Modeling of a Super-Spreading Event of the Mers-Corona Virus during the Hajj Season using Simulation of the Existing Data

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Abstract: The Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) has exhibited super-spreading events in recent years. In this work, we investigate the effects a possible super-spreading event in one of the largest annual mass gatherings: the Hajj season in the Kingdome Saudi Arabia (KSA). Since the KSA has the most significant confirmed number of MERS-CoV, we assume that super-spreaders are only from the local population. By the use of an extended SIR model, we considered two subpopulations: local and non-local pilgrims, were calculated the basic reproduction number and final size of the epidemic. Simulation of the existing data gives find the estimation of the basic reproduction number is less than one, although the final size of the epidemic shows proportionality to the super-spreading effect.

Keywords: Corona, Hajj, Super-spreader, Mathematical modeling, Mers-Corona.

INTRODUCTION

The Middle East respiratory syndrome corona virus, Mers-CoV, is a virus from corona virus family which started in Saudi Arabia in 2012 [9]. The virus attacks respiratory system causing fever, cough, and shortness of breath; the fatality rate is more than 35% [9, 20]. The largest number of cases were in Saudi Arabia, South Korea, and the United Arab Emirates. The cases of Mers-CoV in Saudi Arabia and the United Arab Emirates were caused to direct or indirect infection of the human by camels. These two countries import camels from aboard, particularly from the Horn of Africa countries and Sudan, where the camels showed tolerance to the virus [12]. However, the South Korean cases were originally caused by a superspread case of a health care worker in Saudi Arabia [4], creating a large outbreak in South Korea. More recently, there have been indications of a possible super-spreading event in one of the hospitals in Riyad in Saudi Arabia from a female case of Mers-CoV [22].

The concept of the super-spreaders has been documented in several diseases such as Typhoid [11], Tuberculosis [13, 14], Ebola hemorrhagic fever [15] as well as in people with HIV/HCV co-infection [16]. The superspreader also has ties with other Corona-type virus such as SARS-CoV. In fact, it was reported in [17] that during the Beijing SARS outbreak, the majority of patients did not infect others and a few patients infected

a high number of people, making these patients superspreaders. A similar super-spreading event happened in Hong Kong [19].

The huge burden of a super-spreading event requires the understanding of its impact on the public health especially if this event happens in a large human gathering such as the Hajj, where more than 2.5 million pilgrims from more than 20 countries [21] gather and massively move to perform their religious rituals. Therefore, our goal is to investigate the dynamics of a possible spreading event in the hajj. The aim is to measure, depending on the value of the basic reproduction number, the level of the prevalence of the virus.

Therefore, we will investigate a mathematical model that considers two type pilgrims: outside pilgrims, the non-locals, and insider pilgrims, which represents the people performing Hajj and living in Saudi Arabia; we call them locals. We also assume that the superspreaders are local. We justify this assumption by the fact that recent findings suggest the possibility of having a super-spreader from the locals. Hence, we will consider two patches of populations: local pilgrims and non-local pilgrims. In the local category, there are six classes, S susceptible, E exposed, I infectious, P super-spreader, H hospitalized and R recovered. The only difference between local and non-local pilgrims is that the non-local pilgrims have no super-spreaders. We have assumed that E, I, P and H classes only can infect.

Our work is inspired by the model of South Korea Mers-CoV outbreak [4] and on the general data of

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Mers-CoV [2]. These models considered the asymptotic population but did not study the impact of the super-spreader. Other models [7] have used the super spreader class of population in the case of SARS, but have not investigated the impact of the other possible populations (such as exposed and hospitalized).

MATERIAL AND METHOD

The aim of this model is to introduce a possible super-spreading event in the Hajj season and assess the impact of this event on the total pilgrims in the Hajj season. The model is to have a simple assumption: the super-spreaders are from the local population in the KSA. Therefore, we will divide the populations into two groups: local pilgrims L and non-local pilgrims N.

We divide the population L as follows

$$L = S_L + E_L + I_L + P + H_L + R_L \tag{1}$$

with S_L the susceptible local pilgrims, E_L is the exposed local pilgrims, I_L infected local pilgrims, P represents super-spreaders in the local pilgrims, H_L the hospitalized local pilgrims and R_L the recovered local pilgrims.

The Non-local pilgrims N is divided in to

$$N = S_N + E_N + I_N + H_N + R_N (2)$$

We also assume that the exposed, infected and hospitalized populations are infected with MERS-CoV. and they are infectious MERS-CoV to susceptible individuals. Therefore, we assume the infection rate of the local is defined by:

$$\lambda_{L} = \frac{\beta_{L} \left(I_{L} + \in_{L} E_{L} + \theta_{L} H_{L} \right)}{S_{L} + E_{L} + I_{L} + P + H_{L} + R_{L}}$$
(3)

and for the non-local

$$\lambda_{N} = \frac{\beta_{N} \left(I_{N} + \epsilon_{N} E_{N} + \theta_{N} H_{N} \right)}{S_{N} + E_{N} + I_{N} + H_{N} + R_{N}} \tag{4}$$

with β_i , (i = L, N) is the human-to-human transmission rate, among the class of pilgrims i, per unit time (day), ∈, quantifies the relative transmissibility of the exposed pilgrims, and θ_i quantifies the relative transmissibility of the hospitalized patients pilgrims.

Hence, the system of equations that represents the locals pilgrims is

$$\dot{S}_{L} = -\lambda_{L}S_{L} - \lambda_{N}S_{L}$$

$$\dot{E}_{L} = \lambda_{L}S_{L} + \lambda_{N}S_{L} - \alpha_{L}E_{L}$$

$$\dot{I}_{L} = p\alpha_{L}E_{L} - (\gamma_{L}^{1} + \gamma_{L}^{2})I_{L}$$

$$\dot{P} = (1 - p)\alpha_{L}E_{L} - v_{L}P$$

$$\dot{H}_{L} = \gamma_{L}^{1}I_{L} + v_{L}P - \xi_{L}H_{L}$$

$$\dot{R}_{L} = \gamma_{L}^{2}I_{L} + \xi_{L}H_{L}$$
(5)

and the system of equations that represents the nonlocals pilgrims is

$$\dot{S}_{N} = -\lambda_{L}S_{N} - \lambda_{N}S_{N}$$

$$\dot{E}_{N} = \lambda_{L}S_{L} + \lambda_{N}S_{N} - \alpha_{N}E_{N}$$

$$\dot{I}_{N} = \alpha_{N}E_{N} - (\gamma_{N}^{1} + \gamma_{N}^{2})I_{N}$$

$$\dot{H}_{N} = \gamma_{N}^{1}I_{N} + \xi_{N}H_{N}$$

$$\dot{R}_{N} = \gamma_{N}^{2}I_{N} + \xi_{N}H_{N}$$
(6)

with α_i , (i = N, L) is the rate at which a pilgrim leaves the exposed class and becomes a regular infected (with probability p) or super-spreader (with probability 1 - p). This probability is assumed to be p = 1 for the nonlocal pilgrims since we have assumed the superspreading is restricted to the local pilgrims. γ^1 the rate at which a regularly infected pilgrim get hospitalized and γ^2 the rate at which a regularly infected pilgrim recovers without hospitalization. A super-spreader has a rate v_i of hospitalization. Finally, ξ_i stands for the rate of recovery of the pilgrim by hospitalization.

RESULTS

The basic reproduction number, denoted by R_0 , represents the expected number of secondary cases produced by a single infection in a completely susceptible population. This threshold quantifies the intensity of the spread of the disease in a population. If R_0 < 1 then the virus infection die out in the population and if $R_0 > 1$ then the virus infection persists in the population, which could lead to a pandemic.

To calculate the R₀ of our models of Mers-Corona or SARS, we use a technique similar to the one described by [3]. For this purpose, we write the following: We define the vector x as follows:

$$x = \left[E_L, E_N, I_L, I_N, P, H_L, H_N\right]^{\mathrm{T}}$$

We have

$$\dot{x} = F(x) - V(x) \tag{7}$$

$$F(x) = \begin{bmatrix} \lambda_{L}S_{L} + \lambda_{N}S_{L} \\ \lambda_{L}S_{N} + \lambda_{N}S_{N} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad V(x) = \begin{bmatrix} \alpha_{L}E_{L} \\ \alpha_{N}E_{N} \\ -p\alpha_{L}E_{L} + (\gamma_{L}^{1} + \gamma_{L}^{2})I_{L} \\ -\alpha_{N}E_{N} + (\gamma_{N}^{1} + \gamma_{N}^{2})I_{N} \\ -(1-p)\alpha_{L}E_{L} + v_{L}P \\ -\gamma_{L}^{1}I_{L} - v_{L}P + \xi_{L}H_{L} \\ -\gamma_{N}^{2}I_{N} + \xi_{N}H_{N} \end{bmatrix}$$

We take F and V as

$$F = \frac{\partial F}{\partial x_j} \quad and \quad V = \frac{\partial V}{\partial x_j}$$

where we get the linearization of the equation (7) at the disease free equilibrium given by

$$\dot{x} = (F - V)x$$

The matrices F, V are given by

and

$$V = \begin{bmatrix} \alpha_L & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha_N & 0 & 0 & 0 & 0 & 0 & 0 \\ -p\alpha_L & 0 & \gamma_L^1 + \gamma_L^2 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\alpha_N & 0 & \gamma_N^1 + \gamma_N^2 & 0 & 0 & 0 & 0 \\ -(1-p)\alpha_L & 0 & 0 & 0 & v_L & 0 & 0 & 0 \\ 0 & 0 & -\gamma_L^1 & 0 & -v_L & \xi_L & 0 & 0 \\ 0 & 0 & 0 & -\gamma_N^1 & 0 & 0 & \xi_N \end{bmatrix}$$

We need to find the ${\rm V\,}^{-1}$, which is given by

We have
$$\dot{x} = F(x) - V(x)$$
 (7)
$$\dot{x} = F(x) - V(x)$$
 (7) with
$$V(x) = \begin{bmatrix} \lambda_L S_L + \lambda_N S_L \\ \lambda_L S_N + \lambda_N S_N \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad V(x) = \begin{bmatrix} \alpha_L E_L \\ \alpha_N E_N \\ -p \alpha_L E_L + (\gamma_L^1 + \gamma_L^2) I_L \\ -\alpha_N E_N + (\gamma_N^1 + \gamma_N^2) I_N \\ -(1-p)\alpha_L E_L + v_L P \\ -\gamma_L^1 I_L - v_L P + \xi_L H_L \\ -\gamma_N^2 I_N + \xi_N H_N \end{bmatrix}$$

$$\beta b = \left[\beta_L \in_L \quad \beta_N \in_N \quad \beta_L \quad \beta_N \quad \beta_L \quad \beta_L \beta_L \quad \beta_N \theta_N \right]$$

$$\beta b = \begin{bmatrix} \beta_L \in_L & \beta_N \in_N & \beta_L & \beta_N & \beta_L & \beta_L \theta_L & \beta_N \theta_N \end{bmatrix}$$

$$Q = \begin{bmatrix} \frac{1}{L} & 0\\ 0 & \frac{1}{N}\\ 0 & 0\\ 0 & 0\\ 0 & 0\\ 0 & 0\\ 0 & 0 \end{bmatrix}$$

$$y = \begin{bmatrix} S_L \\ S_N \end{bmatrix}$$

from the technique in [1]

$$R_{0} = \frac{S_{L}^{0}\beta_{L}}{L} \left(\frac{p}{\gamma_{L}^{1} + \gamma_{L}^{2}} - \frac{p-1}{v_{L}} + \frac{\epsilon_{L}}{\alpha_{L}} + \frac{\theta_{L}\left(\gamma_{L}^{1} + \gamma_{L}^{2} - \gamma_{L}^{2}p\right)}{\xi_{L}\left(\gamma_{L}^{1} + \gamma_{L}^{2}\right)} \right) + \frac{S_{N}^{0}\beta_{N}}{N} \left(\frac{1}{\gamma_{N}^{1} + \gamma_{N}^{2}} + \frac{\epsilon_{N}}{\alpha_{N}} + \frac{\theta_{N}\gamma_{N}^{1}}{\xi_{N}\left(\gamma_{N}^{1} + \gamma_{N}^{2}\right)} \right)$$

The three plots in Figure 1 show the contour plot of the three main variables that impact superspreaders class: α , p and v. The first plot show that probability to become a regular infected p have a strong effect in R_0 when it's between (0 - 0.15) while the hospitalization rate of super-spreader ν is between (0 - 0.95) which imply that 85% of the people that leave exposed class E to be a super-spreader to have an epidemic. The second plot shows that the rate of leaving exposed class to become an infected α should be between (0 - 0.2) while the hospitalization rate of super-spreader v is between (0 - 0.2) which imply that the epidemic will happen if the length of virus in patients are long. The third plot shows that probability to become a regular infected p is not infected by the rate of leaving exposed class to become an infected α .



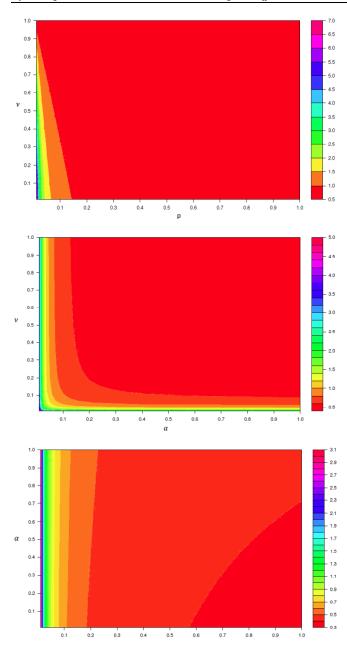


Figure 1: The contour plot of ${\rm R}_0$ with respect to the parameters of the super-spreading effects, which are α , p, and v.

THE FINAL SIZE

We will combine the two populations of non-local and local population to have one final size for all the population

$$S = \begin{bmatrix} S_L \\ S_N \end{bmatrix}, \quad E = \begin{bmatrix} E_L \\ E_N \end{bmatrix}, \quad I = \begin{bmatrix} I_L \\ I_N \end{bmatrix}$$

$$P = \begin{bmatrix} P \\ 0 \end{bmatrix}, \quad H = \begin{bmatrix} H_L \\ H_N \end{bmatrix}, \quad R = \begin{bmatrix} R_L \\ R_N \end{bmatrix}$$

and here we will combine the parameters

$$\Lambda = \begin{bmatrix} \lambda_L & \lambda_N \\ \lambda_L & \lambda_N \end{bmatrix}, \hat{\alpha} = \begin{bmatrix} \alpha_L & 0 \\ 0 & \alpha_N \end{bmatrix}, \hat{\gamma}^1 = \begin{bmatrix} \gamma_L^1 & 0 \\ 0 & \gamma_n^1 \end{bmatrix}$$

$$\hat{\gamma}^2 = \begin{bmatrix} \gamma_L^2 & 0 \\ 0 & \gamma_n^2 \end{bmatrix}, \hat{\xi} = \begin{bmatrix} \xi_L & 0 \\ 0 & \xi_n \end{bmatrix}, \hat{v} = \begin{bmatrix} v_L & 0 \\ 0 & 0 \end{bmatrix}$$

$$\hat{p} = \begin{bmatrix} p & 0 \\ 0 & 1 \end{bmatrix} \hat{\beta} = \begin{bmatrix} \beta_L & 0 \\ 0 & \beta_N \end{bmatrix} \hat{\epsilon} = \begin{bmatrix} \epsilon_L & 0 \\ 0 & \epsilon_N \end{bmatrix}$$

$$\hat{\theta} = \begin{bmatrix} \theta_L & 0 \\ 0 & \theta_N \end{bmatrix} \hat{\lambda} = \begin{bmatrix} \lambda_L \\ \lambda_N \end{bmatrix}$$

So those are the equations for the total population

$$\dot{S} = -\Lambda S$$

$$\dot{E} = \Lambda S - \hat{\alpha} E$$

$$\dot{I} = \hat{p} \hat{\alpha} E - (\hat{\gamma}^1 + \hat{\gamma}^2) I$$

$$\dot{P} = (1 - \hat{p}) \hat{\alpha} E - \hat{v} P$$

$$\dot{H}_L = \hat{\gamma}^1 I + \hat{v} P - \hat{\xi} H$$

$$\dot{R}_L = \hat{\gamma}^2 I + \hat{\xi} H$$

$$\hat{\beta} b = \begin{bmatrix} \hat{e} \hat{\beta} & \hat{\beta} & \hat{\beta} & \hat{\theta} \hat{\beta} \end{bmatrix}$$

$$V = \begin{bmatrix} \hat{\alpha} & 0 & 0 & 0 \\ -\hat{p} \hat{\alpha} & \hat{\gamma}^1 + \hat{\gamma}^2 & 0 & 0 \\ -(1 - \hat{p}) \hat{\alpha} & 0 & \hat{v} & 0 \\ 0 & -\hat{\gamma}^1 & -\hat{v} & \hat{\xi} \end{bmatrix}$$

$$\begin{bmatrix} \frac{1}{\hat{\alpha}} & 0 & 0 & 0 \\ \frac{\hat{p}}{I + \hat{v}^2} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{\hat{\alpha}} & 0 & 0 & 0 \\ \frac{\hat{p}}{\hat{\gamma}^1 + \hat{\gamma}^2} & \frac{1}{\hat{\gamma}^1 + \hat{\gamma}^2} & 0 & 0 \\ \frac{-(1-\hat{p})}{\hat{v}} & 0 & \frac{1}{\hat{v}} & 0 \\ \frac{(\hat{\gamma}^1 + \hat{\gamma}^2 - \hat{\gamma}^2 \hat{p})}{\hat{\xi}(\hat{\gamma}^1 + \hat{\gamma}^2)} & \frac{-\hat{\gamma}^1}{\hat{\xi}(\hat{\gamma}^1 + \hat{\gamma}^2)} & \frac{1}{\hat{\xi}} & \frac{1}{\hat{\xi}} \end{bmatrix}$$

Therefore, the final size will be

$$\ln\left(\frac{S^{0}}{S^{\infty}}\right) = \frac{R_{0}}{S^{0}} \left[S^{0} - S^{\infty}\right] + 1^{0} \hat{\beta} \left(\frac{1}{\hat{\gamma}^{1} + \hat{\gamma}^{2}} + \frac{\hat{\gamma}^{1} \hat{\theta}}{\hat{\xi} (\hat{\gamma}^{1} + \hat{\gamma}^{2})}\right) + P^{0} \hat{\beta} \left(\frac{1}{\hat{v}} + \frac{\hat{\theta}}{\hat{\xi}}\right)$$
(8)

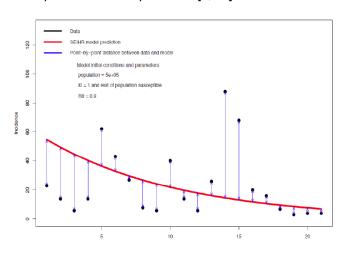
By comparing the final size of SARS calculated in [1], the equation (8) shows, clearly, the final size of the MERS-CoV is augmented by the effect superspreading event. This finding also shows the impact of the hospitalization capacity in reducing the final size.

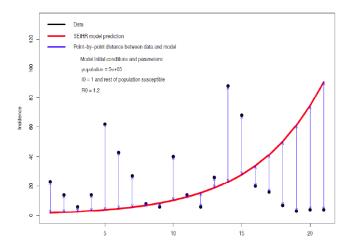
PARAMETERS ESTIMATION AND DATA FITTING

First, we estimate the parameters based on the existing models of Mers SARS Corona models [2, 4]. These are the only models that used data. Next, we will use the 2014-2016 MERS-Corona outbreak in the KSA data to estimate the reproduction number without the super-spreading effect. This estimation will help us to predict the effect of a possible super-spreading event during the Hajj season.

The Table **1** shows the parameters used later on in our data fitting.

Next, we fit our model the existing MERS-CoV in 2014-2016 season using Least Squares and the Monte Carlo parameter sweep method [5, 18]





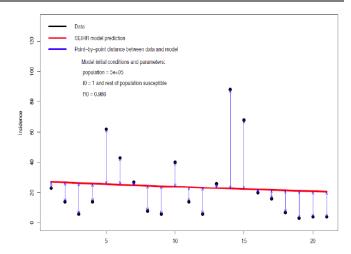


Figure 2: The data fitting of the confirmed Mers-Cov cases, KSA, 2014-2016 season using the least square method. The plots show three cases $R_0 = 0.9$, $R_0 = 1.2$ and the best fit to the data which $R_0 = 0.986$.

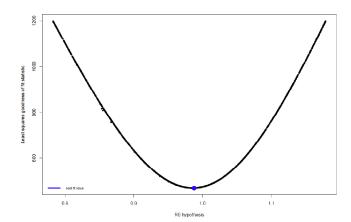


Figure 3: We have estimated the best R_0 with the lowest least square value.

CONCLUSION AND DISCUSSION

In this work, we aimed to study a possible superspreading event of MERS-CoV in the Hajj season. The scenario of having supers-spreaders in the Hajj season can not be omitted since there are previous indication of such an incident in Saudi Arabia. Moreover, spreading of MERS-CoV in south Korea, in the year 2015, is an indicator of emerging of disease. Hence, it is important to build an understanding of the dynamics of the disease a case of super-spreading in Hajj season. If this scenario even happens, it will lead to a world wide event. This is because the pilgrims come from 20 different countries. The graph of prevalence shows that effect will be more in the non-local pilgrims. By using differential equations, we considered two subpopulations of pilgrims: local and non-local. In each population, we have similar class S susceptible, E exposed, I infectious, H hospitalized, R recovered.

Table 1: Parameters Estimation Base on the Literature

Parameter	Value	Reference
$oldsymbol{eta}_{\!\scriptscriptstyle L}$	0.036-0.0835	[1]
\in_L	0.1-0.5	[1, 4]
$ heta_{\scriptscriptstyle L}$	1-22	[2, 4]
$\alpha_{\scriptscriptstyle L}$	0.15	[4]
p	1-1	Assumed
$\boldsymbol{\gamma}_L^1$	0.6403	[4]
γ_L^2	0.2	[4]
v_L	0-0.5	[2]
$\xi_{\scriptscriptstyle L}$	9 x 10 ⁻⁵	[2]
$oldsymbol{eta}_{\scriptscriptstyle N}$	0.036-0.0835	[4]
\in_{N}	8.8 x 10 ⁻⁶	[2]
$ heta_{\scriptscriptstyle N}$	1-22	[4]
$\alpha_{_{N}}$	0.15	[4]
γ_N^1	0.6403	[4]
γ_N^2	0.2	[4]
$\xi_{\scriptscriptstyle N}$	9 x 10⁻⁵	[2]

We assumed that super-spreaders P are only from the local. This assumption is justifiable because the data have shown that all the cases were mainly originated from Saudi Arabia. We calculated the basic reproduction num- ber R₀ which represented the number of cases one case generated on average over the course of its infectious period. We also found the final size of the possible pandemic. We used recent studies that estimated R₀ of MERS-CoV to get all of parameters of our model. Our numerical simulations showed a prevalence graph for the local that looked like a bell reflecting the peak seen in the current disease data. For non-local, we found the prevalence would keep on increasing until it goes to a steady state. This finding is alarming because it means that MERS-CoV could lead to the world spreading the disease, particularly that there are over 20 nationalities of pilgrims in the Hajj season.

As an extension of our work, we could investigate the efficacy of some control measures, such as procedure mask, to reduce the spread of the disease during the Hajj season.

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