Al-Mukhtar Journal of Educational Sciences
Vol: 6, P: 167–175 6/30/2023
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Effect of Being Vaccinated Against Covid-19 Without Any Other Therapeutic Interventions: A Compartmental Mathematical Model

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Abstract

DOI: https://doi.org/10.54172/aaqkpp38

A mathematical model for covid-19 is formulated, it is based on a compartmental system of nonlinear ordinary differential equations focusing on vaccination and excluding any other interventions, and hence the proposed mode is divided into eight compartmental classes, namely, susceptible (S), first dose (V_1), the second dose(V_2), booster dose vaccinated V_3, exposed (E), asymptomatic (A), symptomatic (I), and recovery(R). The basic reproduction number R_0 is calculated by the next-generation matrix (NGM) method. Comparison of the resulting value of R_0 with its corresponding for the general model which includes hospitalized (H) shows the importance of keeping a bit of healthcare beside vaccinations to get the best results to combat the epidemic.

Keywords: *COVID-19, Next Generation Matrix, Basic Reproduction Number, Double Dose Vaccination, Booster Vaccination Dose, Therapeutic Interventions.*

أثر الاكتفاء بالتطعيم ضد وباء كورونا دون أي تدخلات طبية أخرى: نموذج رياضي

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المستخلص

نموذج رياضي لوباء كورونا مؤسس على نظام من المعادلات التفاضلية غير الخطية تمت صياغته وتحليله. النموذج يركز على الاكتفاء بتلقي التطعيم دون أي تدخلات علاجية أخرى، وبالتالي فقد قسم الى ثمانية أقسام:

1. أصحاء قابلون للإصابة عند المخالطة $S(t)$
2. حاصلون على جرعة أولى من التطعيم $V_1(t)$
3. حاصلون على جرعة ثانية من التطعيم بشرط حصولهم على جرعة أولى $V_2(t)$
4. حاصلون على جرعة معززة من التطعيم بعد حصولهم على الجرعتين الأوليتين $V_3(t)$
5. مصابون في فترة حضانة المرض لا تظهر عليهم أعراض ولا ينقلون العدوى الى غيرهم $E(t)$
6. مصابون في فترة حضانة المرض لا تظهر عليهم أعراض ولكنهم ينقلون العدوى الى غيرهم $A(t)$
7. مصابون تظهر عليهم الأعراض وينقلون العدوى الى غيرهم $I(t)$
8. متعافون اكتسبوا مناعة ولكنها ليست دائمة فهم عرضة للانتقال الى القسم الأول $R(t)$

باستخدام طريقة مصفوفة الجيل القادم NGM تم حساب قيمة رقم التكاثر الأساسي R_0 ثم مقارنتها بنظيرتها في النموذج العام والذي يشمل قسم تاسع يمثل التدخلات العلاجية $H(t)$. وقد بينت الدراسة أهمية الأخذ بشيء من الرعاية الصحية بالإضافة الى التطعيم للحصول على أفضل النتائج في مكافحة الوباء والقضاء عليه.

الكلمات المفتاحية: *كوفيد 19، مصفوفة الجيل التالي، رقم التكاثر الأساسي، جرعة التطعيم المزدوجة، جرعة التطعيم الداعمة، التدخلات العلاجية.*

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Introduction

The World Health Organization (WHO) first declared COVID-19 as a threat to the international community on January 30, 2020, and then as a pandemic on March 11, 2020 [1]. On April 04, 2022, there have been 492,271,251 confirmed cases worldwide with 6,178,291 deaths and 427,442,919 recovered. These numbers are exponentially growing day by day [2]**.** On March 07, 2023, there have been 680,817,071 confirmed cases worldwide with 6,806,074 deaths and 653,716,966 recovered [3]. However, after strenuous efforts of precautionary and medical processes that culminated in the discovery of vaccinations, the intensity of the epidemic began to wane. Today (at the time of writing), May, 1st, 2023, there have been 687,121,872 confirmed cases worldwide with 6,863,851 deaths and 659,671,069 recovered. https://www.worldometers.info/coronavirus/.

During the first and second waves of the COVID-19 pandemic, non-pharmaceutical interventions (NPIs) were the only available measures to reduce the burden on healthcare systems and save lives. As of December 2020, multiple vaccines against COVID-19 were approved but travel restrictions and social distancing are still needed, especially because of the spreading of highly transmissible variants of concern [4]. Prior to December 2020, the implementation of non-pharmaceutical interventions (NPIs), including school/business closures, physical distancing, and mask-wearing, was the main tool to control the spread of SARS-CoV-2. However, with the development of effective vaccines against SARS-CoV-2, in December 2020 many countries were able to initiate vaccination campaigns [5–7]. The most recommended strategy was prioritizing the elderly and high-risk populations, followed by essential workers, and then the general public [8–10]. At the initial stage of vaccine distribution, strict NPIs were kept in place to avoid potential virus resurgence. After almost six months of immunization, the focus shifted to establishing an optimal vaccination strategy in order to safely lift NPIs while avoiding virus resurgence [11].

Researchers have contributed a lot in forecasting, and understanding the transmission dynamics, the fatality of SARS-CoV-2, and the evolution of the pandemic, to help in the fight against this new global problem. Among the researchers, statisticians, epidemiologists, and mathematicians contributed to formulating models to capture the transmission dynamics of COVID-19 and forecasting the evolution of the pandemic among different populations amidst government interventions. These mainly included statistical models [9-18], deep-learning models [19-24], and mathematical models [1,14,25,26]. Statistical models offer more precise models and deep-learning techniques are the key to high-quality predictive models [27]. However, both statistical and deep-learning models require real data to make predictions. But with mathematical models, a set of mathematical equations that mimic the current situation is written, and solving them for certain parameters provide information about the disease characteristics [28]. Some of their advantages include mathematical models representing the real situation of the problem being solved and they do not require all data to be available for

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it to be fitted as deductions from known information about the situation can be used. Also, they can handle sudden changes and complexity with ease. Since the start of the COVID-19 pandemic, mathematical models have been at the forefront of determining and forecasting the spread of COVID-19 and shaping government policies around the world [28]. A seminal paper in 1927 introduced the Susceptible, Infectious, and Recovered (SIR), a mathematical model for infectious diseases [29]. Since then, with advances in information technology and fast computing methods, many variations of the SIR model have been developed. Because mathematical models can easily be understood and definite conclusions about the COVID-19 outbreak can be made from them, Susceptible, Exposed, Infectious and Recovered (SEIR), a modification of SIR and a cascade of other modifications have been constructed and developed for predicting COVID-19 since its declaration as a global pandemic [30-42]. However, statistical and deep-learning models would require real data in substantial amounts to perform any forecasting or prediction. On the other hand, these new developments can easily be modeled with little or no data with mathematical models [43].

Main Text

To investigate the importance of keeping a bit of healthcare besides vaccinations to get the best results to combat the epidemic, the extended SEIR model [3] is modified by eliminating the compartment $H(t)$ which was represented medical treatments, Table 1. represents all the parameters used in COVID-19 transmission model, and hence the new proposed model is as shown in the Flow chart 1.

Table 1

A detailed description of state variables and relevant parameters of the model

Variable	Description
$S(t)$	Susceptible
$V_1(t)$	First dose vaccinated
$V_2(t)$	The second dose of vaccinated
$V_3(t)$	Booster dose
$E(t)$	Exposed
$A(t)$	Asymptomatic
$I(t)$	Symptomatic
$H(t)$	Hospitalized
$R(t)$	Recovered
Λ	Recruitment rate into a susceptible population
σ	Rate of loss of immunity
β_a	Rate of transmission from S to E due to contact with A
β_i	Rate of transmission from S to E due to contact with I

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β_s	$= \beta_a A + \beta_i I$
λ	Rate of vaccination with the first dose
μ	Natural human death rate
ε_1	Efficacy of the first dose
ε_2	Efficacy of the second dose
η	Rate of transmission from V_1 to V_2
ω	Rate of transmission from $V_2$to V_3
π	Rate of transmission from V_3 to S
α	Progression rate from E to either A or I
κ	The proportion of asymptomatic infectious people
φ	Rate of transmission from A to I
γ	Rate of recovery of the asymptomatic human population
ψ	Rate of recovery of the symptomatic population
h	Rate of transmission from I to treatment
δ	Rate of death due to the COVID-19 disease
ρ	Rate of recovery due to treatment

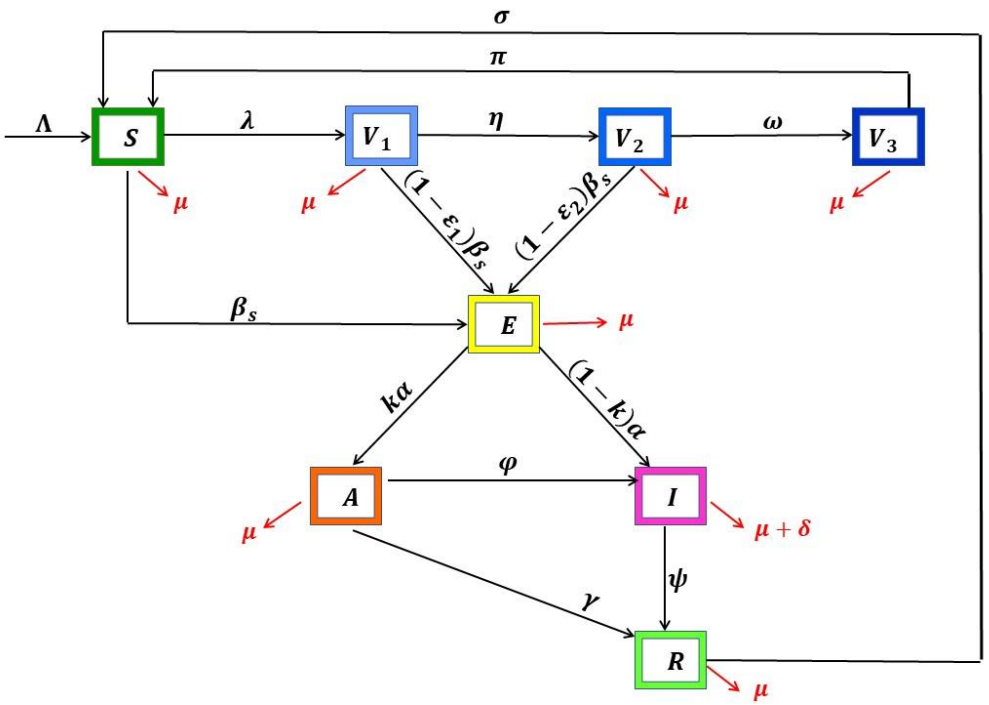

Figure 1. Flow chart of the proposed model

The constructed mathematical model is given by:

$$\dot{S} = \Lambda + \sigma R - [\beta_s + \lambda + \mu]S + \pi V_3$$
$$\dot{V}_1 = \lambda S - [(1-\varepsilon_1)\beta_S + \eta + \mu]V_1$$
$$\dot{V}_2 = \eta V_1 - [(1-\varepsilon_2)\beta_S + \omega + \mu]V_2$$
$$\dot{V}_3 = \omega V_2 - [\pi + \mu]V_3$$
$$\dot{E} = \beta_S S + (1-\varepsilon_1)\beta_S V_1 + (1-\varepsilon_2)\beta_S V_2 - (\alpha + \mu)E$$
$$\dot{A} = \kappa\alpha E - [\varphi + \gamma + \mu]A$$
$$\dot{I} = (1-\kappa)\alpha E + \varphi A - [\psi + \mu + \delta]I$$
$$\dot{R} = \gamma A + \psi I - (\sigma + \mu)R$$

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The infected subsystem:

$$\dot{E} = \beta_s S + (1-\varepsilon_1)\beta_s V_1 + (1-\varepsilon_2)\beta_s V_2 - (\alpha+\mu)E$$
$$\dot{A} = \kappa\alpha E - [\varphi+\gamma+\mu]A$$
$$\dot{I} = (1-k)\alpha E + \varphi A - [\psi+\mu+\delta]I$$

Decomposition of the infected subsystem:

$$\mathcal{F} = \begin{bmatrix} \beta_s S + (1-\varepsilon_1)\beta_s V_1 + (1-\varepsilon_2)\beta_s V_2 \\ 0 \\ 0 \end{bmatrix}$$

$$\mathcal{M} = \begin{bmatrix} -(\alpha+\mu)E \\ \kappa\alpha E - [\varphi+\gamma+\mu]A \\ (1-k)\alpha E + \varphi A - [\psi+\mu+\delta]I \end{bmatrix}$$

The decease-free equilibrium:

$$DFE(S_0 \quad V_{10} \quad V_{20} \quad V_{30} \quad 0 \quad 0 \quad 0 \quad 0\ );$$
$$S_0 = \frac{\Lambda + \pi V_{30}}{\mu+\lambda}$$

$$V_{10} = \frac{\lambda}{\mu+\eta} S_0 = \frac{\lambda(\Lambda+\pi V_{30})}{(\mu+\eta)(\mu+\lambda)}$$
$$V_{20} = \frac{\eta}{\mu+\omega} V_{10} = \frac{\eta}{\mu+\omega}.\frac{\lambda(\Lambda+\pi V_{30})}{(\mu+\eta)(\mu+\lambda)}$$
$$V_{30} = \frac{\omega}{\mu+\pi} V_{20} = \frac{\omega}{\mu+\pi}.\frac{\eta\lambda(\Lambda+\pi V_{30})}{(\mu+\omega)(\mu+\eta)(\mu+\lambda)}$$

then

$$(\mu+\pi)(\mu+\omega)(\mu+\eta)(\mu+\lambda)V_{30} = \omega\eta\lambda(\Lambda+\pi V_{30})$$
$$[(\mu+\pi)(\mu+\omega)(\mu+\eta)(\mu+\lambda) - \omega\eta\lambda\pi]V_{30} = \omega\eta\lambda\Lambda$$

and hence,

$$V_{30} = \frac{\omega\eta\lambda\Lambda}{(\mu+\pi)(\mu+\omega)(\mu+\eta)(\mu+\lambda) - \omega\eta\lambda\pi}$$

The Jacobian of this decease-free equilibrium for $\mathcal{F}$ and $\mathcal{M}$ are (respectively)

$$F = \begin{bmatrix} 0 & \beta_A S_0 + (1-\varepsilon_1)\beta_A V_{10} + (1-\varepsilon_2)\beta_A V_{20} & \beta_I S_0 + (1-\varepsilon_1)\beta_I V_{10} + (1-\varepsilon_2)\beta_I V_{20} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$M = \begin{bmatrix} -(\alpha+\mu) & 0 & 0 \\ \kappa\alpha & -[\varphi+\gamma+\mu] & 0 \\ (1-k)\alpha & \varphi & -[\psi+h+\mu+\delta] \end{bmatrix}$$

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Since the matrix has two zero rows, the next generation matrix of the system is taken by the spectral radius of $NGM = -E^T F M^{-1} E$ where $E^T = (1 \quad 0 \quad 0)$ and

$$M^{-1} = \begin{bmatrix} \frac{-1}{\alpha+\mu} & 0 & 0 \\ \frac{-k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)} & \frac{-1}{\varphi+\gamma+\mu} & 0 \\ \frac{-1}{\psi+\mu+\delta}\left[\frac{(1-k)\alpha}{\alpha+\mu}+\frac{k\alpha\varphi}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right] & \frac{-\varphi}{(\varphi+\gamma+\mu)(\psi+\mu+\delta)} & \frac{-1}{(\psi+\mu+\delta)} \end{bmatrix}$$

and hence,

$(-E^T F)(M^{-1}E) =$

$-(0 \quad \beta_A S_0 + (1-\varepsilon_1)\beta_A V_{10} + (1-\varepsilon_2)\beta_A V_{20} \quad \beta_I S_0 + (1-\varepsilon_1)\beta_I V_{10} + (1-\varepsilon_2)\beta_I V_{20})$

$$\begin{pmatrix} \frac{-1}{\alpha+\mu} \\ \frac{-k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)} \\ \frac{-1}{\psi+\mu+\delta}\left[\frac{(1-k)\alpha}{\alpha+\mu}+\frac{k\alpha\varphi}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right] \end{pmatrix}$$

which reduces to a single element. Therefore, the basic reproduction number of the system is

$$R_0 = -[\beta_A S_0 + (1-\varepsilon_1)\beta_A V_{10} + (1-\varepsilon_2)\beta_A V_{20}]\left[\frac{-k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right] - [\beta_I S_0 + (1-\varepsilon_1)\beta_I V_{10} + (1-\varepsilon_2)\beta_I V_{20}]\{\frac{-1}{\psi+\mu+\delta}\left[\frac{(1-k)\alpha}{\alpha+\mu}+\frac{k\alpha\varphi}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right]\}$$

$$= \beta_A[S_0 + (1-\varepsilon_1)V_{10} + (1-\varepsilon_2)V_{20}]\left[\frac{k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right] + \beta_I[S_0 + (1-\varepsilon_1)V_{10} + (1-\varepsilon_2)V_{20}]\left[\frac{(1-k)\alpha}{(\psi+\mu+\delta)(\alpha+\mu)}+\frac{k\alpha\varphi}{(\psi+\mu+\delta)(\alpha+\mu)(\varphi+\gamma+\mu)}\right]$$

$$= [S_0 + (1-\varepsilon_1)V_{10} + (1-\varepsilon_2)V_{20}]\left\{\beta_A\left(\frac{k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right) + \beta_I\left(\frac{(1-k)\alpha}{(\psi+\mu+\delta)(\alpha+\mu)} + \frac{k\alpha\varphi}{(\psi+\mu+\delta)(\alpha+\mu)(\varphi+\gamma+\mu)}\right)\right\}$$

$$R_0 = [S_0 + (1-\varepsilon_1)V_{10} + (1-\varepsilon_2)V_{20}]\left\{\beta_A\left(\frac{k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right) + \beta_I\left(\frac{\alpha[\varphi+(1-k)(\gamma+\mu)}{(\psi+\mu+\delta)(\alpha+\mu)(\varphi+\gamma+\mu)}\right)\right\}$$

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This result consists of its analogy when health care provides, except for the absence of h, which expresses the rate of transmission from I to treatment H. [3]

$$R_{03} = [S_0 + (1-\varepsilon_1)V_{10} + (1-\varepsilon_2)V_{20}]\left\{\beta_A\left(\frac{k\alpha}{(\alpha+\mu)(\varphi+\gamma+\mu)}\right) + \beta_I\left(\frac{\alpha[\varphi+(1-k)(\gamma+\mu)]}{(\psi+h+\mu+\delta)(\alpha+\mu)(\varphi+\gamma+\mu)}\right)\right\}$$

Conclusion

- Although F and M are 4×4 matrices when medical care was available and 3×3 if not; However, the statements of R_{03} and R_0 were compatible, this confirms the validity and stability of the next generation matrix (NGM) method in calculating the basic reproduction number.
- The appearance of h in the statements of R_{03} without R_0 specifically in the denominator indicates its contribution to make $R_{03} < R_{0,}$ which means that the addition of extra care to vaccinations contributes to the reduction of the basic reproduction number, and hence to combat the epidemic.

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