# A Novel Approach To Analyse Infectivity Of Pre-Symptomatic Sars-Cov-2 Carriers Against Testing Delays

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**Summary**
One of the biggest times trial, COVID-19 that has affected the entire human race, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Amidst a lot of research going on with regards to the prediction on growth and transmission through Symptomatic carriers of the virus, the vulnerability of the spread of infection by pre-symptomatic carriers of SARS-COV-2 is also a matter of grave concern. Pre-Symptomatic carriers either don't realize that they are potential suspects of the virus or ignore the significance of otherwise mild symptoms resulting in delayed medical diagnosis and testing. The proposed work presents an analysis of clinical characteristics of 450 contacts who had onset of very low to mild COVID-19 symptoms with varying delays in exposure to medical care facilities for testing or treatment. The results show that 20% of the subjects were pre-symptomatic and establishes that the pre-symptomatic cases where the first medical intervention was delayed with a delay factor greater than the Series Interval were responsible for spreading 61% of the total infection.

***Keywords:***
*SARS-CoV2, symptomatic, pre-symptomatic, logistic regression, Series Interval*

## 1. Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by a recently discovered coronavirus. Originated in Wuhan, China, the World Health Organization declared it as a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020. Till date, more than 7.96 million cases of COVID-19 have been reported in more than 188 countries and territories, resulting in more than 434,000 deaths [1].

Cases who have acquired the virus infection and are pre-symptomatic with very mild to mild symptoms but are ignorant and have not been tested or exposed to medical intervention early may work as sleeper cells to spread the infection to a large population. The study, published in the journal Science[3], finds that about 4 in 5 people with confirmed coronavirus in China were likely infected by people who didn't know they had it.

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A lot of researches have been carried out in recent times to delve deep to understand the growth, spread, and containment of the bizarre CoV-2 virus. On the one hand, the symptomatic carriers of the virus have certainly attracted medical attention and just-in time intervention to contain the spread. On the other hand, lack of awareness, limited testing and facilities, ignorant mindset, disease phobia, and other socio-psychological factors have contributed to non-surfacing of the pre-symptomatic carriers. The nations who have been instrumental in carrying out large scale testing are able to restrict the spread to 10-20% of the population. This is a clear signal of curbing the spread at the root through potential carriers, if any.

The proposed work carries out a novel analysis exploiting the epidemiological dynamics of the infectivity of the virus to find the infectivity potential of the virus through pre-symptomatic carriers. The next section discusses some of the related research works.

## 2. Related Works

Margaretha et al. (2014), in their paper discuss that the series Interval of a disease which is infectious in nature can be a good criteria to allow investigators identify epidemiological links between cases and transmission models. Xie Z (2020), in his research presents the extent of SARS-CoV-2 infection in children. Zhang Y (2020) in their paper presents the epidemiological characteristics of an outbreak of 2019 novel coronavirus (COVID-19) in China.

Wang et al. (2020) finds that presumed hospital-related transmission was suspected if a cluster of health professionals or hospitalized patients in the same wards became infected and a possible source of infection could be tracked. Ming Gao et al. (2020) finds that the although asymptomatic carriers are liable to spread infection but infectivity of some asymptomatic SARS-CoV-2 carriers

might be weak. Teo (2020) uses a smartphone pulse oximeter to detect Silent Hypoxia in Covid-19 Pneumonia at a nearly stage. The detection of an initial drop of oxygen saturation level to detect CoVid19 infected patients who begin suffering from pneumonia can be treated with highly invasive procedures such as intubation and mechanical ventilation.

Chun Ka Wong et al. (2020) propose an Artificial intelligence mobile health platform to detectCOVID-19. In this approach, authors use a randomized controlled trial protocol by using a wearable biosensor explore the potential of using wearable biosensors to continuously monitor multidimensional physiological parameters for early detection of COVID-19 clinical progression.

In another research, Murugan et al. (2020) use a Fiber-Optic Biosensor device to rapidly detectCOVID-19. Ap lasmonic fiber-optic absorbance biosensor (P-FAB), which is developed with the collaboration of the association of the other, has been invented. This P-FAB is a hand-held diagnostic device based on a U-bent optical fiber probe used to detect the COVID-19.

Jiang et al. (2020) proposed RGB-based infrared sensors to detect respiratory infections. The images of people wearing a mask are captured from a thermal camera; a deep learning neural network is performed to work on the classification between healthy and abnormal respiration conditions. Won et al. (2020) developed a safe and low-cost Detection Protocol for COVID-19 at laboratory-based. This protocol is based on rtPCR and is composed of accessible specimen collection via Trizol-based RNA purification and swab sample. This approach focused on detecting negative cases rather than detecting positive covid-19 cases. Ozturk et al. (2020) proposed an x-ray based automatic COVID-19 detection by using deep neural networks. In this approach, the authors discussed detecting the infected area with the help chest x-ray by using a heatmap.

Based on the above works, this research paper carries out a mathematical analysis and quantification of the correlation between the epileptological parameters and late medical intervention to establish the infectivity potential of the novel corona virus. The next section discusses the epileptological parameters of the novel coronavirus.

## 3. Epidemiology of the virus

The Severe Acute Respiratory Syndrome SARS coronavirus (SARS-CoV) started off from a bat was first identified during 2002-2003 when it first infected humans in the Guangdong province of southern China in 2002. The epidemic at that time affected 26 countries and resulted in more than 8000 cases in 2003 with a Case-Fatality-Rate of 10%. A decade later, Middle East respiratory syndrome (MERS), a viral respiratory disease, was caused by another mutant of novel coronavirus (a mutated form of the virus from the coronavirus family) and was first identified in Saudi Arabia in 2012.

Furthermore, in the year 2019-2020 SARS-CoV-2 or novel corona virus, COVID-19 outbroke from Wuhan China. All these three forms of virus belong to the same family. Table 1 draws a comparison of the epidemiology of the three coronaviruses.

Table 1: Epidemiology Parameters of three mutants of CORONA Virus

| Parameter | Significance | SARS-CoV | MERS | COVID-19 |
|---|---|---|---|---|
| **Case Fatality Rate** | Rate of Deaths w.r.t total infected cases | 10% | 34% | 3.7% |
| **Reproductive Ratio(R0)** | Rate of Spread of Infection | 1.3 | <1 | 3 |
| **Series Interval (SI)** | Duration 0f transmission of infection from primary to secondary cases | 2.2 to 2.8 | 2.5 | 5 to 7.5 |
| **Category** | Animal to Animal Transmission | Zoonotic | Zoonotic | Zoonotic |

The factors Reproductive Ratio and Series Interval are crucial because they allow investigators to identify epidemiologic links between cases and serve as an crucial parameter in epidemic transmission models used to design infection control strategies [5].

As the world is fighting hard to overcome the spread of the highly contagious corona virus and flatten the infection inflation curve, lot of ways are being researched to contain the pandemic. Logically, there could be three ways to curb this deadly virus:

1. Expose the entire population without any restriction so that almost all get infected and develop natural resistance for further infection.
2. Isolation or lockdown with testing to restrict the spread
3. Developing a Vaccination as a long-term solution

The practical viability of option 1 is extremely irrational; option 3 is the most evident solution keeping the past outbreaks in history. In the event of non-availability of vaccines against the virus till date, early testing and classification of the novel coronavirus disease and instantly quarantine the infected people due to unavailability of specific drugs is the only way to cure and control.

## 4. Proposed Work

The proposed work attempts to analyze the mathematic correlation between onset of symptoms in potential carriers and the time gap in seeking medical intervention using the epidemiological dynamics of the novel corona virus. Open access freely available datasets 'kaggle' were used for the study. The main contributions of the present work are as follows:

1. Establishing a correlation between the onset of symptoms and delay in seeking medical test as one of the key factor in spreading the disease.
2. Quantifying the rate of potential infection spread through such pre-symptomatic carriers.

The subsequent subsections discussspecific contribution in detail.

### 4.1 Correlation between the onset of symptoms and delay in seeking medical test

COVID-19 is a deadly virus that is spread from Human-to-Human. One of the important factors in spreading the infection that is ignored is the difference between the onset of symptoms in an individual and the day of a seeking medical test.
With reference to Table 1 indicated in section 3, as per the epidemiology of the pandemic viruses, two parameters that decide the spread chain of a virus are R0 (Reproductive Rate) and Series Interval (SI). For the novel corona virus COVID-19, the R0=3 and the SI=6 (median value considered). The spread chain is explained in Fig 1.

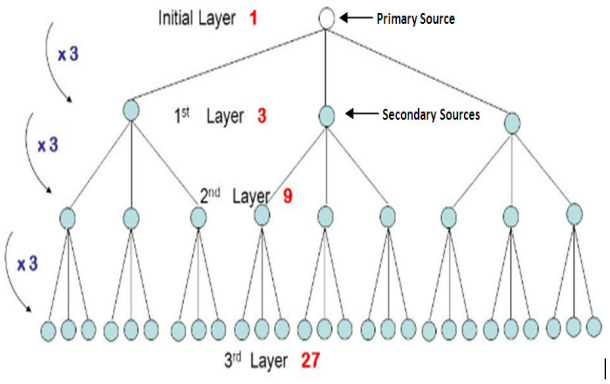


Fig 1: Exponential Growth Chain of COVID-19 (with$R_0$=3)

The R0 score indicates one infected person can infect 3 contacts, 3 can infect 9, 9 can infect 27; hence the spread curve is exponential, which is highly undesirable. Further, the Series Interval (SI) determines that given a primary source who is infected with the viral load irrespective of being Symptomatic, Asymptomatic or Pre-Symptomatic, when can he transmit the virus. That means how fast a transmission can spread. The higher the value the desirable it is, the lower the value, the alarming it is.

When compared with the other counterparts of this virus, SI of COVID-19 is certainly better, but R0 is not desirable. In our case, the value of SI ranges from 5-7.5, which means an infected person can infect a secondary contact anywhere between 5th of 7.5th of him getting infected.

Given a situation when the primary carrier out of ignorance or unaware of being infected (in the case of Asymptomatic/Pre-Symptomatic carriers) does not seek medical testing within day1 to day5, the person becomes a vulnerable source for the spreading the infection to his contacts, which can, in turn, spread the infection further and so on and the chain becomes endless.

Fig 2 shows the plot of the subjects w.r.t the date of onset of symptom/infection and date of medical intervention in testing/diagnosis.

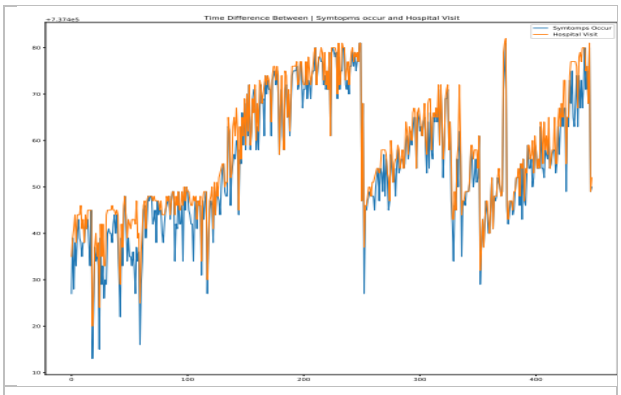


Fig 2: Plot of onset of symptom/infection(Blue line) and hospital visit (Orange line)

The count plot in Fig 3 shows the count of carriers who are subjected to medical testing soon after they had onset of the symptoms or developed viral load, hence were isolated from the uninfected population. There is a subset of the population who were pre-symptomatic and were not exposed to medical testing within the safe window i.e before the SI interval, which is <5, and the count plot is shown in Fig 4. These carriers thus kept mingling with the healthy ones in the normal course and unknowingly spread the infection.

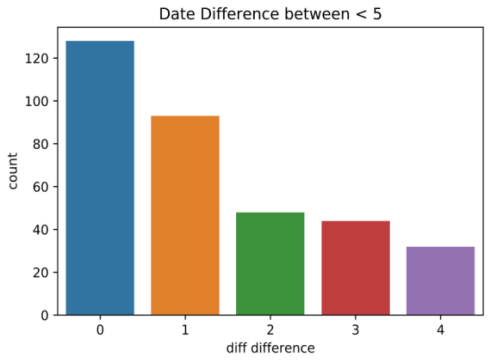


Fig 3: Count plot of Carriers who were diagnosed early

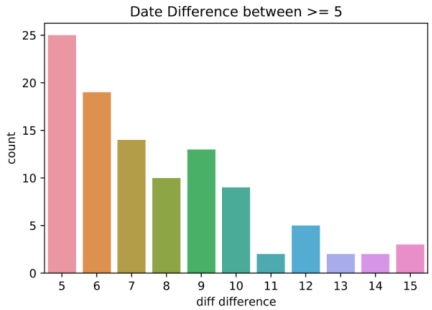


Fig 4: Count plot of Carriers who were diagnosed in the SI window or later

Table 2: Testing Window and it's Frequency Distribution

| Testing Window w.r.t SI | Frequency Distribution count | % w.r.t Pre-Symp (out of 450) | |
|---|---|---|---|
| When it is < 5 | 339 | 75.3% | |
| When it is = 5 | 32 | 7.1% | Combined =24.6% |
| When it is > 5 | 79 | 17.5% | |

As enumerated in Table 2, around 24.6% of the pre-symptomatic population did not get medical testing on time, either due to various reasons like insufficient testing approach or other socio-psychological factors, hence were responsible for propagating the infection to a healthy set of the population.

The next subsection quantifies the vulnerability of infection.

### 4.2 Quantifying the rate of potential infection spread through such pre-symptomatic carriers

This section presents a mathematical quantification for the percentage of the population who are pre-symptomatic and infected but are not subjected to the medical protocol or isolated from the healthy population. As seen in the Table 2 about 24.6% of population sought medical intervention on or after day 5, which means that these subjects were within the Series Interval window and most potent to spread the infection to their secondary contacts.

Consider the Susceptible->Exposed->Infectious-> Recovered (SEIR Model), as shown in Fig 5.Susceptible (S) set is the entire set of the population that is vulnerable to catch population. Exposed (E) set is the set of population that has been exposed to the infection. Infected (I) is the set of population that is already infected. Recovered (R), is the set of population who has already been infected and has recovered.

Let's formulate the mathematical Susceptible->Exposed->Infectious (SEIR Model).

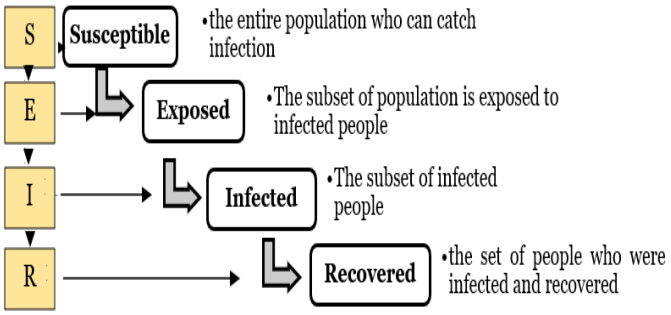


Fig 5 : SEIR Model

At any given time t,

N = total population which is assumed to be constant

$$S(t)+E(t)+I(t)+R(t)=N \quad (1)$$

The rate of change of each of the factors is given by-

Rate of change of S is proportional to the sum of no. of susceptible persons coming in contact with either Infected persons (S*I) or Exposed persons (S*E). The terms aSI and qSE is denoted with -ve sign because these set of population will leave this group and join the Infected or Exposed group respectively.

$$\frac{dS}{dt} = -aSI - qSE \quad (2)$$

Rate of change of E is proportional to the sum of no. of susceptible persons coming in contact with either Infected persons (S*I) or Exposed persons (S*E) minus the Exposed population who become infected.

$$\frac{dE}{dt} = aSI - cE + qSE \quad (3)$$

Rate of change of I is proportional to the Exposed population who become infected minus Infected ones who get recovered.

$$\frac{dI}{dt} = cE - bI \qquad (4)$$

Rate of change of R is proportional to the Infected population who had recovered.

$$\frac{dR}{dt} = bI \qquad (5)$$

In the Eq (3) the Exposed population which is latent group capable of spreading the infection contains a factor +qSE, defined as the no. of susceptible population coming in contact with Exposed population. The exposed population is the pre-symptomatic ones ($n_v$) who are still not in the infected category but are latent and can infect others. Thus, qSE is defined by-

$$qSE = {n_v}^{R_0} \qquad (6)$$

Thus Eq (3) is rewritten as

$$\frac{dE}{dt} = aSI - cE + {n_v}^{R_0} \qquad (7)$$

Or

$$\frac{dE}{dt} \propto {n_v}^{R_0} \qquad (8)$$

Which is an exponential term, hence undesirable. In the instant case, $n_v = 104$ (people who sought medical intervention within or after the SI Window) which comprises of 24.6%. Table 3 shows the number of persons who could be infected by the 24.6% population at worst case. The average case column shows the global average growth rate of infection i.e., on an average of 3%(approx.) increase in cases per day has been recorded [2] as per global corona growth rate.

Table 3: Infection Rate of Exposed Population

| Day | EXPOSED (Worst case) | Average (as per Global growth rate 3%) | % case per 1 lakh |
|---|---|---|---|
| Day 5 | 104 | 3.12 | 0.00312 |
| Day 6 | 312 | 9.36 | 0.00936 |
| Day 7 | 936 | 28.08 | 0.02808 |
| Day 8 | 2808 | 84.24 | 0.08424 |
| Day 9 | 8424 | 252.72 | 0.25272 |
| Day 10 | 25272 | 758.16 | 0.75816 |
| Day 11 | 75816 | 2274.48 | 2.27448 |
| Day 12 | 227448 | 6823.44 | 6.82344 |
| Day 13 | 682344 | 20470.32 | 20.47032 |
| Day 14 | 2047032 | 61410.96 | 61.41096 |

The mathematical analysis shows that about 61410 persons will get infected by these 104 people. Thus 24.6% percent of the latent vulnerable population contributes to 61% of the healthy population per 1 lakh. The infection inflation curve is shown in Fig 5.

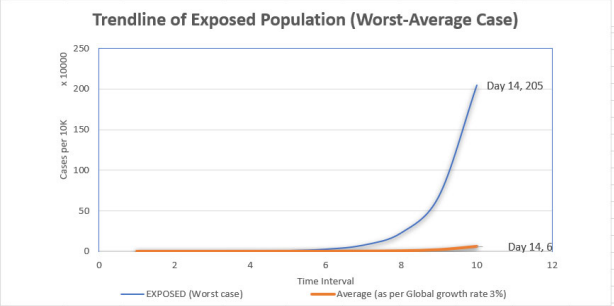


Fig 5: Infection Inflation curve

For containing the pandemic, the factor $\frac{dE}{dt}$ should be equal to zero over a time period.

$$\int_{t0}^{t1} \frac{dE}{dt} = 0 \qquad (9)$$

That means $aSI - cE + qSE = 0$

If we are able to control qSE to minimal, by restricting multiplication S and E then Infected cases will reduce and the subsequently I becomes zero, I=0 hence

$$\frac{dE}{dt} = 0 \qquad (10)$$

Thus isolating the S from E is the key idea, which is possible only when we identify the pre-symptomatic cases early and isolate before the SI window starts. The next section concludes the research findings.

## 5. Conclusion

The aim of this research paper is to predict the effect of covid-19 carriers in the coming days if there are latent carriers in the population. Clinical researches and online reports on the ongoing pandemic reveal that more than 50% of the infection is spread by carriers who actually do not know that they are affected.

Epidemiology dynamics of the virus shows that isolating the susceptible population from Exposed population early is the key idea, which is possible only when we identify the pre-symptomatic cases early and isolate before the SI window starts.

This paper presents a novel approach considering two key factors for interpolating the spread of COVID-19 infection,

R0 and Series Interval and mathematically establishes that isolating Suspected Population from the Exposed population before the SI window starts could contain the spread of the virus.

The analysis has been quantified using SEIR model. The results so obtained show that 24% of carrier population is possible to spread the infection to 60% of healthy population in every 1 lakh population.

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