3.2)) we get

$$\begin{aligned}
\max_{0\le r\le t}|\phi_1(r)| &\le \int_0^t h(1+|X_0|)ds + A\int_0^t h(1+|X_0|)ds \\
&= h(1+|X_0|)(1+A)\int_0^t ds \\
&= h(1+A)\big(1+|X_0|\big)t
\end{aligned}$$

For $n = 2$, applying lemma 1 and 2, lipschitz and linear growth conditions we get

$$\begin{aligned}
\max_{0\le r\le t}\left|\phi_2(r)\right| &= \max_{0\le r\le t}\Big|\int_0^r (f(s,X_1(s)) - f(s,X_0(s)))ds \\
&\quad + \max_{0\le r\le t}\int_0^r (G(s,X_1(s)) - G(s,X_0(s)))dW(s)\Big| \\
&\le \max_{0\le r\le t}\Big|\int_0^r (f(s,X_1(s)) - f(s,X_0(s)))ds\Big| \\
&\quad + \max_{0\le r\le t}\Big|\int_0^r (G(s,X_1(s)) - G(s,X_0(s)))dW(s)\Big| \\
&\le \max_{0\le r\le t}\int_0^t |(f(s,X_1(s)) - f(s,X_0(s)))|ds \\
&\quad + A\max_{0\le r\le t}\int_0^r |(G(s,X_1(s)) - G(s,X_0(s)))|ds
\end{aligned}$$

$$
\begin{aligned}
&\leq \int_0^t |(f(s, X_1(s)) - f(s, X_0(s)))(s))| ds \\
&\quad + A \int_0^t |(G(s, X_1(s)) - G(s, X_0(s)))| ds \\
&\leq \int_0^t c|X_1(s) - X_0(s)|) ds + A \int_0^t c|X_1(s) - X_0(s)| ds \\
&= c(1 + A) \int_0^t |X_1(s) - X_0(s)| ds \\
&\leq c(1 + A) \int_0^t h(1 + A)\big(1 + |X_0|\big) s ds \\
&= \frac{hc(1 + A)^2\big(1 + |X_0|\big)t^2}{2!}
\end{aligned}
$$

Therefore, by induction we can assert that for $n \geq 0$

$$
\begin{aligned}
\max_{0\leq r\leq t} \big|\phi_{n+1}(r)\big| &= \max_{0\leq r\leq t} \Big| \int_0^r (f(s, X_n(s)) - f(s, X_{n-1}(s))) ds \\
&\quad + \max_{0\leq r\leq t} \int_0^r (G(s, X_n(s)) - G(s, X_{n-1}(s))) dW(s)\Big| \\
&\leq \max_{0\leq r\leq t} \Big| \int_0^r (f(s, X_n(s)) - f(s, X_{n-1}(s))) ds\Big| \\
&\quad + \max_{0\leq r\leq t} \Big| \int_0^r (G(s, X_n(s)) - G(s, X_{n-1}(s))) dW(s)\Big| \\
&\leq \max_{0\leq r\leq t} \int_0^t |(f(s, X_n(s)) - f(s, X_{n-1}(s)))| ds \\
&\quad + A \max_{0\leq r\leq t} \int_0^r |(G(s, X_n(s)) - G(s, X_{n-1}(s)))| ds \\
&\leq \int_0^t |(f(s, X_n(s)) - f(s, X_{n-1}(s)))(s))| ds \\
&\quad + A \int_0^t |(G(s, X_n(s)) - G(s, X_{n-1}(s)))| ds \\
&\leq \int_0^t c|X_n(s) - X_{n-1}(s)|) ds + A \int_0^t c|X_n(s) - X_{n-1}(s)| ds \\
&= c(1 + A) \int_0^t |X_n(s) - X_{n-1}(s)| ds \\
&\leq c(1 + A) \int_0^t hc^n(1 + A)^n\big(1 + |X_0|\big) s^n ds \\
&= \frac{hc^n(1 + A)^{n+1}\big(1 + |X_0|\big)t^{n+1}}{(n + 1)!}
\end{aligned}
$$

As the convergence of

$$\sum_{n=0}^{+\infty} \frac{hc^n(1+A)^{n+1}\big(1+|X_0|\big)t^{n+1}}{(n+1)!}$$

exists, it is obvious that

$$\sum_{n=0}^{+\infty} \max_{0\leq r\leq t} |\phi_{n+1}(r)|\big) < +\infty.$$

Hence by the Weierstrass M-test stated in [7, p. 227], $X_n(t)$ converges uniformly in the finite interval of time $[0, T]$. If we denote the limit by $X(t)$ (i.e. $X(t) = \lim_{n\to\infty} X_n(t)$), then equation (3.1) becomes

$$X(t) = X_0 + \int_0^t f(s, X(s)ds + \int_0^t g(s, X(s)dW(s)$$

Thus, the proof of existence of solution completed as required. ■

Uniqueness can also be proved as follows.Suppose the two solutions $X(t)$ and $Z(t)$ are defined as

$$X(t) = X_0 + \int_0^t f(s, X(s)ds + \int_0^t g(s, X(s)dW(s)$$

$$Z(t) = X_0 + \int_0^t f(s, Z(s)ds + \int_0^t g(s, Z(s)dW(s)$$

Then, after applying lemma 1, 2 and lipschitz assumption we can obtain that

$$\begin{aligned}
\max_{0\le r\le t}|X(r)-Z(r)|) &= \max_{0\le r\le t}\Big|\int_0^r \big(f(s,X_(s))-f(s,Z(s))\big)ds \\
&\quad + \int_0^r \big(G(s,X(s))-G(s,Z(s))\big)dW(s)\Big| \\
&\le \max_{0\le r\le t}\Big|\int_0^r \big(f(s,X(s))-f(s,Z(s))\big)ds\Big| \\
&\quad + \max_{0\le r\le t}\Big|\int_0^r \big(G(s,X(s))-G(s,Z(s))\big)dW(s)\Big| \\
&\le \max_{0\le r\le t}\int_0^r |f(s,X(s))-f(s,Z(s))|ds \\
&\quad + A\max_{0\le r\le t}\int_0^r |G(s,X(s))-G(s,Z(s))\big|ds \\
&\le \int_0^t |f(s,X(s))-f(s,Z(s))|ds \\
&\quad + A\int_0^t |G(s,X(s))-G(s,Z(s))\big|ds \\
&\le \int_0^t c|X(s)-Z(s)|ds + A\int_0^t c|X(s)-Z(s)\big|ds \\
&= c(1+A)\int_0^t c|X(s)-Z(s)|ds
\end{aligned}$$

By the Gronwall's inequality [9, p. 45] we found that

$$\max_{0\le r\le t}|X(r)-Z(r)|) \le 0.e^{c(1+A)t} = 0$$

This implies $X(t) = Z(t)$, and hence uniqueness of solution is proved as desired.

4. Conclusion

In the successive accumulation of further and boosted understanding of the dynamics of infectious diseases transmission, it is paramount importance to keep on developing models for the spread of healthcare associated infections. Such models have a tremendous role in understanding the transmission ways, and thereby provide clues how the control, intervention and prevention strategies have to be. In this study, we formulated a co-infection model with two types of strains of MRSA, namely, HA-MRSA and CA-MRSA with the introduction of random component. Here, it has be described that the number of rows and columns for the diffusion matrix are different. We showed a step by step procedure on how to develop the co-infection model with inclusion of random component which makes the process stochastic with discrete time. The existence and uniqueness of solution hold. It is shown that The procedure can be applied to similar studies in antimicrobial-resistant infections.

Competing Interest

None of the authors have any competing interests.

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