Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: July 31, 2022

Citation: Sergio Celaschi, 2022. Confirmed first year expansion of COVID-19 pandemic in Brazil, Medical Research Archives, [online] 10(7). https://doi.org/10.18103/mra.v10i7.2899

DOI
https://doi.org/10.18103/mra.v10i7.2899

ISSN: 2375-1924

RESEARCH ARTICLE

Confirmed First Year Expansion of COVID-19 Pandemic in Brazil

Sergio Celaschi*[1]

[1]CTI Renato Archer, Rod. D Pedro I (SP-65), Km 143,6 - CEP 13069-901, Campinas – SP, 13069, Brazil

* sergio.celaschi@cti.gov.br

ABSTRACT

Background: COVID-19 was first reported in Brazil in February 2020 – EPI week # 9. One semester latter, the country became one of the worst affected globally. After twelve months from the first reported case, the number of confirmed cases and deaths crossed 10 million and 248.5 thousand, respectively. Since the start of the epidemic in Brazil, several types of Non-pharmaceutical Interventions - NPI have been adopted with varied success. This work aims to confirm previous forecasts reported on September, 2020 for the expansion of the COVID-19 pandemic in Brazil, the most populated South American country with over 120 million inhabitants.

Methods: The methodology employed in this work was presented in a previous publication. In such methodology, a first series of published data, determines the epidemiological parameters that govern the dynamics of the compartmental model, and adjust the model parameters aiming to forecast the COVID-19 evolutionary outbreak in a longer period. The deterministic and compartmental model provides predictions of the time series of infected individuals and fatalities in the studied population. A SEIR compartmental model was previously selected to estimate outcomes to the dynamics of the COVID-19 epidemic breakout in Brazil. This model takes into account two dominant lineages of the SARS-CoV-2, and a time-varying reproduction number R(t) to estimate the epidemic behavior. Compartments for individuals vaccinated, and newer prevalent SARS-Cov-2 variants were not included. A time-dependent incidence weight on R(t) accounted for Non Pharmaceutical Interventions (NPI).

Results: The cohort study was set as a city population-based analysis. Population-based sample, 3,862,311 during the first study period, was the number of confirmed cases on infected individuals. A previous analysis, restricted to the city of S. Paulo - Brazil, was applied to predict the consequences of holding for posterior NPI releases, and indicates the appearance of a second wave starting last quarter of 2020. A second series of official data available from September 1st, 2020 to February 28, 2021, covering the whole Brazilian country, confirms the forecasts previously reported for the evolution of infected people and fatalities.

Conclusion: This work quantifies the importance of the adopted and enforced Non-pharmaceutical Interventions - NPI to control the spread of the COVID-19 pandemic in Brazil, as predicted by a compartmental model. By February 28, 2021, the number of confirmed cases reached 10,551,259 - 5% bellow predicted average of accumulated cases, and fatalities accounted for 254,942 - 4% above accumulated average of estimated deaths. After March 1st, 2021 new peaks on reported numbers of daily new infected and new fatalities appeared and were label as the second wave. They resulted as a combination to the presence of the prevalent SARS-CoV-2 P1 variant, the progressive NPIs realise, and the increased number of vaccinated individuals. Regarding the original SARS-CoV-2 form and its variant, the only model assumption is their distinct incubation rates.

Keywords: COVID-19; Brazil; confirmed forecast; NPI and mitigation policy; second wave; prevalent variants; vaccination.

Introduction

COVID-19 was first reported in Brazil in February 2020 – EPI week # 9. One semester latter, the country became one of the worst affected globally. As other South American countries, Brazil comprises many states with vulnerable communities, and a relatively weak social protection system. It has been widely noticed that public health regulations proved to be ineffective in preventing the proliferation of the virus.[1] After twelve months from the first reported case, the number of confirmed cases and deaths crossed 10 million and 248.5 thousand, respectively. Facts that rise doubts on the availability of public health care for the sections of society that cannot afford private care.[2] Since the start of the epidemic in Brazil, several types of Non-pharmaceutical Interventions - NPI have been adopted with varied success by the country's 27 federal units and 5,596 municipalities. Virus transmission has dropped substantially in most units. However, by September 2020, the estimated reproduction number remains above the unit.[3] Thus, only mitigation (and not suppression) of the epidemic has been achieved so far. Current interventions remain insufficient to extinguish virus transmission in Brazil. Closer surveillance of viral transmission quantifying the impact of different control measures on transmission may help to minimize future infections. Moreover, continued monitoring of the genetic diversity of the virus lineages circulating globally became necessary. As recently suggested, virus diversity are of prime importance in the SARS-CoV-2 transmission.[4] While the COVID-19 pandemic continues in the Americas, new highlights into the Brazilian are: the high SARS-CoV-2 transmission through the country; the role of its large urban centres; the lack of simultaneous lockdown regions; the non-equitable access to tests and reports. Those factors potentially contributed to sustain pandemic spread. By the end of February 2020, before the implementation of NPIs and travel bans, different SARS-Cov-2 lineages had emerged in Brazil from Europe. In the beginning, the epidemic had spread mostly locally and within-state borders.[5]

The primarily intent of this work was to build a simple epidemiological and compartmental model to predict an initial series of results for the basic dynamics of the Covid-19 epidemic breakout in the city of S. Paulo, Brazil where the first cases were confirmed. This study was reported on May, 2020.[6] Later on, by June 2021, a latter publication confirmed the forecasts previously reported for the evolution of infected people and fatalities associated to the epidemic outbreak in the city of S. Paulo.[7] After having built and applied this epidemiological model to the outbreak at the city of S. Paulo, a quantified model on the COVID-19 outbreak as a national dynamics, selecting Brazil as a cohort study case was reported.[8] Epidemiological models are commonly stochastic, network-based, spatially diffusive, using meta-population approaches.[9] However, the parameters of dynamic deterministic models are directly related to interpretable physical processes.[10] As a drawback, deterministic models impose restrictive analysis, once the dynamics of the host population and the virus are not deterministic. The population has free will, and the virus undergoes favourable mutations upon natural selection.[4] Host dynamics was account for into the model by spreading the use of time-varying reproduction number.[11] Regarding the pathogen, the variant SARS-CoV-2 D614G mutation,[4] which became globally proposed as dominant, was incorporated in our model. In short, the methodology employed is the application of a modified SEIR Model. The model takes in consideration two lineages of the SARS-CoV-2, and a time-varying reproduction number to account for changes in the dynamics of the COVID-19 transmission behaviour. This work aims to confirm previous forecasts reported on September, 2020 for the expansion of the COVID-19 pandemic in Brazil, the most populated South American country with over 120 million inhabitants.[9] Such a methodology can be applied worldwide to predict forecasts of the outbreak in any infected country.

The SARS-CoV-2 Increasing Frequency on Global Distribution

Even though SARS-CoV-2 sequence diversity is reported to be low, natural selection acts upon favourable mutations.[12] Persistence of the pandemic might enable accumulation of immunologically relevant mutations. Identification of spike amino acid variant has been reported which increasing frequency globally but not necessarily brings evidence of positive selection for 614G.[13] Spike protein determines the infectivity of the virus, and its transmissibility in the host. Recent studies suggest that the observed increased transmission reported in Europe and Americas were associated with the most dominant variant,[4] and presented experimental evidence that the so called D614G spike variant is associated with greater infectivity as well as higher viral loads. The results are explained assuming the virus being more infectious. On the other hand, the authors did not find evidence of G614 effects on disease severity. As reported

elsewhere, the Spike protein 614 polymorphism has little variance in growth rates among clusters and presented no significant difference in initial growth rates.[13] Those facts are incorporated in our model and evidences are demonstrated, assuming the same time-varying R_t number for both Spike protein 614 morphisms.

SARS-CoV-2 has a dual nature: tragically lethal to many persons and surprisingly harmless to others. Infected persons who remain asymptomatic and pre-symptomatic (here on named non-symptomatic) play a significant role in the ongoing COVID-19 pandemic. The absence symptoms in persons infected with SARS-CoV-2 does not mean an absence of harm. The procedure to classify non-symptomatic hosts is to carry repeated observations of the individual over time in a group of individuals sharing a statistical factor. Therefore, the prevalence of non-symptomatic SARS-CoV-2 infection has to be included in modelling any COVID-19 pandemic outbreak. Applying statistical analysis on published and reliable data,[14] the percentage value of non-symptomatic and symptomatic hosts were estimated to be respectively $(54 \pm 9)\%$ and $(46 \pm 9)\%$.

Serial Intervals and Inference of time-varying reproduction number

Serial interval (SI) is an essential metric for estimating other epidemiological parameters, which in turn are used to predict disease trends, interventions and health care demands. SI depends on the pathogen incubation period which quantifies the biological process of relevant virus mutation and disease progression and tends to follow distributions resulting from genetic differences.[15] Variations in SI can occur and may have significant implications for the transmission dynamics affecting the estimation of epidemic parameters. The real-time transmissibility of an infectious disease is often characterized by the instantaneous Reproduction Number (R_t), which is defined as the expected number of secondary infections caused by an infector within a short time window. Equivalently, R_t can be expressed as the transmission rate $\beta(t)$ divided by the rate γ at which infected people recover or die. The aim of control interventions is typically to reduce the R_t value. A number of methods are available to estimate effective reproduction numbers during epidemics[16] which provide a superior dynamics of the epidemic. With this aim, a method for estimating the instantaneous reproduction number using branching processes was developed.[17] This statistical framework was extended to allow adding data on known pairs of index and secondary cases from which the serial interval is directly estimated[11]. In this work, the time-varying reproduction number was estimated following a procedure available on-line.[18]

Estimative of Infected Individuals and Fatal Outcomes

There are two measures used to assess the proportion of infected individuals with fatal outcomes, the infection fatality ratio (IFR), which estimates this proportion of deaths among all infected individuals, and case fatality ratio (CFR), which estimates this proportion of deaths among identified confirmed cases. The level of transmission is generally underestimated for infectious diseases, which difficulty the IFR estimative.[19] A significant proportion of infected people are undetected because they are non-symptomatic, and fail to present at healthcare facilities. Furthermore, during 2020 testing capacity had been limited in Brazil, and restricted to people with severe cases and priority risk groups. To accurately measure IFR, the complete number of infections, and deaths caused by the disease must be known. Recently, a careful evaluation of the IFR was reported to the COVID-19 outbreak in Brazil, and a country-wide average IFR of 1.05% (95% CRI: 0.96 – 1.17%) was obtained.[20] On the other hand, reliable CFRs are generally obtained at the end of an outbreak, after most infected individuals either died or recovered. CFR calculated using the above relation during ongoing epidemics is influenced by lags in report dates for cases and deaths. Obtaining both IFR and CFR from available data would allow estimating the fraction of symptomatic hosts to apply in the model.

Modelling COVID-19 Brazilian Pandemics

Epidemiological models are useful in estimating main parameters of a pathogen spread like SARS-CoV-2. Mathematically, such models may evaluate the efficacy of specific interventions, identify efficient strategies, and forecast future scenarios.[21] Models provide estimative on the basic and effective reproduction numbers, i.e., the number of new infections caused by each infectious individual, the case fatality ratio (CFR), which estimates this proportion of deaths among identified confirmed cases. They also may quantify the infection fatality ratio (IFR), clarifying ambiguities create by asymptomatic infected hosts and delays between incubation, infection and heal/death. Important to note that official reported

confirmed COVID-19 cases may miss asymptomatic infections, which can bias estimates of disease severity and IFR, so epidemiological models could help reduce this uncertainty. The Susceptible-Exposed-Infected-Removed - SEIR model was previously adapted in this study to take into account the original SARS-Cov-2 D-form and its dominant G-variant with; their own incubation rates, a pre-estimated fraction of symptomatic hosts, and a pre-inferred time-varying reproduction number. COVID-19 has a latent or incubation period, during which the individual is said to be infected but not infectious. Members of this population in latent stage are labelled Exposed (but not infectious). Taken into consideration the original SARS-Cov-2 D-form and its dominant G-variant labelled as D and G, the deterministic model with the groups: Susceptible, Exposed (D and G), Infected (D and G), and Removed (recovered and deaths/fatalities) is labelled as the $SE_DE_GI_DI_GR$ Model. The number of fatalities is assumed dependent on the confirmed COVID-19 cases (Infected D and G). This dependence is not linear neither monotonic, and was previously obtained from official reported cumulative values. COVID-19 cases in Brazil are reported by public health and private services, and interrelated on a website which summarizes daily the aggregated counts.[22] Worth to mention that by the time this study was conducted, estimative on the number of sub notifications and information on the number of non-symptomatic were unreliable. Under those assumptions, the set of ordinary differential equations – ODE governing our $SE_DE_GI_DI_GR$ model follows;

$$\frac{dS(t)}{dt} = -\beta(t).[I_D(t) + I_G(t)].\frac{S(t)}{N} \quad (1)$$

$$\frac{dE_D(t)}{dt} = \beta(t).I_D(t).\frac{S(t)}{N} - \sigma_D.E_D(t) \quad (2)$$

$$\frac{dE_G(t)}{dt} = \beta(t).I_G(t).\frac{S(t)}{N} - \sigma_G.E_G(t) \quad (3)$$

$$\frac{dI_D(t)}{dt} = -\gamma_o.I_D(t) + \sigma_D.E_D(t) \quad (4)$$

$$\frac{dI_G(t)}{dt} = -\gamma_o.I_G(t) + \sigma_G.E_G(t) \quad (5)$$

$$\frac{dRe(t)}{dt} = \gamma_o.I_D(t) + \gamma_o.I_G(t) \quad (6)$$

where $S(t)$, $E_D(t)$, $E_G(t)$, $I_D(t)$, $I_G(t)$, and $Re(t)$, are respectively daily numbers of Susceptible, Exposed (D and G), Infected (D and G), Removed (recovered and deaths) individuals. $S(t) + E_D(t) + E_G(t) + I_D(t) + I_G(t) + Re(t) = N$ = Constant. $\beta(t) = R(t)/\gamma_o$, where $R(t)$ is the time-varying reproduction number. $R(t=0) = R_o$. γ_o is the removed rate that infected individuals (symptomatic and non-symptomatic) recover, leaving the infected groups $I_D(t)$ and $I_G(t)$. The accumulated SARS-Cov-2 confirmed cases are obtained from:

$$C(t) = \alpha_s.\int_0^t [E_D(\tau) + E_G(\tau)].d\tau \quad (7)$$

where $\alpha_s = 0.47 \pm 0.09$ is the estimated fraction of symptomatic individuals. Major assumptions for this model are: $\sigma_D = 0.5$ and $\sigma_G = 0.25$ are respectively the incubation rates for D and G SARS-CoV-2 exposed hosts. It is assumed that both D and G groups share the same $R(t)$ time dependence. In short, N, σ_D and σ_G are the only fitting parameters to data. The susceptible number $N=60 \times 10^6$ (28.7% of the Brazilian population) is chosen as the minimum number of susceptible to account for the accumulated confirmed cases in the study period. Fatalities were modelled as a function of the confirmed cases $C(t)$, and this dependence, obtained from official reported cases and deaths, is not linear neither monotonic as discussed latter.

Methodology

The methodology employed in this work was presented in a previous publication, and illustrated in a flowchart diagram[7]. Such a methodology was applied to forecast the COVID-19 outbreak in S. Paulo, the largest populated city in Brazil, selected as a first reliable cohort study. In such methodology, a first series of published data, determines the epidemiological parameters that govern the dynamics of the compartmental model, and adjust the model parameters aiming to forecast the COVID-19 evolutionary outbreak in a longer period. The deterministic and compartmental model provides predictions of the time series of infected individuals and fatalities in the studied population.

Simulations of average epidemic outbreak scenarios were arbitrarily dependent on the level of NPIs enforcement and release. Forecasts pointed how such NPI policies alter the contamination pattern and suggested the existence of a second epidemic wave.

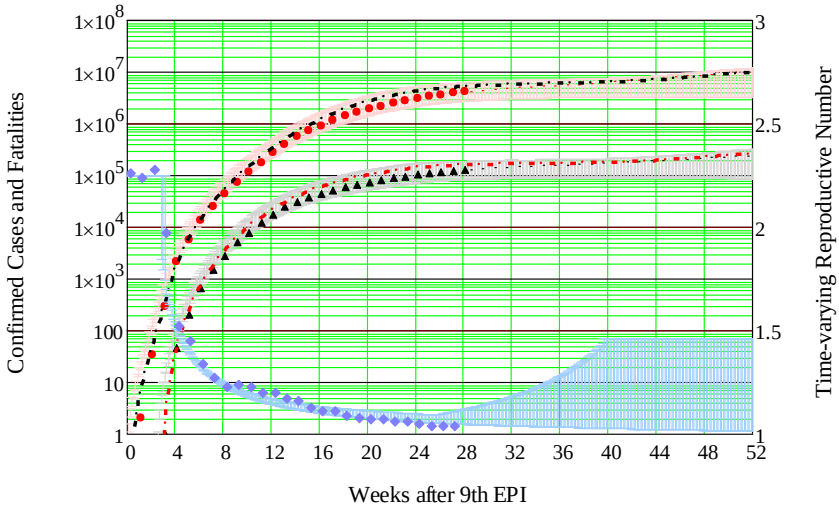
Results

A first series of official published data,[22] from February 25th to August 19th, 2020 EPI Week #9, was previously reported on September 2020.[8] In this first report, the deterministic SEIR model was selected to estimate outcomes to the dynamics of the COVID-19 epidemic breakout in Brazil. All model's parameters were adjusted aiming to forecast one year of the COVID-19 evolutionary outbreak.

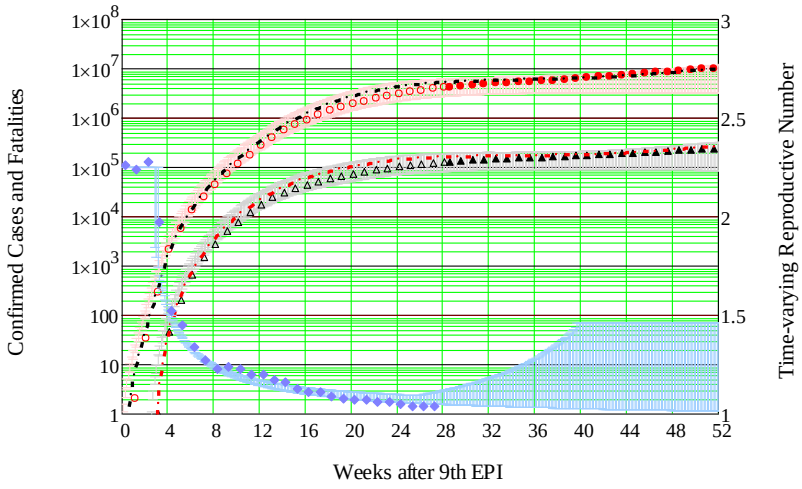
All model parameters presented in Fig 1a were estimated by minimizing the mean squared quadratic errors. A key parameter in deterministic transmission models is the reproductive number R, which is quantified by both, the pathogen and the susceptible population in which it circulates. Thus, a single pathogen, like the SARS-CoV-2, will have different R values depending on lineage and transmission dynamics of the population experiencing the outbreak. When infection is spreading through a population that may be partially non-symptomatic, an accurate estimation of the instantaneous R value is crucial to plan and control the infection.[11] During the COVID-19 outbreak in Brazil, the methodology to estimate the basic reproduction number was presented in a previous publication.[8] The time-varying reproduction number was estimated from a Gamma Distribution Time Generation (Mean Value = 3.6, Variance = 4.8) on confirmed cases from February 25th to August 19th.

The complete estimated sequence of *R(t)* values as well as its Credible Intervals (5 – 95)% is presented in Fig. 1a where time is shown in units of EPI weeks. Time-varying R(t) describes COVID-19 time shifts incidence. Rapid epidemic growth phases are associated with R(t) values higher than 2. In contrast, epidemic decline phases may be characterized by $2 > R > 1$. The beginning of the pandemic spread in Brazil presented, for a one-week time window, R-values larger than 2. However, after two weeks, R(t) shows a monotonic decline, reaching values 4% above the unit, as a consequence of collective acquired immunity and NPI regional interventions across de country (Fig.1a). NPIs in Brazil was implemented between EPI week #10 and #12 across the countries' 27 federal states, and consisted of social distancing, mask wearing, school, and stores closures. At the start of the epidemics, value of $R_o > 2$ was reported in São Paulo concurrent with the timing of state mandatory NPIs.[6]

$SE_DE_GI_DI_GR$ model fittings to data on accumulated confirmed cases (symptomatic infected individuals), and fatalities are show in Fig. 1. The only fitting values are: $N = 6x10^7$ (28.7% of Brazilian population), $\beta(t=0) = 1.265$, $\sigma_D = 0.25$, $\sigma_G = 2\sigma_D$. Initial conditions: $S(0) + E(0) = N$, $E(0) = E_D(0) + E_G(0) = 8$, $I_D(0) = I_G(0) = R_e(0) = 0$. The fitting to the infected individuals (logarithmic scale) presents standard deviation SD = 0.08 over six orders of magnitude. The SARS-Cov-2 spike variant G associated with greater infectivity and higher viral loads is modelled by a higher (two fold) incubation rate σ_G as compared to σ_D. The fraction of symptomatic hosts $\alpha_S = 0.47 \pm 0.09$ within 95% credible interval was estimated comparing IFR to CFR reported values[20]. The estimated mean value and deviation are consistent with previous analysis.[14] Fatalities were modelled as a function of the confirmed cases *C(t)*. By the end of 2020, the predicted numbers of confirmed cases in Brazil, within 95% credible intervals, may reach 6 Million (5 - 7) and fatalities would accounts for 184 thousand (134 – 218). The total number of infected individuals is estimated to reach (13 ± 1) Million, 6.2% of the population.



(a)



(b)

Figure 1. (a) The first series of data previously reported[8] on confirmed cases and fatalities are shown by open red circles, and open black triangles respectively. The fitting average values shown by black (confirmed cases) and red (fatalities) dashed lines are: $N = 6.10^7$, $\beta_o = 1.265$, $\sigma_D = 0.25$, $\sigma_G = 2\sigma_D$ $\alpha_s = 0.47$. Vertical bars represent 5 to 95% CRI. (b) Second series of official published data on confirmed cases and fatalities, added in this report, are shown by solid red circles, and black triangles respectively. Shadow gray and rose areas represent 5 to 95% CRI. Right vertical axis shows the time-varying R(t) (solid blue diamond) as the result of control interventions. Blue shadow indicates the range of arbitrarily maintaining or releasing the NPIs over specific time periods.

As mentioned before, COVID-19 was first reported in Brazil in February 2020. Early June 2020, Brazil began averaging about 1,000 deaths per day from Covid-19, joining the United States as the countries with the world's largest death tolls. Then, starting in August 2020, the spread of the virus reduced, and the daily death toll began to drop. In a short period of time, shopping malls, restaurants and beaches started to draw crowds again. Tourist attractions reopened in several cities, and case numbers started rising and daily death tolls shot above 500 a day again. Major cities such as São Paulo, Rio de Janeiro, and Recife found hospital bed occupation rates reaching over 80%, and pressure increased on Brazilian authorities to re-establish restrictive measures. A key parameter in deterministic transmission models is the basic reproductive number R_o, which is quantified by both, the pathogen and the particular population in which it circulates. Thus, a single pathogen, like the SARS-CoV-2, will have different R_o values depending on the characteristics and transmission dynamics of the

population experiencing the outbreak. Accordingly, $R(t)=\psi(t).R_o$ becomes dependent on the NPI policy $\psi(t)$. Once more, the analysis of a time-varying reproductive number R(t) continue to be applied to forecast the consequences of arbitrarily maintaining or releasing the NPIs over specific time periods.

Discussion

A second series of official published data shown in Fig. 1b confirms the forecasts reported many months earlier, presenting the consequences of maintaining or empirically release the NPIs over specific time periods.[7] As the result, the average fitting value to confirmed cases (logarithmic scale) for the whole study period presents standard deviation SD = 0.097 and root mean square RMS = 0.11. By the end of the study period, the official number of confirmed cases reached 10.6 Million an increase of 2.5 folds on the population-based sample (4.2 Million), with 9% deviation under the predicted average value. The reported fatalities accounted for 255 Thousand (16% under the average of predicted deaths). In short, the previous forecasts reported nationally for the expansion of the COVID-19 epidemic through the Brazilian country with over 210 million inhabitants are confirmed by the epidemiological SEIR model as shown in Fig. 1b. After the beginning of March 2021 new sharp peaks appears on the reported numbers of daily new infected and new fatalities. These were caused by a combined result to the appearance of the prevalent SARS-CoV-2 P1 variant, and the increased number of vaccinated individual, as commented later.

The data ratio, fatalities to confirmed cases, presents a temporal evolution that is not linear neither monotonic (Fig. 2). The non-zero ratio of deaths/(confirmed cases) by COVID-19 (open red circles), begins two weeks after the first reported case, rises monotonically, after roughly seven weeks reaches a maximum of 7%, and drops continuously to a ratio around 2.6%. Possible explanations are many: Increased number of tests and reports available after the first weeks of the epidemic outbreak raises the number of confirmed cases; ICU improved medical procedures; among others. COVID-19 was detected in Brazil in the 9th EPI week of 2020, and testing procedures for the SARS-CoV-2 virus was effectively included in the surveillance four weeks later. Such a time dependent ratio was included in the compartmental model. . Data points for the first 35 EPI weeks (open red circles) were previously reported on.[8] Data points for the last 25 EPI weeks (solid red circles) added after the model was published, granted confidence to this forecast.

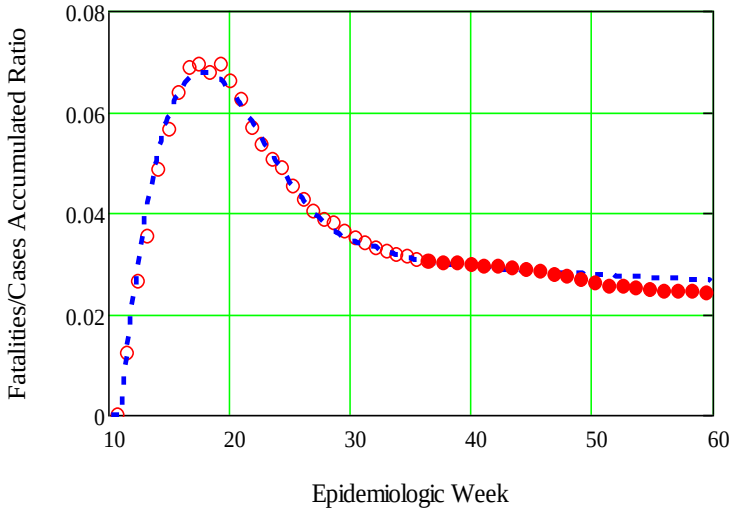
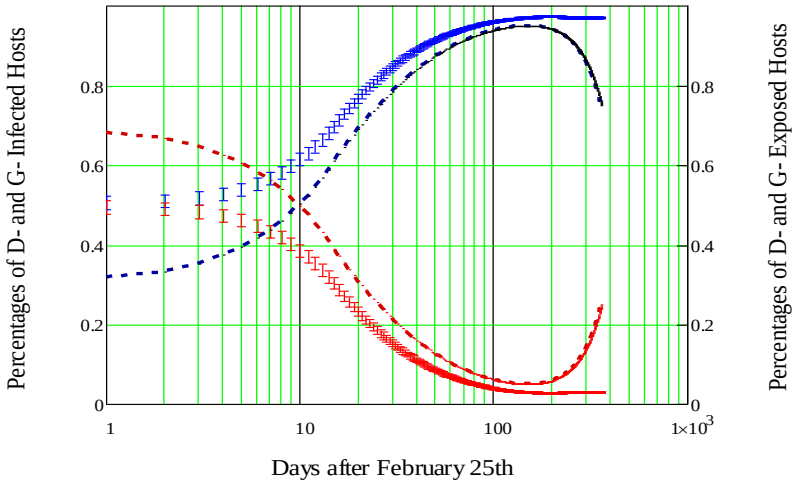
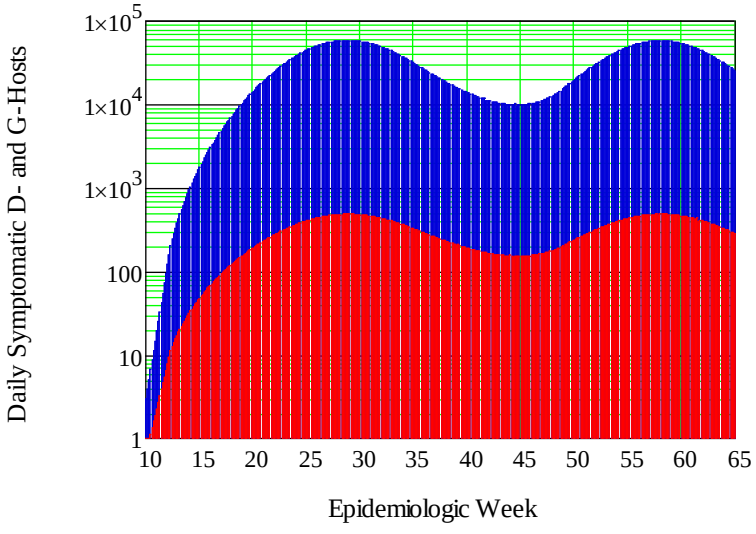


Figure 2. Time dependence of the Fatalities/(Confirmed Cases) ratio. This ratio presents a time-dependence that is not linear neither monotonic. The non-zero ratio of deaths/(confirmed cases) by COVID-19 (open red circles), begins three weeks after the first reported case, rises monotonically, after roughly seven weeks reaches a maximum of 7%, and drops steadily to a ratio around 2.5 %. The fitting equation (dashed blue curve) to the experimental data multiplied by Eq.7 allows estimating the accumulated fatalities as shown in Fig. 1

Regarding the original SARS-CoV-2 D-form and its G-variant, the only distinction in modelling is their own incubation rates. Additionally, it is assumed both forms produce the same disease severity/fatalities, and share the same instantaneous reproductive number, which is an oversimplified assumption. The initial percentage values set in the ODE for individuals exposed to the original D-form and its G-variant were respectively 66% and 34%. Figure 3a presents the evolution of exposed and infected host to the original D-form and its G-variant according to model. These results confirm the prevalence of the G-variant SARS-CoV-2 form in COVID-19 pandemic as globally predicted. The G-variant form reaches a maximum of 96% of exposed individuals as previously reported for South America.[6] The resulted D- to G-shift in the epidemiologic spread suggests that the G-variant form may have a fitness advantage. These findings support continuing surveillance of SARS-CoV-2 mutations to support development of immunological interventions.



(a)



(b)

Figure 3. (a) Estimated evolution of exposed and infected host to SARS-CoV-2 original D-form and G-variant. Broken red and blue lines present respectively the evolution of D and G exposed hosts to SARS-CoV-2. Vertical red and blue bars are respectively the evolution $\alpha_S = 0.47 \pm 0.09$ *and E(0)=* 6 ± 2 *of D and G infected hosts. (b) Model prediction of the evolution of symptomatic infected host to SARS-CoV-2 original D-form and G-variant. Red and blue shades present respectively, according to model, the evolution of D and G exposed hosts to SARS-CoV-2.*

Novel SARS-CoV-2 lineage P.1 first identified in Manaus has been associated with potentially higher transmission rates, and was widespread across all Brazilian regions.[23, 24] On the other hand, a preliminary study conducted by Institute Butantan,[25] suggests the vaccination in Brazil by CoronaVac can neutralize variants P.1 and P.2 of SARS-CoV-2. P.1 was first worldwide reported on January 10, 2021, after been detected in four travellers from Brazil at Haneda airport in Tokyo. It was considered a "variant of concern" because it is more transmissible. Epidemiologists believe P.1 is one of the major causes for recent jump in COVID-19 cases and deaths, alongside the relaxing of mobility restrictions and the slow initial pace of vaccination. Since February 15 2021, in a period of 12 weeks, the variant P.1 of Covid-19, which emerged in Manaus, increased its representativeness in the cases of the São Paulo city from 0% to 91%. The estimate was based on virus samples taken from patients at Hospital São Paulo and confirms the prevalent spread of the new lineage.[26] As the result of this explosive spread, after March 2nd, sharp peaks appear on the reported numbers of daily new infected and new fatalities. These sharp peaks are caused by the combined results of the appearance of the prevalent SARS-CoV-2 P1 variant and the increased number of vaccinated individuals. As mentioned previously, compartments for individuals' vaccinated and additional prevalent SARS-Cov-2 variants were not included in this simple model, restricted to the first 52 EPI weeks, and their combined effects were not predicted. In short, during second half of 2020 a second wave was spreading fast in Brazil as in Europe, and across other continents. In the 30th to 45th epidemiological weeks, corresponding to the tail of the first wave, there was a substantial decline in cases and deaths, as modelled in this cohort study, and presented in Fig. 3. The end of this period also characterizes the division between the end of the first wave and beginning of the second one, in agreement to a recent publication.[27]

Brazil is the largest country in South America. The time interval comprising the first confirmed case in S. Paulo, and the first confirmed death in the Tocantins (in the Amazon forest), the last Brazilian state to report a COVID-19 fatality encompass 8 EPI weeks. Applying a single time frame for a close surveillance of viral transmission across the country limits an overall analysis. An alternative to overall visualize the pandemic stage is to follow the dependence of new weekly cases on their cumulative values, as shown in Fig. 4. Solid black circles are official reported values, and red points and dashed line are average predicted values. This alternative view clearly estimates the predicted, at the end of the first EPI wave, numbers of confirmed cases in the vicinity of 6 Million.

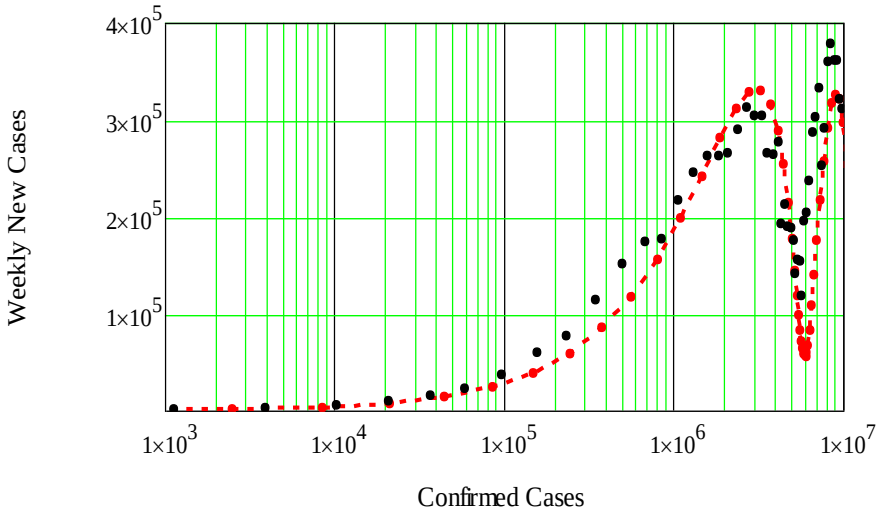


Figure 4. Weekly new cases and deaths (figure inset) versus confirmed cases and deaths respectively. Solid black circles are official reported values, and red solid circles are average predicted values. This alternative view clearly shows the first and second wave periods, and the estimated numbers of confirmed cases (vicinity of 13 Million), and fatalities over 330 thousand.

Conclusions

This work confirms the forecasts previously reported for the evolution of infected people, fatalities, and the appearance of a second wave starting last quarter of 2020 associated to the pandemic outbreak throughout the Brazilian country.[8] Cohort study was set as a country population-based analysis on confirmed COVID-19 cases on exposed symptomatic individuals. The analysis was applied to predict the consequences of the progressive NPI releases previously enforced during the first semester of 2020. An updated series of published confirms the forecasts previously reported for the evolution of infected people and fatalities associated to this pandemic outbreak. By the end of the study period, the official number of confirmed cases reached 10.6 Million an increase of 2.5 folds on the population-based sample (4.2 Million), with 5% deviation under the predicted average value. The reported fatalities accounted for 255 Thousand (4% under the average of predicted deaths). In short, the previous forecasts reported nationally for the expansion of the COVID-19 epidemic through the Brazilian country with over 210 million inhabitants were confirmed during the study period. After the beginning of March 2021 new peaks appears on the reported numbers of daily new infected and new fatalities. These were caused by a combined result to the appearance of prevalent SARS-CoV-2 P1 variant, the progressive NPI realise, and the increased number across de country of vaccinated individual.

Acknowledgments

The author thanks the financial support granted by FUNTTEL - Fundo para o Desenvolvimento Tecnologico das Telecomunicações - Brasil. This paper reflects only the author's views and the Agencies are not responsible for any use that may be made of the information contained therein. This manuscript is an updated version the preprint reported on MedRxiv - doi: https://doi.org/10.1101/2020.09.25.20201558.

Contributions

S. Celaschi wrote the entire manuscript and prepared all the figures.

Funding

Financial support granted by FUNTTEL - Fundo para o Desenvolvimento Tecnologico das Telecomunicações. Financial grant # 01.16.0053.01 FINEP/MCTI from the Brazilian Ministry of Science, Communications, and Innovation.

Role of the Sponsor

The sponsors had no role in the preparation, review or approval of the manuscript and decision to submit the manuscript for publication. Any opinions, findings, and conclusions or recommendations expressed in this article are those of the author and do not necessarily reflect the views of the FUNTTEL/FINEP.

Declaration of Competing Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of Data availability

All data presented in this study is public available.

Ethical Approval

The manuscript does not contain experiments on animals and humans; hence ethical permission is not required.

References

1. Zegarra-Valdivia JA, Chino-Vilca BN, Ames-Guerrero R. " Knowledge, attitudes, and perception susceptibility towards the COVID-19 pandemic in Latin American region" Medical Research Archives [Online]. Volume 10, Issue 4 April 2022.
2. de Souza WM, Buss LF, Candido DS et al. Epidemiological and clinical characteristics of the COVID-19 epidemic in Brazil. Nature Hum. Behav. 4, 856–865, 2020.
3. Felix HC, Fontenele J. Instantaneous R calculation for COVID-19 epidemic in Brazil. medRxiv preprint. https://doi.org/10.1101/2020.04.23.20077172.
4. Qianqian L, et al., The Impact of mutations in SARS-CoV-2 spike on viral infectivity and antigenicit. Cell, July 2020, https://doi.org/10.1016/j.cell.2020.07.012.
5. Darlan SC.Evolution and epidemic spread of SARS-CoV-2 in Brazil. medRxiv preprint https://doi.org/10.1101/2020.06.11.20128249.
6. Celaschi S. Quantifying effects, forecasting releases, and herd immunity of the Covid-19 epidemic in S. Paulo – Brazil". medRxiv preprint https://doi.org/10.1101/2020.05.20.20107912.
7. Celaschi S. Second wave analysis and confirmed forecasts of the SARS-Cov-2 epidemic outbreak in São Paulo, Brazil. SciMedicine Journal. Vol. 3, Special Issue "COVID-19", 2021, DOI: 10.28991/SciMedJ-2021-03-SI-10.
8. Celaschi S. Modeling COVID-19 as a national dynamics with a SARS-CoV-2 prevalent variant: Brazil - a Study Case. MedRxiv. https://doi.org/10.1101/2020.09.25.20201558.
9. Zlojutro A, Rey D, Gardner L, A decision-support framework to optimize border control for global outbreak mitigation. Nature Sci Rep. 9, 2216 2019. doi.org/10.1038/s41598-019-38665-w.
10. Kissler SM, Tedijanto C, Goldstein E, et al.Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. Science. 14 Apr 2020. DOI: 10.1126/science.abb5793.
11. Thompson RN, et al. Improved inference of time-varying reproduction numbers during infectious disease outbreaks. Epidemics. 2019. DOI: https://doi.org/10.1016/j.epidem.2019.100356.
12. Fauver, JR, et al. Coast-to-coast spread of SARS-CoV-2 during the early epidemic in the United States. Cell. 181, 990–996.e5 2020.
13. Volz E, Hill V, et al. Evaluating the effects of SARS-CoV-2 spike mutation D614G on transmissibility and pathogenicity. medRxiv preprint DOI: https://doi.org/10.1101/2020.07.31.20166082.
14. Obadia et al. The Ro package: a toolbox to estimate reproduction numbers for epidemic outbreaks. BMC Medical Informatics and Decision Making. Vol. 12: 147. Published online 2012 Dec 18. DOI: 10.1186/1472-6947-12-147.
15. Ali ST, Lin Wang E, et al. Serial interval of SARS-CoV-2 was shortened over time by NPI interventions, Science 28 Aug 2020: Vol. 369, Issue 6507, pp. 1106-1109 DOI: 10.1126/science.abc9004.
16. Kimihito I, et. al. Relative instantaneous reproduction number of Omicron SARS-CoV-2 variant with respect to the Delta variant in Denmark. J. of Medical Virology. Short Comm., Dec. 2021. https://doi.org/10.1002/jmv.27560.
17. Cori, A, Ferguson, NM, Fraser C., Cauchemez S. "A new framework and software to estimate time-varying reproduction numbers during epidemics". Am. J. Epidemiol., 178, 1505–1512, 2013.
18. Thompson RN, et al. See [11], https://shiny.dide.imperial.ac.uk/epiestim/ Site visited on May, 30, 2022.
19. Estimating mortality from COVID-19, WHO reference number: WHO-2019-nCoV-Sci_Brief-Mortality-2020.1 Scientific Brief 4 Aug. 2020.
20. Marr V, and Quartin, M. An estimate of the COVID-19 infection fatality rate in Brazil base on a seroprevalence survey. medRxiv preprint. DOI: https://doi.org/10.1101/2020.08.18.20177626.
21. Grassly N, Fraser C, Mathematical models of infectious disease transmission. Nature Rev Microbiol 6, 477–487, 2008. DOI: 10.1038/nrmicro1845.
22. https://covid.saude.gov.br/ . Visited on May 25, 2022.

23. Lamarca AP. et al. Genomic surveillance of SARS-CoV-2 tracks early interstate transmission of P.1 lineage and diversification within P.2 clade in Brazil. medRxiv preprint. DOI: https://doi.org/10.1101/2021.03.21.21253418
24. Faria NR. Genomics and epidemiology of a novel SARS-CoV-2 lineage in Manaus, Brazil. medRxiv preprint. DOI: https://doi.org/10.1101/2021.02.26.21252554
25. https://static.poder360.com.br/2021/04/estudo-preliminar-coronavac-11.Abr. 2021. Page visited on April 25, 2020.
26. https://agencia.fapesp.br/study-suggests-the-brazilian-variant-emerged-in-november-is-more-transmissible-and-can-cause-reinfection/35414/. Page visited on April 25, 2020.
27. Zeiser FA, et al., First and second COVID-19 waves in Brazil: A cross-sectional study of patients' characteristics related to hospitalization and in-hospital mortality. Lancet Reg. Health Am. 2022 Feb; 6:100107. DOI: 10.1016/j.lana.2021.100107. Epub 2021 Nov 1. PMID: 34746913; PMCID: PMC8557995.