Qualitative analysis of a mathematical model with presymptomatic individuals and two SARS-CoV-2 variants

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Abstract

The SARS-CoV-2 continues to spread across the world. During this COVID-19 pandemic, several variants of the SARS-CoV-2 have been found. Some of these new variants like the VOC-202012/01 of lineage B.1.1.7 or the most recently B.1.617 emerging in India have a higher infectiousness than those previously prevalent. We propose a mathematical model based on ordinary differential equations to investigate potential consequences of the appearance of a new more transmissible SARS-CoV-2 strain in a given region. The proposed mathematical model incorporates the presymptomatic and asymptomatic subpopulations in addition to the more usual susceptible, exposed, infected, and recovered subpopulations. This is important from a realistic point of view since it has been found recently that presymptomatic and asymptomatic individuals are relevant spreaders of the SARS-CoV-2. Using the next-generation matrix method, we find the basic reproduction number, $\mathcal{R}_0$, an important threshold parameter that provides insight regarding the evolution and outcome of a certain instance of the COVID-19 pandemic. The local and global stability of system equilibria are also presented. In particular, for the global stability we construct a Lyapunov functional and use the LaSalle invariant principle to prove that if the basic reproduction ratio is less than unity, the infection-free equilibrium is globally asymptotically stable. On the other hand, if $\mathcal{R}_0 > 1$ the endemic equilibrium is globally asymptotically stable. Finally, we present numerical simulations to numerically support the analytic results and to show the impact of the introduction of a new more contagious SARS-CoV-2 variant in a population.

Keywords SARS-CoV-2 variant · Global stability analysis · Mathematical modeling · Basic reproduction number

Mathematics Subject Classification 34D20 · 34D23 · 34D45 · 37N25

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1 Introduction

The current COVID-19 pandemic has caused more than 150 million confirmed cases and more than 3 million deaths (end of April 2021) (Johns Hopkins University and Medicine 2020). These numbers are undoubtedly an underestimate due to asymptomatic carriers, as well as delayed reporting and underreporting (Alves et al. 2020; Arvisais-Anhalt et al. 2020; Azmon et al. 2014; Burki 2020; Do Prado et al. 2020; Lau et al. 2020; Ivorra et al. 2020; Rasjid et al. 2021; Reis et al. 2020; Saberi et al. 2020). For instance, delayed reporting can be due to factors such as limited infrastructure, confirmation of reports by laboratory, as well as logistical problems (Sarnaglia et al. 2021). Reporting delay as a crucial issue because it distorts the relationship between the reported disease incidence and the true value. Some of these inaccuracies are related to the surveillance of an epidemic, which is a fundamental aspect of public health policies. The issue of underreporting cases is relevant in most surveillance systems, and has been documented and studied in several scientific articles (Bernard et al. 2014). For instance, for the COVID-19 pandemic in Brazil, it has been estimated an average underreporting of 40.68% (range 25.9–62.7%) for COVID-19-related deaths (Veiga e Silva et al. 2020). A good epidemic surveillance program requires resources and commitment from the health authorities. During the last semester of 2020 and beginning of 2021, several variants of the SARS-CoV-2 virus have been detected and some of them are considered more contagious and deadly (Faria et al. 2021; Lemieux and Li 2021; Plante et al. 2020; Davies et al. 2021; Leung et al. 2021; Wang et al. 2021). These new more contagious SARS-CoV-2 variants can have a great impact on the number of infected cases, prevalence, hospitalizations and deaths. People, researchers, and media are concerned about the consequences of having a more transmissible SARS-CoV-2 variant (Kupferschmidt 2021; Le Page 2021; van Oosterhout et al. 2021; Galloway et al. 2021). At the end of 2020, a few countries started with the inoculation of vaccines against the SARS-CoV-2 virus, but for several countries the vaccines are not yet available or the amount of vaccines is small for the population (Benest et al. 2021; Dinleyici et al. 2020; Haque and Pant 2020; Koirala et al. 2020; Lurie et al. 2020; Yamey et al. 2020). In countries where a vaccination program is advancing quickly, it is necessary to construct an alternative model with more classes and parameters, among which is the vaccinated class. For example, in previous works, both discrete and continuous mathematical models have included several subclasses of the vaccinated class where the individuals have less probability to get infected, transmit the virus, or die (Paltiel et al. 2020; Martinez-Rodriguez et al. 2021).

The spread of the SARS-CoV-2 virus is influenced by many factors that are not yet fully well understood (Mandal et al. 2020; Reis et al. 2020; Wang et al. 2020; Pinky and Dobrovolny 2020; Dobrovolny 2020a,b). Among these, it is known that social behavior, mobility, age, weather variables, and virus mutation can affect the dynamics of the death rate and transmission of the SARS-CoV-2 virus in the human population (Zhang et al. 2020; Ran et al. 2020; Yang and Duan 2020; Zebrowski et al. 2021). The main aim of this article is on the impact of the introduction of a new SARS-CoV-2 variant. This allows insight into the consequences of the appearance of new SARS-CoV-2 variants in some countries. The viruses mutate all the time and, therefore, the SARS-CoV-2 can acquire mutations that provide advantages to be able to spread easily (Altmann et al. 2021; Grubaugh et al. 2020; Li et al. 2020; Korber et al. 2020; Lemieux and Li 2021; Plante et al. 2020; van Dorp et al. 2020). A new variant of the SARS-CoV-2 virus was detected in England in the last quarter of 2020, and it is recognized as the VOC-202012/01 of lineage B.1.1.7. (Rahimi and Abadi 2021; Leung et al. 2021; Fiorentini et al. 2021; Galloway et al. 2021). Since October 2020, England has faced an increase in the number of infected cases and deaths. In addition, testing results

showed that the new SARS-CoV-2 variant VOC-202012/01 was prevalent and its proportion increased at the end of 2020 in England (Public Health England 2021). Several researchers and institutions have mentioned that some new SARS-CoV-2 variants are more contagious than previous variants (Leung et al. 2021; Walensky et al. 2021; Wang et al. 2021; Galloway et al. 2021). For instance, in Leung et al. (2021), the authors found that variant VOC-202012/01 is estimated to present a value of R_0 1.75 times higher than the 501N variant, meaning it is 75% more transmissible compared with the 501N strain. Furthermore, this variant VOC-202012/01 became the dominant strain in England in November/December 2020. Additional variants are appearing in different countries (Walensky et al. 2021; Rahimi and Abadi 2021). In addition to variant VOC-202012/01, a new SARS-CoV-2 variant (B.1.617) emerging in India (Gupta 2021; Thiagarajan 2021) has been found recently. India has the the highest daily tally of new SARS-CoV-2 infections ever recorded in the world, 360,960 (Thiagarajan 2021). Some researchers have considered the possibility that this new wave in India might be due to the circulation of new SARS-CoV-2 variants and suggest they may have an advantage over pre-existing strains (Gupta 2021; Thiagarajan 2021). Thus, based on the appearance of these new variants, it is important to develop mathematical models to study the potential consequences of new strains of the SARS-CoV-2.

Mathematical models are useful and have been used extensively to study and understand the dynamics of many epidemics in different places around the world (Murray 2002; Brauer et al. 2001; Rios-Doria and Chowell 2009; González-Parra et al. 2011; Andreasen et al. 2008; Roberts and Tobias 2000; Legrand et al. 2007; Thompson et al. 2006; Kim et al. 2020, 2017). Furthermore, the models can be used investigate the effect of different health policies on these epidemics. Mathematical models can generate outcomes that are generally difficult to predict and sometimes counterintuitive since the epidemic phenomena are nonlinear and complex. It is important to mention that these models help to provide knowledge and scientific support to design public health policies. Several studies have developed models to study the COVID-19 pandemic (Kucharski et al. 2020; Stutt et al. 2020; Ferguson et al. 2020; Dobrovolny 2020a; Doménech-Carbó and Doménech-Casasús 2021; Kong et al. 2021; Mumbu and Hugo 2020; IHME COVID-19 Forecasting Team 2020; Ivorra et al. 2020; Mbogo and Orwa 2021; Kuniya 2020; Zhong et al. 2020). The mathematical models have parameters and these are subject to some amount of uncertainty. Thus, performing mathematical analysis allows the understanding of different potential outcomes of an epidemic or pandemic. Therefore, we are able to predict that under certain conditions the epidemic would decrease or increase. The mathematical analysis allows the determination of necessary and sufficient conditions for an epidemic disappearance.

It has been found that the SARS-CoV-2 is mutating and its transmission has become more efficient (Zhang et al. 2020; Pachetti et al. 2020; van Dorp et al. 2020; Li et al. 2020; Walensky et al. 2021). There is an extensive new literature regarding new variants of the SARS-CoV-2 and their main characteristics (Zhang et al. 2020; Grubaugh et al. 2020; Plante et al. 2020; Zhu et al. 2020; Korber et al. 2020; Walensky et al. 2021). In this research work, we construct a compartmental mathematical model based on differential equations to study the effect of introducing a new more contagious SARS-CoV-2 variant in a population. The mathematical model takes into account the higher transmission rate of a new SARS-CoV-2 variant. The subpopulations of presymptomatic and asymptomatic for each SARS-CoV-2 variant are included in the mathematical model. This is an important feature of the constructed mathematical model. It has been argued that presymptomatic and asymptomatic individuals are major contributors in the spread of the SARS-CoV-2 (Al-Qahtani et al. 2020; Bai et al. 2020; Buitrago-Garcia et al. 2020; Byambasuren et al. 2020; Clarke et al. 2020; Gandhi et al. 2020; Johansson et al. 2021; Slifka and Gao 2020; Teixeira 2020; Zhao et al. 2020). In

addition, the mathematical model includes individuals that go to the hospital, even though it is assumed that they are not able to transmit the virus due to careful prophylaxis actions. Besides the construction of the mathematical model, we find the basic reproduction number $\mathcal{R}_0$ using the method of the next generation matrix. The local stabilities of the infection-free and endemic equilibrium states are studied by means of the linearization method (Brauer et al. 2001; Hethcote 2005). It is important to mention that the basic reproduction number $\mathcal{R}_0$ is of interest since it is related to the effective reproduction number $\mathcal{R}_t$ which is a key indicator of the evolution, or dynamics, of the COVID-19 pandemic. We constructed a Lyapunov functional and then used the LaSalle invariant principle to prove that if the basic reproduction ratio is less than unity, the infection-free equilibrium is globally asymptotically stable. To the best of our knowledge these results have not been presented before.

This paper is organized as follows. In Sect. 2, we present the mathematical model of SARS-CoV-2 transmission and disease progression. Section 3, is devoted to the stability mathematical analysis. In Sect. 4, the numerical simulation results using the constructed mathematical model of SARS-CoV-2 transmission are shown, and the last section is devoted to discussion and conclusions.

2 Mathematical model with presymptomatic and two SARS-CoV-2 variants

We develop a mathematical model based on a deterministic system of nonlinear differential equations that considers two variants of SARS-CoV-2. This mathematical model includes two SARS-CoV-2 variants with different contagiousness. It also takes into account the subpopulations of presymptomatic and asymptomatic individuals for each SARS-CoV-2 variant. This is an important feature that has not been included in many COVID-19 models. The model considers a scenario where the preexistent SARS-CoV-2 variant has a lower contagiousness than a new SARS-CoV-2 variant that is introduced in some region or country. Specifically, we can consider a situation in which the second variant is the VOC-202012/01 of lineage B.1.1.7. It also can be applied for other SARS-CoV-2 variants, such as the SARS-CoV-2 variant B.1.617 emerging in India (Gupta 2021; Thiagarajan 2021).

The model includes individuals in the susceptible ($S(t)$), latent ($E(t)$), presymptomatic ($P(t)$), infected ($I(t)$), asymptomatic ($A(t)$), and hospitalized ($H(t)$) classes, as shown in Fig. 1. The transition of individuals from one class to another depends on the stage of the disease. An individual would belong to just one of these classes at any one time, depending on the COVID status. The model also assumes that individuals infected with one SARS-CoV-2 variant have full immunity against the other variant due to the adaptive immune response (Amador Pacheco et al. 2019; Brauer 2017; Meskaf et al. 2020; Shayak et al. 2021). The classes latent, presymptomatic, infected and asymptomatic have two disjoint groups related to variants one and two. Initially, a susceptible individual can get the SARS-CoV-2 and right away transits to the latent class (with either variant one or two). In this latent stage the individual cannot spread the virus. The individuals remain in this phase for a time $1/\alpha$ (average). The individuals in the latent classes $E_1(t)$ and $E_2(t)$ then transit into the presymptomatic classes ($P_1(t)$ or $P_2(t)$, respectively), where the individuals do not have symptoms but they are able to spread the virus (Buitrago-Garcia et al. 2020; Slifka and Gao 2020; Teixeira 2020). After this stage, the individuals in classes $E_1(t)$ and $E_2(t)$ can transit into the infective symptomatic ($I_1(t)$ or $I_2(t)$, respectively) or asymptomatic classes ($A_1(t)$ or $A_2(t)$), respectively), where they are able to transmit the SARS-CoV-2 to other

individuals. The symptomatic and asymptomatic people stay in the infectious phase for a certain time with mean $1/\gamma$. The asymptomatic individuals transit to the recovered class at a rate γ . Finally, infected individuals with symptoms might transit to the recovered ($R(t)$) or hospitalized classes ($H(t)$), as can be seen in Fig. 1. As expected, the critical cases go to the hospital and then the person can recover or might die due to COVID. It is important to remark that, as in many other proposed models in the literature, we consider that once the person is in the recovered class it stays there. i.e., it has full-immunity against the SARS-CoV-2. Future studies would determine how long this immunity lasts.

Mathematical modeling using differential equations has become a very useful tool for the understanding of the dynamics of virus transmission (Murray 2002; Brauer et al. 2001; Hethcote 2005; Rios-Doria and Chowell 2009; Andreasen et al. 2008; González-Parra et al. 2011; Roberts and Tobias 2000; Legrand et al. 2007). Thus, here we follow a classical methodology for modeling epidemics and in particular the current COVID-19 pandemic. This approach allows us to study the local and global behavior of the dynamics of SARS-CoV-2 virus transmission with two variants. In particular, the population is divided into susceptible individuals ($S(t)$), two classes of latent individuals ($E_{1,2}(t)$), two classes of presymptomatic individuals ($P_{1,2}(t)$), two classes of infectious individuals ($I_{1,2}(t)$), two classes of asymptomatic individuals ($A_{1,2}(t)$), hospitalized $H(t)$ and recovered $R(t)$. The model takes into account that individuals infected with one SARS-CoV-2 variant have full cross-immunity against the other variant due to the adaptive immune response (Amador Pacheco et al. 2019; Brauer 2017; Meskaf et al. 2020; Shayak et al. 2021). The total population size is given by

$$N(t) = S(t) + E_1(t) + P_1(t) + I_1(t) + A_1(t) + H(t) + R(t) \\ + E_2(t) + P_2(t) + I_2(t) + A_2(t). \quad (1)$$

Notice that the total population $N(t)$ does not include the death class $D(t)$. The diagram of the mathematical model is illustrated in Fig. 1, and it is represented by the following system of nonlinear differential equations

$$\begin{aligned} \dot{S}(t) &= \Lambda - dS(t) - \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) + \beta_{P_2} P_2(t) \right. \\ &\quad \left. + \beta_{I_2} I_2(t) + \beta_{A_2} A_2(t) \right) S(t), \\ \dot{E}_1(t) &= \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) \right) S(t) - (d + \alpha) E_1(t), \\ \dot{P}_1(t) &= \alpha E_1(t) - (d + p) P_1(t), \\ \dot{I}_1(t) &= (1 - a) p P_1(t) - (d + h + \gamma) I_1(t), \\ \dot{A}_1(t) &= a p P_1(t) - (d + \gamma) A_1(t), \\ \dot{E}_2(t) &= \left(\beta_{P_2} P_2(t) + \beta_{I_2} I_2(t) + \beta_{A_2} A_2(t) \right) S(t) - (d + \alpha) E_2(t), \\ \dot{P}_2(t) &= \alpha E_2(t) - (d + p) P_2(t), \\ \dot{I}_2(t) &= (1 - a) p P_2(t) - (d + h + \gamma) I_2(t), \\ \dot{A}_2(t) &= a p P_2(t) - (d + \gamma) A_2(t), \\ \dot{H}(t) &= h I_1(t) + h I_2(t) - (d + \delta + \rho) H(t), \\ \dot{R}(t) &= \gamma \left(I_1(t) + I_2(t) + A_1(t) + A_2(t) \right) + \rho H(t) - d R(t), \end{aligned} \quad (2)$$

Fig. 1 Graphical representation of the COVID-19 mathematical model (2), with state variables and parameters

The model has eleven state variables, denoting the susceptible individuals ($S(t)$), two subpopulations of exposed individuals ($E_{1,2}(t)$), two subpopulations of presymptomatic individuals ($E_{1,2}(t)$), two subpopulations of infectious individuals ($I_{1,2}(t)$), two subpopulations of asymptomatic individuals ($A_{1,2}(t)$), hospitalized $H(t)$ and recovered $R(t)$. The meaning of the parameters are shown in Table 1. Thus,

H₁. The initial conditions of the model satisfy

$$\begin{aligned} S(0) > 0, E_1(0) \geq 0, P_1(0) \geq 0, I_1(0) \geq 0, A_1(0) \geq 0, H(0) \geq 0, R(0) \geq 0, \\ E_2(0) \geq 0, P_2(0) \geq 0, I_2(0) \geq 0, A_2(0) \geq 0. \end{aligned} \quad (3)$$

H₂. The parameters holds that

$$\beta_{P_2} > \beta_{P_1} > 0, \beta_{I_2} > \beta_{I_1} > 0, \beta_{A_2} > \beta_{A_1} > 0, \text{ and } \alpha, a, h, \gamma, p, \rho, \delta \in (0, 1). \quad (4)$$

2.1 Positivity on the solutions

Using the classical theory of ordinary differential equations (Lambert 1973; Fred Brauer 1989), it follows that the Cauchy system proposed in (2) is well posed. Furthermore, since system (2) represents interaction between subpopulations, from a biological point of view it must be shown that if (3) is satisfied, the solutions of model (2) will remain positive for all time $t > 0$. The following theorem states:

Theorem 1 Suppose that (3) and (4) are satisfied. Then the solution

$$Z(t) := (S(t), E_1(t), P_1(t), I_1(t), A_1(t), H(t), R(t), E_2(t), P_2(t), I_2(t), A_2(t))$$

of (2) remains positive and uniformly bounded for all $t > 0$.

Proof We consider the following

$$\begin{aligned} \mathcal{C} = \sup \{ \theta > 0 / \forall t \in [0, \theta], S(t) \geq 0, E_i(t) \geq 0, I_i(t) \geq 0, \\ A_i(t) \geq 0, H(t) \geq 0, R(t) \geq 0, P_i(t) \geq 0 \} \end{aligned}$$

for $i = 1, 2$. If $\mathcal{C} < \infty$, then since the solutions are continuous, one gets that

$$\begin{aligned} S(\mathcal{C}) = 0, \text{ or } E_1(\mathcal{C}) = 0, \text{ or } I_1(\mathcal{C}) = 0, \text{ or } A_1(\mathcal{C}) = 0, \text{ or } P_1(\mathcal{C}) = 0, \text{ or } H(\mathcal{C}) = 0, \text{ or } \\ R(\mathcal{C}) = 0, \text{ or } E_2(\mathcal{C}) = 0, \text{ or } I_2(\mathcal{C}) = 0, \text{ or } A_2(\mathcal{C}) = 0, \text{ or } P_2(\mathcal{C}) = 0. \end{aligned}$$

Suppose that $S(C) = 0$ occurs first before the other variables, then

$$\frac{dS(C)}{dt} = \lim_{t \rightarrow C^-} \frac{S(C) - S(t)}{C - t} \leq 0,$$

and using this result in the first equation of system (4), we get the following contradiction

$$\begin{aligned} \dot{S}(C) &= \Lambda - dS(C) - \left(\beta_{P_1} P_1(C) + \beta_{I_1} I_1(C) + \beta_{A_1} A_1(C) \right. \\ &\quad \left. + \beta_{P_2} P_2(C) + \beta_{I_2} I_2(C) + \beta_{A_2} A_2(C) \right) S(C) \\ &= \Lambda > 0. \end{aligned}$$

Next, if we have the case where $E_1(C) = 0$, occurs previously than the other variables, it follows that

$$\frac{dE_1(C)}{dt} = \lim_{t \rightarrow C^-} \frac{E_1(C) - E_1(t)}{C - t} \leq 0,$$

and from the second equation of system (2), we obtain another contradiction

$$\begin{aligned} \dot{E}_1(C) &= \left(\beta_{P_1} P_1(C) + \beta_{I_1} I_1(C) + \beta_{A_1} A_1(C) \right) S(C) - (d + \alpha) E_1(C) \\ &= \left(\beta_{I_1} I_1(C) + \beta_{A_1} A_1(C) \right) S(C) > 0. \end{aligned}$$

Using the same procedure for the rest of the other variables, we arrive to contradictions. Therefore, $C = +\infty$, and thus

$$\begin{aligned} S(t) &\geq 0, E_1(t) \geq 0, I_1(t) \geq 0, A_1(t) \geq 0, P_1(t) \geq 0, H(t) \geq 0, \\ R(t) &\geq 0, E_2(t) \geq 0, I_2(t) \geq 0, A_2(t) \geq 0, P_2(t) \geq 0, \end{aligned}$$

for $t > 0$. Now, from (4) we can obtain

$$\dot{N}(t) = \Lambda - dN(t) - \delta H(t) \leq \Lambda - dN(t), \quad (5)$$

and applying Gronwall inequalities one gets that

$$N(t) \leq \frac{\Lambda}{d} + \left(N(0) - \frac{\Lambda}{d} \right) e^{-dt}, \quad (6)$$

for $t \geq 0$. Then, the right-hand side of inequality (6) is the maximum solution of (5). For the case $t = 0$, $N(0) \leq \frac{\Lambda}{d}$. Thus, $N(t) \leq \frac{\Lambda}{d}$ for $t > 0$. Then, the region

$$\mathcal{O} = \left\{ (S, E_1, I_1, A_1, P_1, H, R, E_2, I_2, A_2, P_2) \in \mathbf{R}_+^{11} / N(t) \leq \frac{\Lambda}{d}, t \geq 0 \right\}, \quad (7)$$

is positively invariant. The solutions of (2) remain bounded. Including, if $N(0) > \frac{\Lambda}{d}$, then either the solution enters $\mathcal{O}$ for infinite time or $N(t)$ approaches to $\frac{\Lambda}{d}$ asymptotically. $\square$

3 Stability analysis

The stability analysis of an epidemiology model, represented by a system of differential equations, is based on finding the steady state solutions, which determine the equilibrium points of interest. For model (2) there is a so-called disease-free equilibrium point (F^*), which is generated assuming that $I_1 = I_2 = 0$ and means that the SARS-CoV-2 virus disappears. It should be noted that since we have births, the system introduces new susceptible individuals and this allows us to obtain endemic equilibrium points. Epidemiological models have different biological parameters and one of particular interest is the one related to the disease-free state called the basic reproduction number $\mathcal{R}_0$. This threshold parameter measures the effect that an infected individual produces when interacting in a population formed only by susceptible individuals (Hethcote 2005; den Driessche and Watmough 2002).

3.1 Disease-free equilibrium point and $\mathcal{R}_0$

Since the first ten equations are independent of the last equation of the system (2), we can omit it since the total population verifies Eq. (1). The disease-free equilibrium (F^*) point of the model (2) is obtained by setting the right-hand side of the model equations (2) to zero, and then using $I_1 = I_2 = 0$, the algebraic system is solved for the state variables. Thus, one obtains that

$$\mathcal{F}^* = (S^0, E_1^0, I_1^0, A_1^0, P_1^0, H^0, E_2^0, I_2^0, A_2^0, P_2^0) = \left(\frac{\Lambda}{d}, 0, 0, 0, 0, 0, 0, 0, 0, 0 \right). \quad (8)$$

The algebraic expression of $\mathcal{R}_0$ for model (2), is described by applying the next generation matrix methodology (den Driessche and Watmough 2002; Van den Driessche and Watmough 2008), which is obtained by calculating the spectral radius of the $\mathcal{F}\mathcal{V}^{-1}$, where the matrix $\mathcal{F}$ represents the new infection cases and the matrix $\mathcal{V}$ symbolizing the transition terms associated with the model (2). For more details about this methodology, the readers are referred to den Driessche and Watmough (2002), Van den Driessche and Watmough (2008). Therefore,

$$\mathcal{F} = \begin{bmatrix} 0 & 0 & \frac{\beta_{P_1}\Lambda}{d} & 0 & \frac{\beta_{I_1}\Lambda}{d} & 0 & \frac{\beta_{A_1}\Lambda}{d} & 0 & 0 \\ 0 & 0 & 0 & \frac{\beta_{P_2}\Lambda}{d} & 0 & \frac{\beta_{I_2}\Lambda}{d} & 0 & \frac{\beta_{A_2}\Lambda}{d} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

and

$$\mathcal{V} = \begin{bmatrix} \alpha + d & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha + d & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\alpha & 0 & d + p & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\alpha & 0 & d + p & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (a-1)p & 0 & d + h + \gamma & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & (a-1)p & 0 & d + h + \gamma & 0 & 0 & 0 \\ 0 & 0 & -ap & 0 & 0 & 0 & d + \gamma & 0 & 0 \\ 0 & 0 & 0 & -ap & 0 & 0 & 0 & d + \gamma & 0 \\ 0 & 0 & 0 & 0 & -h & -h & 0 & 0 & d + \delta + \rho \end{bmatrix}.$$

Thus, the next-generation matrix is given by

$$\mathcal{FV}^{-1} = \begin{bmatrix} \mathcal{R}_{0_1} & 0 & \mathcal{FV}_{13}^{-1} & 0 & \frac{\beta_{I_1} \Lambda}{d(d+h+\gamma)} & 0 & \frac{\beta_{A_1} \Lambda}{d(d+\gamma)} & 0 & 0 \\ 0 & \mathcal{R}_{0_2} & 0 & \mathcal{FV}_{24}^{-1} & 0 & \frac{\beta_{I_2} \Lambda}{d(d+h+\gamma)} & 0 & \frac{\beta_{A_2} \Lambda}{d(d+\gamma)} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

where

$$\mathcal{FV}_{13}^{-1} = \frac{\beta_{P_1} \Lambda}{d(d+p)} + \frac{\beta_{I_1} \Lambda(1-a)p}{d(d+p)(d+h+\gamma)} + \frac{\beta_{A_1} \Lambda ap}{d(d+p)(d+\gamma)},$$

$$\mathcal{FV}_{24}^{-1} = \frac{\beta_{P_1} \Lambda}{d(d+p)} + \frac{\beta_{I_1} \Lambda(1-a)p}{d(d+p)(d+h+\gamma)} + \frac{\beta_{A_1} \Lambda ap}{d(d+p)(d+\gamma)},$$

and

$$\mathcal{R}_{0_1} = \frac{\beta_{P_1} \Lambda \alpha}{d(d+\alpha)(d+p)} + \frac{\beta_{I_1} \Lambda(1-a)p\alpha}{d(d+p)(d+\alpha)(d+h+\gamma)} + \frac{\beta_{A_1} \Lambda ap\alpha}{d(d+p)(d+\alpha)(d+\gamma)},$$

$$\mathcal{R}_{0_2} = \frac{\beta_{P_2} \Lambda \alpha}{d(d+\alpha)(d+p)} + \frac{\beta_{I_2} \Lambda(1-a)p\alpha}{d(d+p)(d+\alpha)(d+h+\gamma)} + \frac{\beta_{A_2} \Lambda ap\alpha}{d(d+p)(d+\alpha)(d+\gamma)}. \quad (9)$$

The biological interpretation of the secondary parameters $\mathcal{R}_{0_1}$ and $\mathcal{R}_{0_2}$, is that they determine the effects of the controls applied on the two variants of SARS-CoV-2 virus, respectively. The final value of the spectral radius of the matrix $\mathcal{FV}^{-1}$ is given by

$$\mathcal{R}_0 = \max \{ \mathcal{R}_{0_1}, \mathcal{R}_{0_2} \}. \quad (10)$$

Now, the value of the basic reproduction number $\mathcal{R}_0$ determines whether the disease becomes an outbreak. Thus, for $\mathcal{R}_0 < 1$, and if the initial conditions of the subpopulations that make up the model (4) are contained in an attractive neighborhood of the disease-free equilibrium ($\mathcal{F}^*$), then the number of infected cases would decrease towards zero. On the other hand, if $\mathcal{R}_0 > 1$, then there would be outbreak, even if just one infected individual is introduced in a region where everyone is susceptible. This is summarized in the following theorem.

Theorem 2 When the parameter $\mathcal{R}_0 < 1$, the disease-free equilibrium state point given in (8) of model (2) is locally asymptotically stable, and if $\mathcal{R}_0 > 1$ then it is unstable.

Proof It is sufficient to apply Theorem 2 given in den Driessche and Watmough (2002). $\square$

3.2 Global stability of disease-free equilibrium point

In the analysis of the global stability of the equilibrium points, it is common to use Lyapunov functions and a useful tool to construct them are the Volterra functions which are based on the following expression:

$$G(x) = x - 1 - \ln(x), \quad (11)$$

where $G(x) \geq 0$, for $x > 0$ and $G(x) = 0$, if $x = 1$. The Volterra approach does not give an explicit form for the Volterra function $G(x)$, and this needs some analysis creativity (Bentaleb and Amine 2019; Taneco-Hernández and Vargas-De-León 2020; O'Regan et al. 2010). We can use this approach to prove that when $\mathcal{R}_0 < 1$, the disease eradication is independent of the initial conditions of the mathematical model (2). This means that the disease-free equilibrium ($\mathcal{F}^*$) is globally asymptotically stable (GAS). This statement is verified by the following result.

Theorem 3 The disease-free equilibrium point (8) of system (2) is globally asymptotically stable if $\mathcal{R}_0 \leq 1$.

Proof In this case, for the analysis of the global steady-state stability of the disease-free equilibrium point, we consider the following Lyapunov function, which is a combination of linear functions and Volterra function, and is given as follows:

$$\begin{aligned} \mathcal{L}_{\mathcal{F}^*}(Z(t)) = & S^0 \left(\frac{S(t)}{S^0} - 1 - \ln \left(\frac{S(t)}{S^0} \right) \right) + E_1(t) + E_2(t) + \frac{S^0 \beta_{I_1}}{d + h + \gamma} I_1(t) \\ & + \frac{S^0 \beta_{I_2}}{d + h + \gamma} I_2(t) + \frac{S^0 \beta_{A_1}}{d + \gamma} A_1(t) + \frac{S^0 \beta_{A_2}}{d + \gamma} A_2(t) \\ & + \left(\frac{S^0 \beta_{P_1}}{d + p} + \frac{S^0 \beta_{I_1}(1 - a)p}{(d + p)(d + h + \gamma)} + \frac{S^0 \beta_{A_1}ap}{(d + p)(d + \gamma)} \right) P_1(t) \\ & + \left(\frac{S^0 \beta_{P_2}}{d + p} + \frac{S^0 \beta_{I_2}(1 - a)p}{(d + p)(d + h + \gamma)} + \frac{S^0 \beta_{A_2}ap}{(d + p)(d + \gamma)} \right) P_2(t), \quad (12) \end{aligned}$$

where $Z(t) = (S(t), E_1(t), I_1(t), A_1(t), P_1(t), H(t), E_2(t), I_2(t), A_2(t), P_2(t),)$, and $\mathcal{L}_{\mathcal{F}^*}$ satisfies

$$\mathcal{L}_{\mathcal{F}^*}(\mathcal{F}^*) = 0,$$

$$\mathcal{L}_{\mathcal{F}^*}(Z(t)) > 0, \text{ for all } Z(t) \neq \mathcal{F}^*,$$

$$\mathcal{L}_{\mathcal{F}^*}(Z(t)) \rightarrow \infty, \text{ as } \|Z\| \rightarrow \infty. \text{ Moreover } \mathcal{L}_{\mathcal{F}^*}(Z(t)) \text{ is radially unbounded.} \quad (13)$$

The time derivative of $\mathcal{L}_{\mathcal{F}^*}(Z(t))$ through the solutions of the model (2) is

$$\begin{aligned} \frac{d\mathcal{L}_{\mathcal{F}^*}(Z(t))}{dt} = & \left(1 - \frac{S^0}{S(t)}\right) \dot{S}(t) + \dot{E}_1(t) + \dot{E}_2(t) + \frac{S^0\beta_{I_1}}{d+h+\gamma} \dot{I}_1(t) \\ & + \frac{S^0\beta_{I_2}}{d+h+\gamma} \dot{I}_2(t) + \frac{S^0\beta_{A_1}}{d+\gamma} \dot{A}_1(t) + \frac{S^0\beta_{A_2}}{d+\gamma} \dot{A}_2(t) \\ & + \left(\frac{S^0\beta_{P_1}}{d+p} + \frac{S^0\beta_{I_1}(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0\beta_{A_1}ap}{(d+p)(d+\gamma)}\right) \dot{P}_1(t) \\ & + \left(\frac{S^0\beta_{P_2}}{d+p} + \frac{S^0\beta_{I_2}(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0\beta_{A_2}ap}{(d+p)(d+\gamma)}\right) \dot{P}_2(t). \end{aligned}$$

After performing some cancellations of similar terms and regrouping the rest of them, one gets that

$$\begin{aligned} \frac{d\mathcal{L}_{\mathcal{F}^*}(Z(t))}{dt} = & -d \frac{(S(t) - S^0)^2}{S(t)} - (d+\alpha)E_1(t) - (d+\alpha)E_2(t) \\ & + \left(\frac{S^0\beta_{P_1}\alpha}{d+p} + \frac{S^0\beta_{I_1}\alpha(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0\beta_{A_1}ap\alpha}{(d+p)(d+\gamma)}\right) E_1(t) \\ & + \left(\frac{S^0\beta_{P_2}\alpha}{d+p} + \frac{S^0\beta_{I_2}\alpha(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0\beta_{A_2}ap\alpha}{(d+p)(d+\gamma)}\right) E_2(t) \\ = & (d+\alpha)(\mathcal{R}_{0_1} - 1)E_1(t) + (d+\alpha)(\mathcal{R}_{0_2} - 1)E_2(t) \\ \leq & (d+\alpha)(\mathcal{R}_0 - 1)(E_1(t) + E_2(t)). \end{aligned}$$

Therefore, when $\mathcal{R}_0 \leq 1$, then $\frac{d\mathcal{L}_{\mathcal{F}^*}(Z(t))}{dt} \leq 0$. Furthermore, $\frac{d\mathcal{L}_{\mathcal{F}^*}(Z(t))}{dt} = 0$, if and only if $E_1(t) = 0$ and $E_2(t) = 0$. Thus, the set

$$\mathcal{L}_{\mathcal{F}^*} = \left\{ Z(t) \in \mathcal{O} : \frac{d\mathcal{L}_{\mathcal{F}^*}(Z(t))}{dt} = 0 \right\}$$

contains only the point $\{\mathcal{F}^*\}$. It follows that by Lyapunov's Theorem, that the disease-free equilibrium $(\mathcal{F}^*)$ is globally asymptotically stable if $\mathcal{R}_0 \leq 1$ in $\mathcal{O}$. $\square$

3.3 Global stability of endemic points

For the health control institutions, it is important to determine the effect of the biological parameters on the transmission of infectious diseases. One way to accomplish this is by means of the solutions of an epidemiological model represented by ordinary differential equations. Besides the desirable disease equilibrium point, the most important stationary solutions are the endemic equilibrium points. They allow us to observe the effect that health control policies like quarantine or lock-down have on the transmission of the disease.

In the mathematical model (2), we are interested in analyzing the behavior of the model's solutions when the transmission rates of the new SARS-CoV-2 are higher than the pre-existing one (Davies et al. 2021; Leung et al. 2021). That is, $\beta_{P_2} > \beta_{P_1}$, $\beta_{A_2} > \beta_{A_1}$, and $\beta_{I_2} > \beta_{I_1}$, with the aim of determining from a qualitative point of view the effect of a second SARS-CoV-2 variant on the overall dynamics of the COVID-10 pandemic in a particular region or country over time. For this, we use the following algebraic system:

$$\begin{aligned}
0 &= \Lambda - dS^* - \left(\beta_{P_1} P_1^* + \beta_{I_1} I_1^* + \beta_{A_1} A_1^* + \beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^*, \\
0 &= \left(\beta_{P_1} P_1^* + \beta_{I_1} I_1^* + \beta_{A_1} A_1^* \right) S^* - (d + \alpha) E_1^*, \\
0 &= \alpha E_1^* - (d + p) P_1^*, \\
0 &= (1 - a) p P_1^* - (d + h + \gamma) I_1^*, \\
0 &= a p P_1^* - (d + \gamma) A_1^*, \\
0 &= \left(\beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^* - (d + \alpha) E_2^*, \\
0 &= \alpha E_2^* - (d + p) P_2^*, \\
0 &= (1 - a) p P_2^* - (d + h + \gamma) I_2^*, \\
0 &= a p P_2^* - (d + \gamma) A_2^*, \\
0 &= h(I_1^* + I_2^*) - (d + \delta + \rho) H^*.
\end{aligned} \tag{14}$$

We can see from the first equation of (14) that $S^* > 0$. Moreover, $\Lambda - dS^* > 0$, this is, $S^* \in \mathcal{O}$. Next, the following proposition allows us to obtain the endemic point.

Proposition 1 Suppose that $\beta_{P_2} > \beta_{P_1}$, $\beta_{A_2} > \beta_{A_1}$, and $\beta_{I_2} > \beta_{I_1}$. Then $E_1^* = P_1^* = I_1^* = A_1^* = 0$.

Proof Let us assume that equality $P_1^* = E_1^* = I_1^* = A_1^* = 0$, is not verified. Hence, assuming that any of the points $P_1^*, E_1^*, I_1^*, A_1^*$ is zero, then a contradiction follows from (14). Now, when $P_1^* > 0, E_1^* > 0, I_1^* > 0, A_1^* > 0$, from (14) one gets that

$$P_2^* = P_1^* \frac{E_2^*}{E_1^*}, \quad I_2^* = I_1^* \frac{E_2^*}{E_1^*}, \quad A_2^* = A_1^* \frac{E_2^*}{E_1^*}.$$

Replacing the above in the sixth equation of system (14), we obtain

$$\begin{aligned}
(\alpha + d) E_2^* &= \left(\beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^* > \left(\beta_{P_1} P_2^* + \beta_{I_1} I_2^* + \beta_{A_1} A_2^* \right) S^* \\
&= \left(\beta_{P_1} P_1^* \frac{E_2^*}{E_1^*} + \beta_{I_1} I_1^* \frac{E_2^*}{E_1^*} + \beta_{A_1} A_1^* \frac{E_2^*}{E_1^*} \right) S^*.
\end{aligned} \tag{15}$$

Thus, equation (15) contradicts the second equation of system (14). Therefore, the equality $P_1^* = E_1^* = I_1^* = A_1^* = 0$, holds if $\beta_{P_2} > \beta_{P_1}$, $\beta_{A_2} > \beta_{A_1}$, and $\beta_{I_2} > \beta_{I_1}$. $\square$

Consequently, Proposition 1 allows us to guarantee a single endemic point if the conditions $\beta_{P_2} > \beta_{P_1}$, $\beta_{A_2} > \beta_{A_1}$, and $\beta_{I_2} > \beta_{I_1}$, hold. Thus,

$$\mathcal{E}^* = (S^*, 0, 0, 0, H^*, E_2^*, P_2^*, A_2^*, I_2^*), \tag{16}$$

where $\mathcal{E}^*$ satisfies

$$\begin{aligned}
0 &= \Lambda - dS^* - \left(\beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^*, \\
0 &= \left(\beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^* - (d + \alpha) E_2^*, \\
0 &= \alpha E_2^* - (d + p) P_2^*, \\
0 &= (1 - a) p P_2^* - (d + h + \gamma) I_2^*, \\
0 &= a p P_2^* - (d + \gamma) A_2^*, \\
0 &= h I_2^* - (d + \delta + \rho) H^*.
\end{aligned} \tag{17}$$

Applying some algebraic manipulations in (17), we get

$$\begin{aligned}
 S^* &= \frac{\Lambda}{d\mathcal{R}_{0_2}}, \\
 E_2^* &= \frac{\Lambda}{d+\alpha} \frac{\mathcal{R}_{0_2}-1}{\mathcal{R}_{0_2}}, \\
 P_2^* &= \frac{\alpha}{d+p} \frac{\Lambda}{d+\alpha} \frac{\mathcal{R}_{0_2}-1}{\mathcal{R}_{0_2}}, \\
 A_2^* &= \frac{ap\alpha}{(d+\gamma)(d+p)} \frac{\Lambda}{d+\alpha} \frac{\mathcal{R}_{0_2}-1}{\mathcal{R}_{0_2}}, \\
 I_2^* &= \frac{(1-a)p\alpha}{(d+h+\gamma)(d+p)} \frac{\Lambda}{d+\alpha} \frac{\mathcal{R}_{0_2}-1}{\mathcal{R}_{0_2}}, \\
 H^* &= \frac{h}{d+\delta+\rho} \frac{(1-a)p\alpha}{(d+h+\gamma)(d+p)} \frac{\Lambda}{d+\alpha} \frac{\mathcal{R}_{0_2}-1}{\mathcal{R}_{0_2}}.
 \end{aligned} \tag{18}$$

Thus, we arrive to the following proposition,

Proposition 2 *The endemic steady-state point $\mathcal{E}^*$ given by (16) of system (2) exists if $\mathcal{R}_{0_2} > \max\{\mathcal{R}_{0_1}, 1\}$.*

Next, we carry out the global stability analysis of the endemic point. We consider two cases. First, $\mathcal{R}_{0_2} > 1 > \mathcal{R}_{0_1}$.

Theorem 4 *Suppose that $\mathcal{R}_{0_2} > 1 > \mathcal{R}_{0_1}$, then the endemic equilibrium point $\mathcal{E}^*$ of system (2) given by (16) is globally asymptotically stable on $\mathcal{O}$.*

Proof Consider the following Lyapunov function:

$$\begin{aligned}
 \mathcal{L}(Z(t)) = & E_1(t) + \frac{S^0\beta_{I_1}}{d+h+\gamma} I_1(t) + \frac{S^0\beta_{A_1}}{d+\gamma} A_1(t) \\
 & + \left(\frac{S^0\beta_{P_1}}{d+p} + \frac{S^0\beta_{I_1}(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0\beta_{A_1}ap}{(d+p)(d+\gamma)} \right) P_1(t) \\
 & + S^* \left(\frac{S(t)}{S^*} - 1 - \ln \left(\frac{S(t)}{S^*} \right) \right) + E_2^* \left(\frac{E_2(t)}{E_2^*} - 1 - \ln \left(\frac{E_2(t)}{E_2^*} \right) \right) \\
 & + \frac{\beta_{I_2}I_2^*S^*}{(1-a)pP_2^*} I_2^* \left(\frac{I_2(t)}{I_2^*} - 1 - \ln \left(\frac{I_2(t)}{I_2^*} \right) \right) \\
 & + \frac{\beta_{A_2}A_2^*S^*}{apP_2^*} A_2^* \left(\frac{A_2(t)}{A_2^*} - 1 - \ln \left(\frac{A_2(t)}{A_2^*} \right) \right) \\
 & + \left(\frac{\beta_{P_2}P_2^*S^* + \beta_{A_2}A_2^*S^* + \beta_{I_2}I_2^*S^*}{\alpha E_2^*} \right) P_2^* \left(\frac{P_2(t)}{P_2^*} - 1 - \ln \left(\frac{P_2(t)}{P_2^*} \right) \right),
 \end{aligned} \tag{19}$$

which verifies (13). Next, applying the time derivative of $\mathcal{L}(Z(t))$ along of the trajectories of (2), we obtain

$$\begin{aligned} \frac{d\mathcal{L}(Z(t))}{dt} = & \dot{E}_1(t) + \frac{S^0 \beta_{I_1}}{d+h+\gamma} \dot{I}_1(t) + \frac{S^0 \beta_{A_1}}{d+\gamma} \dot{A}_1(t) \\ & + \left(\frac{S^0 \beta_{P_1}}{d+p} + \frac{S^0 \beta_{I_1}(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0 \beta_{A_1}ap}{(d+p)(d+\gamma)} \right) \dot{P}_1(t) \\ & + \left(1 - \frac{S^*}{S(t)} \right) \dot{S}(t) + \left(1 - \frac{E_2^*}{E_2(t)} \right) \dot{E}_2(t) \\ & + \frac{\beta_{I_2} I_2^* S^*}{(1-a)pP_2^*} \left(1 - \frac{I_2^*}{I_2(t)} \right) \dot{I}_2(t) + \frac{\beta_{A_2} A_2^* S^*}{apP_2^*} \left(1 - \frac{A_2^*}{A_2(t)} \right) \dot{A}_2(t) \\ & + \left(\frac{\beta_{P_2} P_2^* S^* + \beta_{A_2} A_2^* S^* + \beta_{I_2} I_2^* S^*}{\alpha E_2^*} \right) \left(1 - \frac{P_2^*}{P_2(t)} \right) \dot{P}_2(t), \end{aligned} \quad (20)$$

Then we replace the derivatives of the state variables in (20) and thus obtain

$$\begin{aligned} \frac{d\mathcal{L}(Z(t))}{dt} = & \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) \right) S(t) - (d+\alpha) E_1(t) \\ & + \frac{S^0 \beta_{I_1}}{d+h+\gamma} ((1-a)pP_1(t) - (d+h+\gamma)I_1(t)) \\ & + \frac{S^0 \beta_{A_1}}{d+\gamma} (apP_1(t) - (d+\gamma)A_1(t)) \\ & + \left(\frac{S^0 \beta_{P_1}}{d+p} + \frac{S^0 \beta_{I_1}(1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0 \beta_{A_1}ap}{(d+p)(d+\gamma)} \right) (\alpha E_1(t) - (d+p)P_1(t)) \\ & + \left(1 - \frac{S^*}{S(t)} \right) \left(\Lambda - dS(t) \right) \\ & - \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) + \beta_{I_2} I_2(t) + \beta_{P_2} P_2(t) + \beta_{A_2} A_2(t) \right) S(t) \\ & + \left(1 - \frac{E_2^*}{E_2(t)} \right) \left((\beta_{P_2} P_2(t) + \beta_{I_2} I_2(t) + \beta_{A_2} A_2(t)) S(t) - (d+\alpha) E_2(t) \right) \\ & + \frac{\beta_{I_2} I_2^* S^*}{(1-a)pP_2^*} \left(1 - \frac{I_2^*}{I_2(t)} \right) ((1-a)pP_2(t) - (d+h+\gamma)I_2(t)) \\ & + \frac{\beta_{A_2} A_2^* S^*}{apP_2^*} \left(1 - \frac{A_2^*}{A_2(t)} \right) (apP_2(t) - (d+\gamma)A_2(t)) \\ & + \left(\frac{\beta_{P_2} P_2^* S^* + \beta_{A_2} A_2^* S^* + \beta_{I_2} I_2^* S^*}{\alpha E_2^*} \right) \left(1 - \frac{P_2^*}{P_2(t)} \right) (\alpha E_2(t) - (d+p)P_2(t)). \end{aligned} \quad (21)$$

On the other hand, from (17) we can obtain the following expressions:

$$\begin{aligned} \Lambda = & dS^* + \left(\beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^*, \quad d+\alpha = \frac{\left(\beta_{P_2} P_2^* + \beta_{I_2} I_2^* + \beta_{A_2} A_2^* \right) S^*}{E_2^*} \\ d+p = & \frac{\alpha E_2^*}{P_2^*}, \quad d+h+\gamma = \frac{(1-a)pP_2^*}{I_2^*}, \quad d+\gamma = \frac{apP_2^*}{A_2^*}, \end{aligned} \quad (22)$$

which can be substituted in (21). After performing algebraic operations and rearranging terms, it is possible to obtain

$$\begin{aligned} \frac{d\mathcal{L}(Z(t))}{dt} = & -\frac{d(S(t) - S^*)^2}{S(t)} + \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) \right) S^* \\ & - \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) \right) S(t) \\ & - S^0 \beta_{P_1} P_1(t) - S^0 \beta_{I_1} I_1(t) - S^0 \beta_{A_1} A_1(t) + (d + \alpha) E_1(t) (\mathcal{R}_{0_1} - 1) \\ & + \beta_{P_2} P_2^* S^* \left(3 - \frac{S^*}{S(t)} - \frac{E_2^* P_2(t) S(t)}{E_2(t) P_2^* S^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) \\ & + \beta_{I_2} I_2^* S^* \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* I_2(t) S(t)}{E_2(t) I_2^* S^*} - \frac{I_2^* P_2(t)}{I_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) \\ & + \beta_{A_2} A_2^* S^* \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* A_2(t) S(t)}{E_2(t) A_2^* S^*} - \frac{A_2^* P_2(t)}{A_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right). \quad (23) \end{aligned}$$

Thus,

$$\begin{aligned} \frac{d\mathcal{L}(Z(t))}{dt} \leq & -\frac{d(S(t) - S^*)^2}{S(t)} - \left(\beta_{P_1} P_1(t) + \beta_{I_1} I_1(t) + \beta_{A_1} A_1(t) \right) S(t) \\ & + (d + \alpha) E_1(t) (\mathcal{R}_{0_1} - 1) \\ & + \beta_{P_2} P_2^* S^* \left(3 - \frac{S^*}{S(t)} - \frac{E_2^* P_2(t) S(t)}{E_2(t) P_2^* S^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) \\ & + \beta_{I_2} I_2^* S^* \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* I_2(t) S(t)}{E_2(t) I_2^* S^*} - \frac{I_2^* P_2(t)}{I_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) \\ & + \beta_{A_2} A_2^* S^* \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* A_2(t) S(t)}{E_2(t) A_2^* S^*} - \frac{A_2^* P_2(t)}{A_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right). \quad (24) \end{aligned}$$

We know that the arithmetic mean is greater than the geometric mean. Thus, the following inequalities are verified:

$$\begin{aligned} \left(3 - \frac{S^*}{S(t)} - \frac{E_2^* P_2(t) S(t)}{E_2(t) P_2^* S^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) & \leq 0, \\ \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* I_2(t) S(t)}{E_2(t) I_2^* S^*} - \frac{I_2^* P_2(t)}{I_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) & \leq 0, \\ \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* A_2(t) S(t)}{E_2(t) A_2^* S^*} - \frac{A_2^* P_2(t)}{A_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) & \leq 0. \quad (25) \end{aligned}$$

Accordingly, if $\mathcal{R}_{0_2} > 1 > \mathcal{R}_{0_1}$ then $\frac{d\mathcal{L}(Z(t))}{dt} \leq 0$. Moreover, from (23) it follows that $\frac{d\mathcal{L}(Z(t))}{dt} = 0$ if only if $E_1(t) = I_1(t) = A_1(t) = 0$, $S(t) = S^*$, $A_2(t) = A_2^*$, $I_2(t) = I_2^*$, $P_2(t) = P_2^*$, that is, the set

$$\mathcal{L}\mathcal{E}^* = \left\{ Z(t) \in \mathcal{O} : \frac{d\mathcal{L}(Z(t))}{dt} = 0 \right\} = \{\mathcal{E}^*\}. \quad (26)$$

Applying the Lyapunov–LaSalle asymptotic stability theorem, we can infer that the endemic equilibrium state $\mathcal{E}^*$ is globally asymptotically stable in the positive region $\mathcal{O}$. $\square$

The second case is when $\mathcal{R}_{0_2} > \mathcal{R}_{0_1} > 1$.

Theorem 5 Suppose that $\mathcal{R}_{02} > \mathcal{R}_{01} > 1$. Then the endemic equilibrium point $\mathcal{E}^*$ of system (2) given by (16) is globally asymptotically stable on $\mathcal{O}$.

Proof We define the following Lyapunov function:

$$\begin{aligned} \mathcal{S}(Z(t)) = & \mathcal{R}_{02} S^* \left(\frac{S(t)}{S^*} - 1 - \ln \left(\frac{S(t)}{S^*} \right) \right) + \mathcal{R}_{02} E_1(t) + \frac{S^0 \beta_{I_1}}{d+h+\gamma} I_1(t) + \frac{S^0 \beta_{A_1}}{d+\gamma} A_1(t) \\ & + \left(\frac{S^0 \beta_{P_1}}{d+p} + \frac{S^0 \beta_{I_1} (1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0 \beta_{A_1} ap}{(d+p)(d+\gamma)} \right) P_1(t) \\ & + \mathcal{R}_{02} E_2^* \left(\frac{E_2(t)}{E_2^*} - 1 - \ln \left(\frac{E_2(t)}{E_2^*} \right) \right) \\ & + \frac{\mathcal{R}_{02} \beta_{I_2} I_2^* S^*}{(1-a)pP_2^*} I_2^* \left(\frac{I_2(t)}{I_2^*} - 1 - \ln \left(\frac{I_2(t)}{I_2^*} \right) \right) \\ & + \frac{\mathcal{R}_{02} \beta_{A_2} A_2^* S^*}{apP_2^*} A_2^* \left(\frac{A_2(t)}{A_2^*} - 1 - \ln \left(\frac{A_2(t)}{A_2^*} \right) \right) \\ & + \mathcal{R}_{02} \left(\frac{\beta_{P_2} P_2^* S^* + \beta_{A_2} A_2^* S^* + \beta_{I_2} I_2^* S^*}{\alpha E_2^*} \right) P_2^* \left(\frac{P_2(t)}{P_2^*} - 1 - \ln \left(\frac{P_2(t)}{P_2^*} \right) \right). \end{aligned} \quad (27)$$

This function $\mathcal{S}$ fulfills conditions (13). Next taking the time derivative of $\mathcal{S}(Z(t))$ along the trajectories of system (2), one gets

$$\begin{aligned} \dot{\mathcal{S}}(Z(t)) = & \mathcal{R}_{02} \left(1 - \frac{S^*}{S(t)} \right) \dot{S}(t) + \mathcal{R}_{02} \dot{E}_1(t) + \frac{S^0 \beta_{I_1}}{d+h+\gamma} \dot{I}_1(t) + \frac{S^0 \beta_{A_1}}{d+\gamma} \dot{A}_1(t) \\ & + \left(\frac{S^0 \beta_{P_1}}{d+p} + \frac{S^0 \beta_{I_1} (1-a)p}{(d+p)(d+h+\gamma)} + \frac{S^0 \beta_{A_1} ap}{(d+p)(d+\gamma)} \right) \dot{P}_1(t) \\ & + \mathcal{R}_{02} \left(1 - \frac{E_2^*}{E_2(t)} \right) \dot{E}_2(t) + \frac{\mathcal{R}_{02} \beta_{I_2} I_2^* S^*}{(1-a)pP_2^*} \left(1 - \frac{I_2^*}{I_2(t)} \right) \dot{I}_2(t) \\ & + \frac{\mathcal{R}_{02} \beta_{A_2} A_2^* S^*}{apP_2^*} \left(1 - \frac{A_2^*}{A_2(t)} \right) \dot{A}_2(t) \\ & + \mathcal{R}_{02} \left(\frac{\beta_{P_2} P_2^* S^* + \beta_{A_2} A_2^* S^* + \beta_{I_2} I_2^* S^*}{\alpha E_2^*} \right) \left(1 - \frac{P_2^*}{P_2(t)} \right) \dot{P}_2(t). \end{aligned} \quad (28)$$

Replacing the derivatives of state variables, inserting (20) into (28) and regrouping terms, one gets that

$$\begin{aligned} \frac{d\mathcal{S}(Z(t))}{dt} = & - \frac{\mathcal{R}_{02} d (S(t) - S_2^*)^2}{S(t)} + (d+\alpha) E_1(t) (\mathcal{R}_{01} - \mathcal{R}_{02}) \\ & + (d+\alpha) E_1(t) (\mathcal{R}_{01} - 1) \\ & + \mathcal{R}_{02} \beta_{P_2} P_2^* S^* \left(3 - \frac{S^*}{S(t)} - \frac{E_2^* P_2(t) S(t)}{E_2(t) P_2^* S^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) \\ & + \mathcal{R}_{02} \beta_{I_2} I_2^* S^* \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* I_2(t) S(t)}{E_2(t) I_2^* S^*} - \frac{I_2^* P_2(t)}{I_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right) \\ & + \mathcal{R}_{02} \beta_{A_2} A_2^* S^* \left(4 - \frac{S^*}{S(t)} - \frac{E_2^* A_2(t) S(t)}{E_2(t) A_2^* S^*} - \frac{A_2^* P_2(t)}{A_2(t) P_2^*} - \frac{P_2^* E_2(t)}{P_2(t) E_2^*} \right). \end{aligned} \quad (29)$$

Thus, if $\mathcal{R}_{0_2} > \mathcal{R}_{0_1} > 1$, then $\frac{d\mathcal{J}(Z(t))}{dt} \leq 0$. Moreover, $\frac{d\mathcal{J}(Z(t))}{dt} = 0$ if only if $E_1(t) = I_1(t) = A_1(t) = P_1(t)0$, $S(t) = S^*$, $A_2(t) = A_2^*$, $I_2(t) = I_2^*$, $P_2(t) = P_2^*$. Then by the Lyapunov theorem we can conclude that the endemic equilibrium point $\mathcal{E}$ is globally asymptotically stable on $\mathcal{O}$. $\square$

4 Numerical simulation results

In this section, we present a variety of numerical simulations of the two SARS-CoV-2 variants mathematical model (2). We use different conditions varying the numerical values of the parameters related to the transmissibility of SARS-CoV-2. All the conditions considered are under the assumption that the new SARS-CoV-2 variant (two) is more contagious than variant one. Thus, these numerical simulations allow us to numerically support the previous theoretical results. Furthermore, we can analyze qualitatively the effects of introducing a more contagious SARS-CoV-2 variant in a particular region or country.

The values of the parameters are shown in Table 1. In regard to the initial subpopulations, we vary them to numerically test the local and global theoretical stability results. In addition, we consider different scenarios with regard to the parameters β_{P_1} , β_{I_2} , β_{A_1} , β_{P_2} , β_{I_2} , β_{A_2} in a such way that we obtain scenarios with $\mathcal{R}_0 < 1$ and $\mathcal{R}_0 > 1$. Thus, for each scenario, we perform a numerical simulation and then the steady states can be observed. In this way, we can numerically support the theoretical results obtained in the previous section. It is important to remark that these numerical simulations provide insight into potential pandemic situations. Moreover, we would like to remark that the basic reproduction number $\mathcal{R}_i$ is related to the well-known effective reproduction number $\mathcal{R}_i$ (Yan and Chowell 2019).

As we have mentioned previously, we consider scenarios where a more contagious SARS-CoV-2 variant is introduced in a region or country ($\beta_{I_2} > \beta_{I_1}$, $\beta_{A_2} > \beta_{A_1}$). We assume that the transmission rates in asymptomatic and symptomatic individuals are time-invariant. For the asymptomatic proportion, we choose without loss of generality that the percentage of infections that are asymptomatic is 50% (Centers for Disease Control and Prevention 2020). We varied this percentage and as expected the theoretical results hold.

The numerical simulations were performed using Matlab software, in particular the function ode45. We varied the numerical values of some parameters of the model and the values obtained for the state variables are positive. Thus, it was not necessary to develop a numerical scheme to guarantee the positivity of the variables. In some cases, it is necessary to construct nonstandard schemes to always obtain realistic positive values and avoid spurious solutions (Mickens 2005; González-Parra et al. 2014). Figure 2 shows the dynamics of the susceptible $S(t)$, infected with variant one $I_1(t)$, asymptomatic one $A_1(t)$, hospitalized $H(t)$, presymptomatic two P_2 and asymptomatic two A_2 subpopulations. This particular case is under such conditions that $\mathcal{R}_{0_1} < 1$ and $\mathcal{R}_{0_2} < 1$. Both SARS-CoV-2 variants disappear from the whole population and the system reaches the disease-free steady state $\mathcal{F}^*$. In the next scenario, we consider that the public health conditions are such that both basic reproduction numbers are greater than one ($\mathcal{R}_{0_2} > \mathcal{R}_{0_1} > 1$). In Fig. 3, it can be seen that the solution goes to the endemic steady state $\mathcal{E}^*$. Notice that the less contagious SARS-CoV-2 variant vanishes and the more contagious one keeps circulating in the population. Finally, we consider an interesting case where the preexistent SARS-CoV-2 variant one has a basic reproduction number less than one ($\mathcal{R}_{0_1} < 1$), but the more contagious one has a basic reproduction number greater than one ($\mathcal{R}_{0_1} > 1$). In Fig. 4, we can see the more contagious SARS-CoV-2 variant dominates and the variant one disappears from the population. The solution reaches

Table 1 Values of the parameters for the mathematical model (2) used in the numerical simulations

Parameter	Symbol	Value
Incubation period	α^{-1}	5.2 <i>days</i> Li et al. (2020), IHME COVID-19 Forecasting Team (2020)
Infectious period	γ^{-1}	7 <i>days</i> Li et al. (2020)
Hospitalization rate	h^{-1}	3.5 <i>days</i> $\times$ 0.04 Ferguson et al. (2020), Li et al. (2020), Hoseinpour Dehkordi et al. (2020)
Hospitalization period	ρ^{-1}	10.4 <i>days</i> Ferguson et al. (2020), Li et al. (2020), Hoseinpour Dehkordi et al. (2020)
Death rate (hospitalized)	δ^{-1}	10.4 <i>days</i> $\times$ 0.103 Quah et al. (2020), Paltiel et al. (2020)
Probability of being asymptomatic	a	0.5 Centers for Disease Control and Prevention (2020), Oran and Topol (2020)

Fig. 2 Numerical simulation of the mathematical model (2) when $\mathcal{R}_{02} \approx 0.95 > \mathcal{R}_{01} \approx 0.87$. Both SARS-CoV-2 variants disappear and the system reaches the disease-free steady-state $\mathcal{F}^*$

Fig. 3 Numerical simulation of the mathematical model (2) when $\mathcal{R}_{02} \approx 2.62 > \mathcal{R}_{01} \approx 1.87 > 1$. The more contagious SARS-CoV-2 variant clears the less contagious variant despite the initial amount of cases have this variant. The system reaches the endemic steady state $\mathcal{E}^*$

the endemic steady state $\mathcal{E}^*$. This case is similar to what happened in England with the introduction of a more transmissible SARS-CoV-2 variant (Davies et al. 2021). Thus, it can be seen the importance of increasing the number of public health policies when new more transmissible variants are introduced in a population. Even if the basic reproduction number was less than one before the appearance of the new variant, that would not be enough to control the COVID-19 pandemic.

5 Conclusions

Mathematical modeling in conjunction with mathematical analysis is a useful tool to investigate the spread of different viruses within and between hosts. Thus, it is possible to gain insights on the dynamics of many infectious diseases. This mathematical approach also helps to assess the possible effects of health policies on the evolution of infectious disease processes. Mathematical models provide insights that usually are difficult to anticipate due to the complexity of the spread of the viruses in a population. However, as any mathematical

Fig. 4 Numerical simulation of the mathematical model (2) when $\mathcal{R}_{02} \approx 1.06 > \mathcal{R}_{01} \approx 0.967$. Again as expected the more contagious SARS-CoV-2 variant clears the less contagious variant despite the initial amount of cases have this variant. The system reaches the endemic steady-state $\mathcal{E}^*$

model, there are limitations that we need to be aware to understand the whole real-world situation.

In this work, we designed a mathematical model to study the dynamics of the spread of two different SARS-CoV-2 variants, which have different contagiousness (Davies et al. 2021; Pachetti et al. 2020; Rahimi and Abadi 2021; Wise 2020; Iacobucci 2021). This study was developed taking into account that the new SARS-CoV-2 variant is more contagious than the preexistent one (Davies et al. 2021; Pachetti et al. 2020; Rahimi and Abadi 2021; Wise 2020; Iacobucci 2021).

The spread of the SARS-CoV-2 virus is affected by many factors such as social behavior, mobility, age, weather variables, and virus mutation. In this work we focused on the impact of the introduction of a new SARS-CoV-2 variant. This allows insight into what is happening in some countries with the appearance of new SARS-CoV-2 variants. In the mathematical analysis presented here, we consider that one SARS-CoV-2 variant is more contagious than the other one. We first performed a local stability analysis using the next generation matrix method. We found that the basic reproduction number is given by the maximum of the following two threshold quantities $\mathcal{R}_{01}$ and $\mathcal{R}_{02}$. Next, we did a global stability analysis and obtained two theorems that establish the necessary and sufficient conditions for the asymptotic global stability of disease-free and endemic steady states. For the global stability analysis we found several Lyapunov functionals and used the LaSalle invariant principle to prove the global stability of the steady states. The theoretical results show that the more contagious SARS-CoV-2 variant dominates the other one. Thus, the preexistent SARS-CoV-2 variant disappears after some time, even if it has a basic reproduction number greater than one. The only way that both SARS-CoV-2 variants would disappear is if both basic reproduction numbers are less than one ($\mathcal{R}_{01}, \mathcal{R}_{02} < 1$). We performed numerical simulations to numerically support the theoretical results and to show some qualitative effects of the introduction of a more contagious SARS-CoV-2 variant. Even if public health policies succeed in reducing the basic reproduction number to less than one, the introduction of a new, more contagious, variant would necessitate the implementation of more extreme policies such as radical quarantines and severe lockdowns. The results presented in this work show that a new more infectious SARS-CoV-2 variant will become dominant and the prevalence of the preexistent variant would be reduced. Our results help to support health policies and, most importantly, to raise awareness in the population regarding the consequences of the appearance of new

SARS-CoV-2 variants with higher transmission rates, such as, for example, the current Delta variant.

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