

COVID-19 Follows a Flattened Growth Curve Subsequent to Prolonged Intervention in A Population; Its Implication on Rate of Doubling Time & Plausible Suppression of SARS-CoV-2 Infection.

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ABSTRACT

COVID-19 is fast spreading around the globe in a highly contagious manner. In this article we have described that after prolonged interventions the percentage growth curve for COVID-19 cases showed a flattened nature, after prolonged volatility in number of COVID-19 cases. The stability in the growth curve was continuously maintained from 18 April, 2020 to 29 April, 2020. The significance of this sustained stable curve on survival & doubling time has been discussed. One significant part of the study reflected that the doubling time of COVID-19 cases showed a negative correlation with the percent increase in COVID-19 cases ($R=0.468$). It is plausible that if such negative correlation is maintained with further flattening of the growth curve at a lower level, it may influence the infective ability of nCoV-19 & ultimately have a positive evolutionary implication on the spread of COVID-19 among the population.

Key words: COVID-19; intervention; growth curve; survival; doubling time; correlation

I. **INTRODUCTION**

The novel coronavirus (SARS- COV-2) originated in Wuhan in Hubei province of China during December 2019, and has now spread across the world; the most affected being USA, Italy, Spain & now Germany. Until date there are no therapeutic agents which have shown any promise to control this highly infectious virus from spreading among human population.

SARS virus is an infectious agent belonging to the virus family Coronaviridae, which causes severe respiratory illnesses in humans and animals. SARS (severe acute respiratory syndrome) coronavirus (CoV) is a novel member of this family that causes acute respiratory distress syndrome (ARDS), which is associated with high mortality rates. Its characteristic feature is long latency period before the typical flu-like fever, cough, and shortness of breath manifest. The people infected with this virus may not show any symptoms for up to two weeks, allowing them to pass it on to others in the meantime.

Due to alarming nature of this disaster world-wide and to contain its spread in Indian population, The Hon'ble Prime Minister of India declared one day of 'Janata Curfew' on 22 March 2020, from 7AM to 9 PM followed by 'National Lockdown-I' for 21 days starting from 23rd March, 2020 midnight to Midnight of 14 April, 2020. During this period the number of COVID-19 cases abruptly came down due to break in the chain of virus infection, and showed flattening of growth curve until 31 March, 2020. Following which the number of COVID-19 cases showed fluctuations on several occasions.

Due to such variations the Lockdown was further extended for two weeks until 03 May, 2020 (Lockdown-II).

We have assessed the nature of spread of COVID-19 using a percentage graph which accurately reflects the changes in the spread of the disease (1). In earlier studies we observed that (a) much of the success of Lockdown depends on 'early detection' of the intervention introduced in the population so that fine tuning of the intervention could be made possible; that was ascertained by percentage curve. (b) Any unprecedented changes taking place due to any unforeseen event was clearly detectable at an early stage from the plotted percent graph & (c) The percent graph elucidated that the long term down trend of COVID-19 cases remained intact in the population. In this paper, we have endeavoured to further elucidate the role of prolonged Lockdown on the infectivity of this highly mutable Virus and its possible significance on disease control.

II. METHOD AND RESULTS: The present study was carried out on the data collected from Indian & other countries, which were diagnosed as COVID-19 positive cases, starting from March 03, 2020 until 29 April, from the websites of Government of India and other national News agencies.

The **Figure 1** reflects the total number of positive cases of COVID-19/day until 28 April, 2020. The number was collected at 10 PM each day from National news agencies & other sources. The graph reflected that there was an increase in the number of COVID-19 since 14 March, 2020. 31 March. However, on 01 April, 2020 there was an abrupt rise in the total number of COVID-19 cases due to some unforeseen circumstances and that was

maintained thereafter. Such alterations were visibly reflected in the percentage graph depicted in **Figure-2**. It is clear from Figure-2 that from 24 March 2020 onwards, that is, after Lockdown-I was implemented, there was a significant decrease in percent of COVID-19 cases and that was stably maintained until 31 March 2020. However, on the 1st of April, 2020 the percent graph reflected that there was 2.5 folds increase in COVID-19 cases compared to previous day. This change appeared as 'peak' (P1) in the percentage graph. Subsequently, the percentage graph reflected that there were smaller peaks on 4th April, 2020 (P2), 6th April, 2020 (P3) and 10 April, 2020 (P4) respectively, around 10% point. Between 10th April and 14th April it maintained a similar level. At this point, second Lockdown, designated as Lockdown-II was implemented to run until 17 May, 2020. Since 14th April 2020, the percent of COVID-19 cases came down to around 6% and after remaining volatile for some time the percentage graph stabilised at 4.6% from 26 April, 2020 and the flattened nature of the curve was maintained. In spite of the stability in the percentage graph, the number of patients recovering from COVID-19 was rather low in Indian population compared to other countries with higher number of COVID-19 cases. The results shown are for 29th April, 2020. The result in **Table-1** shows the number of COVID-19 cases who recovered from the disease in different countries compared to that of India (7797). In percentage point, as shown in **Figure-3**, the maximum number of recovery was noted in Germany (75%) and lowest number of recovery was recorded in Russia (10%); though maximum numbers of recovered patients were in the USA (142238), in terms of

percentage point it was only 13.7%. In India the recovery of patients from COVID-19 was rather low (24%). In order to ascertain whether rate of recovery had any correlation with number of recovery, a correlation study was made and the result is shown in **Figure-4**. The figure shows a weak positive correlation (R squared value is 0.468). However, the same graph when plotted for Indian population for a extended period between 21 April, 2020 -02 May, 2020, it showed a better result showing there was room for increase in recovered patients that could impact the survival rate, as shown in **Figure-5** (The R squared value =0.997). In order to ascertain the rate of the disease progression, doubling time of COVID-19 cases was determined. The results are depicted in **Figure-6** which reflects that doubling time of infection steadily increased from 3 days to 10 days following implementation of two Lockdowns. The maximum doubling time of 10 days was as of 28 April, 2020. This appeared to be a 'noteworthy- information'. When correlation coefficient graph was plotted between doubling time of COVID-19 cases and the percent change in COVID-19 progression, it showed a negative correlation between the two variables suggesting that with the increase in one variable there would be a decrease in other; the R squared value being 0.468 (**Figure-7**).

III. DISCUSSION:

The recent disaster caused all over the world by influx of nCoV-2 has prompted a massive global effort to hunt for a cure/vaccine for COVID-19. Unfortunately, until date no drugs/vaccine is available which could help to fight the disease. In recent times much faith was put on the use of drug,

Hydroxychloroquine sulphate, for the treatment of COVID-19 but results obtained so far has not been conclusive.

The rapid spread of nCOV-19 in the USA and other western countries has reemphasized the importance of introducing intervention/lockdown and social distancing at an early stage of COVID-19 progression, in controlling the spread of the disease. Over the last few months, in spite of all efforts, it was not possible to prevent the virus from 'community spread' in western countries. Contrary to situation in the west, India however, was an exception as it introduced physical intervention in the form of a Lockdown on March 23, 2020, when number of COVID-19 positive cases was small. The intervention introduced in March, 2020, had an instant effect in slowing down the spread of the contagious virus (SARS-COV-2). We assessed the spread of COVID-19 by using a percentage curve described earlier (1). It was observed that after introduction of Lockdown a 'stable flat curve' was recorded until 31 March 2020. However, the picture abruptly changed from 1st April 2020 onwards, when there was a substantial increase in COVID-19 positive cases. As illustrated in Figure-2 the percent change in COVID-19 cases continued to be volatile until April 9, 2020. Between 10th April and 14th April it maintained a similar level. Since 14th April 2020, the percent of COVID-19 cases came down to around 6% and after remaining volatile for some time the percentage graph stabilised at 4.6% from 26 April, 2020 and the flattened nature of the curve was maintained until 29 April, 2020.

The silver lining so far, about this highly infectious disease is that there are many instances where individuals with COVID-19 have recovered completely

world-wide including India. Many such recovered patients showed presence of antibodies against the SARS-cov-2 and transfer of 'Plasma' taken from recovered patients were able to cure patients suffering from COVID-19. Studies from South Korea further confirmed the role of immunity, when such recovered individuals were protected from re-infection. In our study we have demonstrated that while Germany had the maximum percent of recovery, Russia had minimum number of recovery from COVID-19 cases. In India, the percentage of recovery was low & correlation study between recovery from the disease and percent of COVID-19 cases, between April 21-May 2, 2020 was strong ($R^2 = 0.997$).

It was clear from this study that due to prolonged implementation of lockdown, there was stability in the growth curve of COVID-19 at a lower level of 4.5%-5%. However, this also appears to be high and there is need to bring it down to much below 5%. However the decrease in the percent of COVID-19 cases was reflected in the doubling time of the COVID-19 cases. The doubling time gradually increased and was at 10 days as of 29 April, 2020. Interestingly, when plotted in a correlation coefficient graph, the percent change in COVID-19 cases showed a negative correlation, albeit weak, with the doubling ($R=0.468$). A negative correlation describes the extent to which two variables move in opposite directions. In this instant case the two variables representing the percentage change in COVID-19 cases and doubling time of COVID-19 cases respectively would be moving in the opposite direction. Simply, meaning greater the doubling time, lower the rate of COVID-19 cases/infection. This result is very significant as because

it addresses the infectivity of the virus which if manipulated by prolonged intervention, could slow/suppress the rate of spread of COVID-19 in the population.

The SARS-CoV-2 is a highly mutating virus which is presently having ~10 strains, of which strain A-2a is most infectious by virtue of mutation, a change in a single amino acid from aspartic acid to glycine in the spike protein of the virus, which is known to increase the ability of novel coronavirus to bind to the ACE-2 receptor on the pulmonary cells in the Lungs of human body. At present strain A-2a is the most prevalent strain in the world; in India ~45% of the COVID-19 cases were found to be infected by this strain.

Therefore, more efforts must be directed to implement social distancing and sustained Lockdown to bring the level of COVID-19 cases down to much less than 5%. Such a change could have a sustained impact on the doubling time of the virus infection which could aid in bringing down the correlation coefficient to a critical level. From the data available, it could be hypothesized that sustained waning in the ability of nCoV-2 to infect fresh targets due to prolonged Lockdown, may have a positive evolutionary significance. The selective advantage acquired in the last few months by A-2a strain to survive better in the population, due to lack of use of the acquired advantage, may be helpful in eliminating the 'gains' obtained by the virus by Natural selection, leading to eventual suppression of this highly infectious virus.

IV. Acknowledgement:

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2. Different News channels of India
3. Thanks to Dr. Prabal Chakravarty to assist me in preparation of Manuscript and for encouragement.

V. References:

1. Chakravarty, P. A Simple Method for Detecting Early Signal in Nature of Progression of Covid-19 in Indian Population. Preprints 2020, 2020040041 (doi: 10.20944/preprints202004.0041.v1).

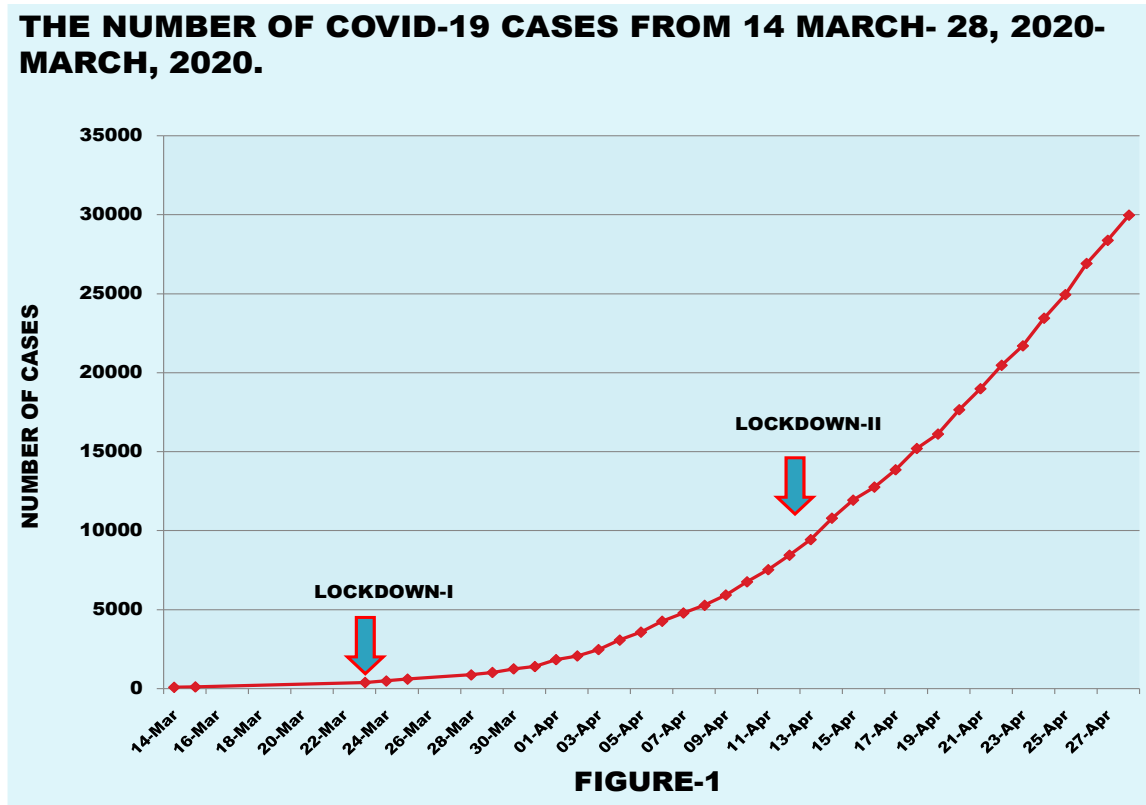
FIGURES FROM 1-7

Figure: 1 The graph shows the number of COVID-19 positive individuals in Indian Population at different time points. As evident from the graph, there is an increase in number of positive cases starting from 14 March, 2020 until 29 April, 2020. The two lockdowns (Lockdown-I & Lockdown-II) are marked on the graph by red arrows.

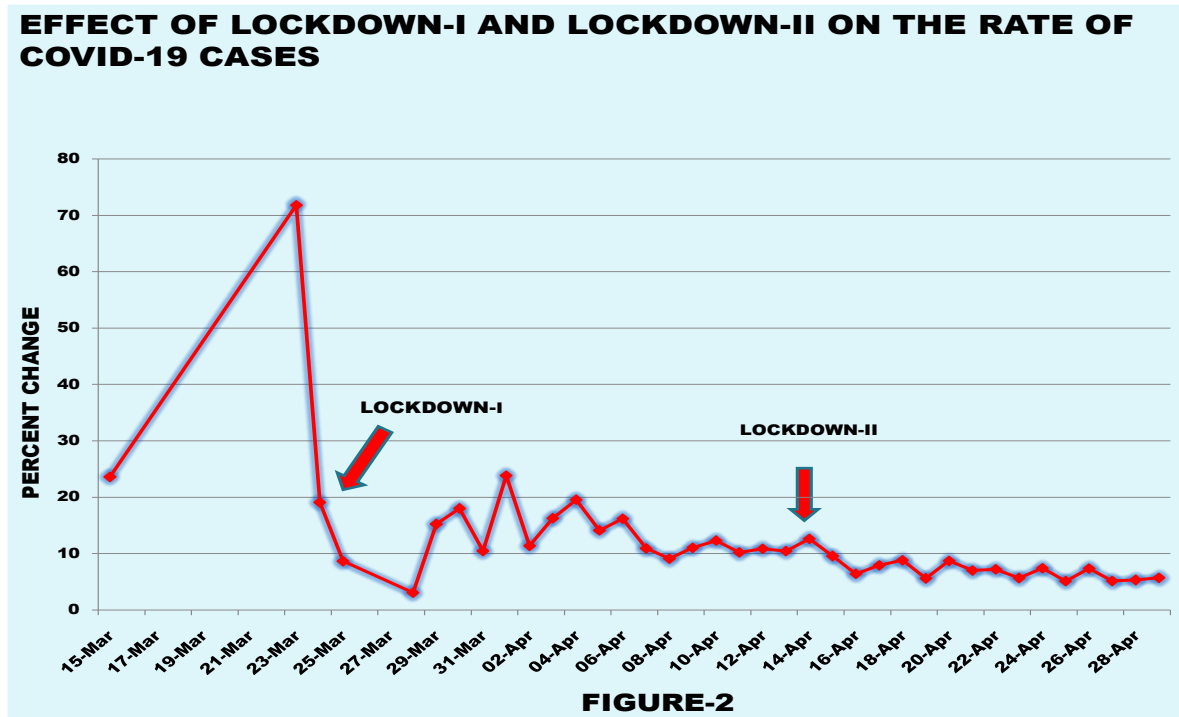
FIGURE-2

FIGURE: 2 The graph shows the percent change in COVID-19 cases from 15 March, 2020 until 28 April, 2020. The graph reflects that the positive effect of 'Lockdown' was maintained from 24 March, 2020 until 31 March, 2020. An abrupt increase in percentage of cases was noted on 01 April 2020 following which there was volatility until 14 April, 2020 when Lockdown-II was initiated. From 18 April, 2020 a flat curve was maintained until 28 April, 2020.

TABLE-1**RECOVERY OF COVID-19 PATIENTS IN INDIA
COMPARED TO OTHER COUNTRIES**

COUNTRY	NUMBER OF COVID-19 CASES	RECOVERED
WORLD	3116992	928930
CANADA	50026	19230
USA	1035765	142238
SPAIN	232128	123903
ITALY	201505	68941
FRANCE	165911	46886
GERMANY	160059	120400
RUSSIA	99399	10286
INDIA	31787	7797

TABLE-1

TABLE-1: The table reflects the number of patients who recovered from COVID-19 in different countries compared to India. Maximum number of recovery was noted in the USA.

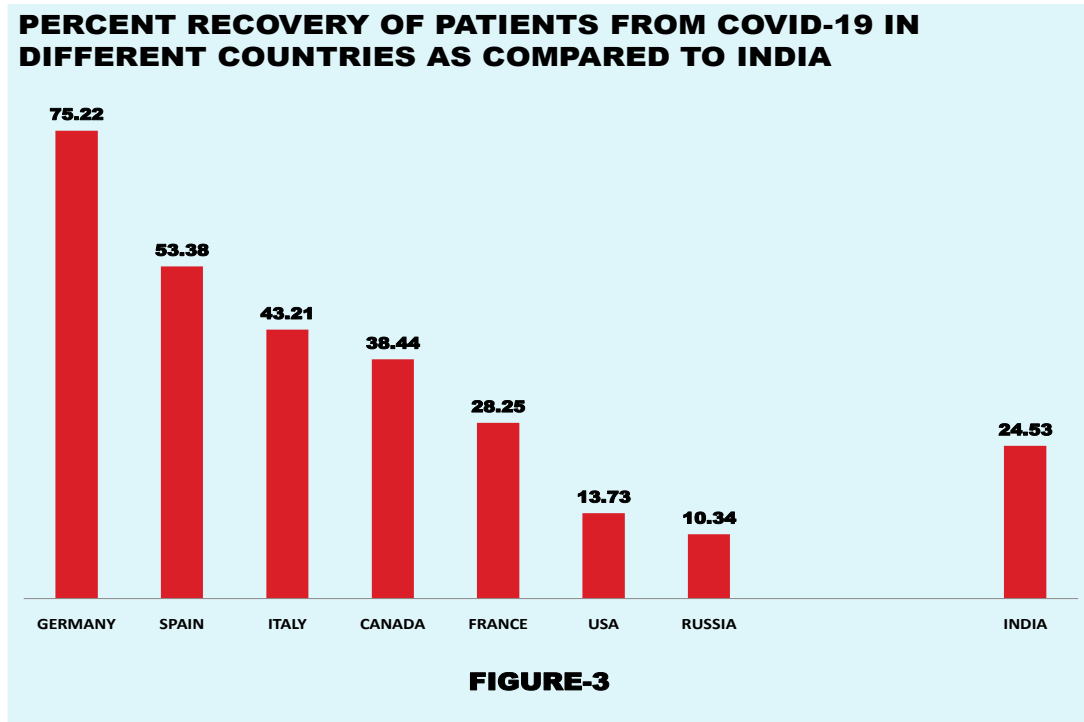
FIGURE-3

FIGURE-3: The graph shows the percent of recovery from COVID-19. The maximum number was recorded in Germany (75%) and the lowest in Russia (10%). India recorded a moderate recovery (24.5%) as on 29 April, 2020.

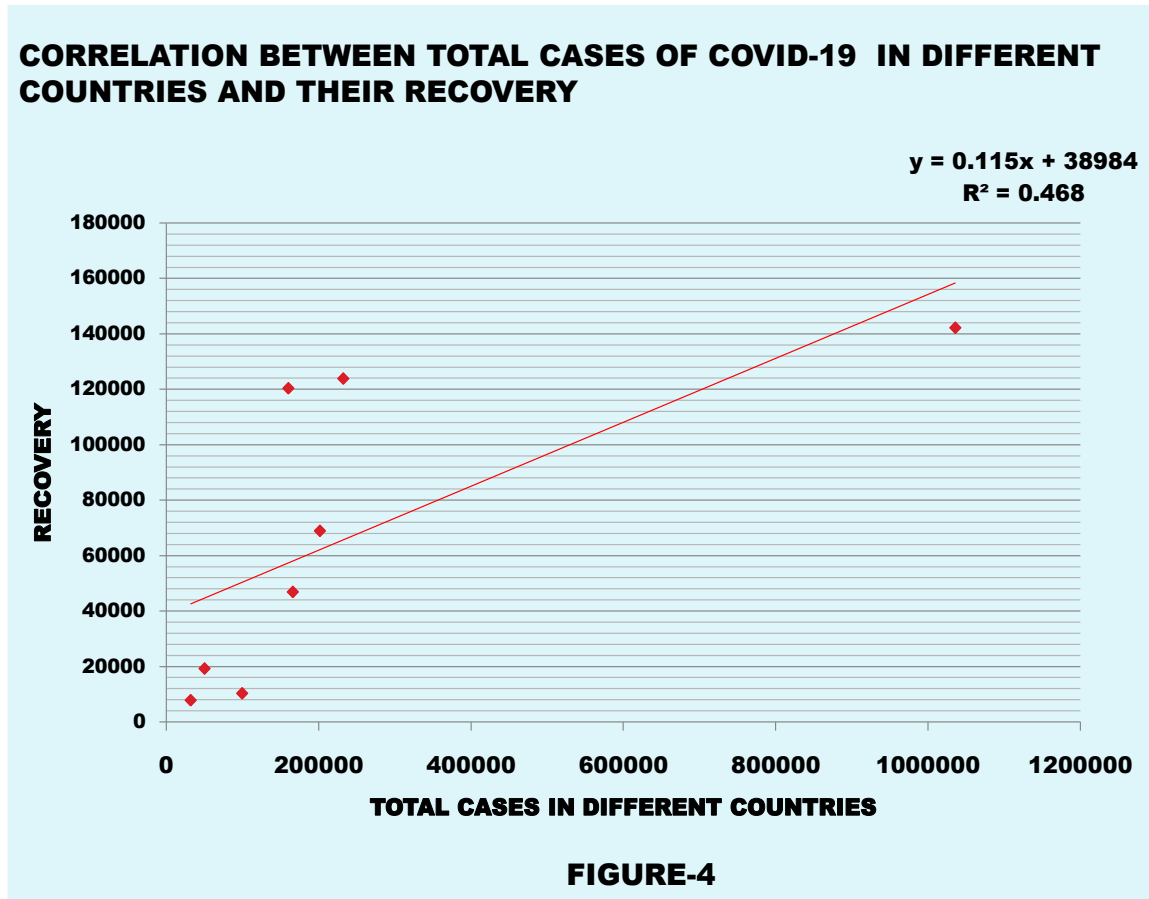
FIGURE-4

FIGURE-4: The Figure shows the correlation of number of cases of COVID-19 cases and their recovery as on 29 April 2020. The graph reflects that recovery has no influence on the rate of COVID-19 cases. The data does not include the data from India.

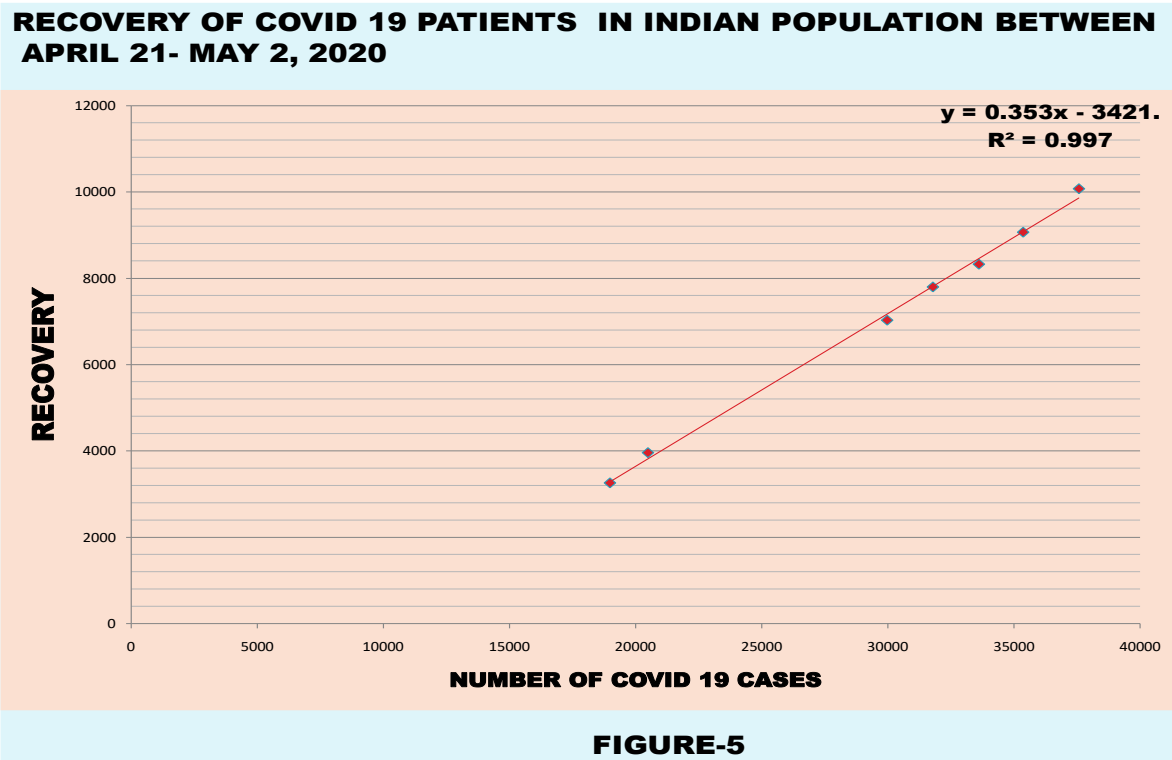
FIGURE: 5

FIGURE-5: The Figure shows the correlation of number of cases of COVID-19 cases and their recovery as on 29 April 2020 in Indian population from April 21- May 2020. The graph reflects that rate of recovery of patients requires to be improved in India.

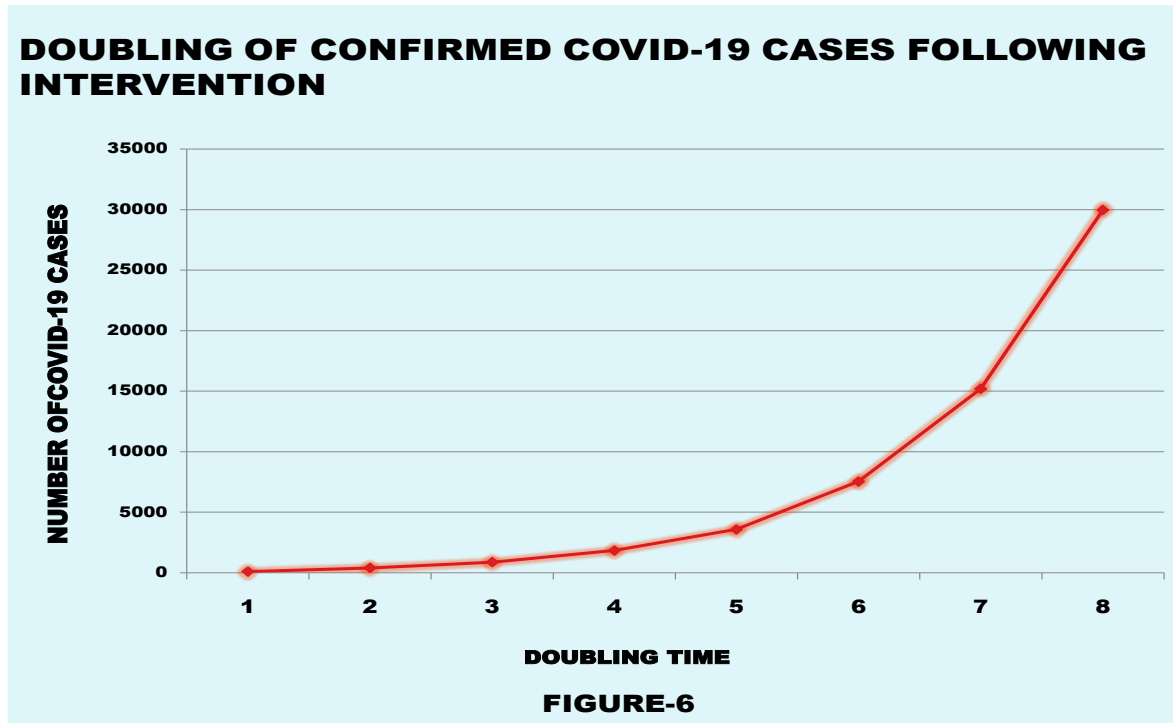
FIGURE-6

FIGURE- 6: The Figure shows the doubling time of COVID-19 cases following intervention. The doubling time has gradually increased to 10 days on 28 April, 2020.

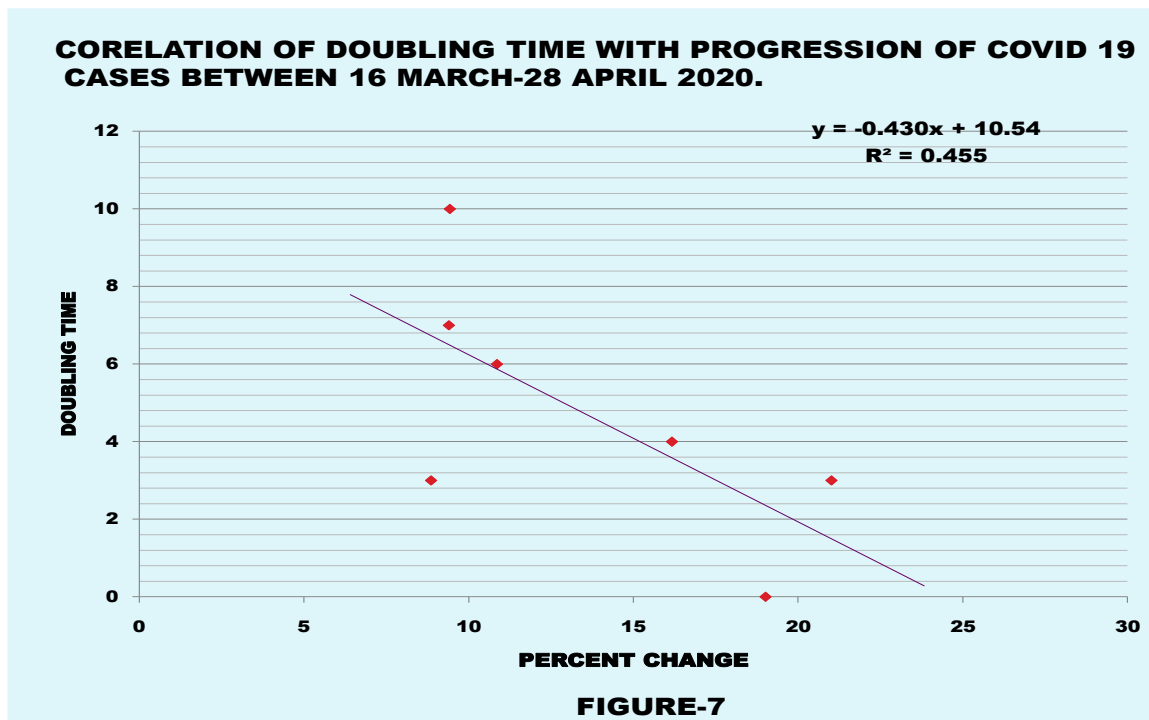
FIGURE: 7

FIGURE 7: The figure shows a weak negative correlation between doubling time and percent increase in COVID-19 cases. It demonstrates that when one variable increases other variable decreases. This has a direct bearing on the rate of increase of COVID-19 cases.