COVID-19 in Indian Population: A Transition from Protective Immunity to Herd Immunity.

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ABSTRACT

COVID-19 is fast spreading around the globe in a highly contagious manner. Until date there are no therapeutic agents/vaccines developed which could control this highly infectious virus from spreading among human population. Our earlier studies showed that implementation of prolonged lockdown had a profound effect on the rate of spread of COVID-19 in the population. The observed increase in doubling time of COVID-19 with a high recovery rate following complete Lockdown reflected that protective immunity was present against the virus among the population. In this article the data from three months post completion of Lockdown, that is during the month of September, 2020 was considered and results reflected that a significant down trend in the rate of COVID-19 with recovery reaching up to 69% of the affected cases of COVID-19 by September 30, 2020. The projection made of the data, up to 30 November, 2020, pointed towards continued decrease in active cases of COVID-19 and the recovery reaching to ~90% at present. The significance of all the data in controlling COVID-19 is discussed.

Key words: COVID-19 – interventions- protective immunity- herd immunity.

I. INTRODUCTION

SARS virus belongs to the family *Coronaviridae*, which is known to cause respiratory illnesses in humans and in animals. Coronavirus (CoV) is a novel member of this family that causes acute respiratory distress syndrome (ARDS), which is associated with high mortality rate. Two main strains of the virus have been identified as G614 and D614. The predominant strain circulating at present is G614 which is highly contagious.

In the past two decades, three deadly human respiratory syndromes associated with coronavirus (CoV) infections have emerged: Severe Acute Respiratory Syndrome (SARS) in 2002, Middle East Respiratory Syndrome (MERS) in 2012, and Coronavirus Disease 2019 (COVID-19) in 2019. These three diseases are caused by the zoonotic CoVs SARS-CoV-1, MERS-CoV, and SARS-CoV-2 respectively (Figure:13).

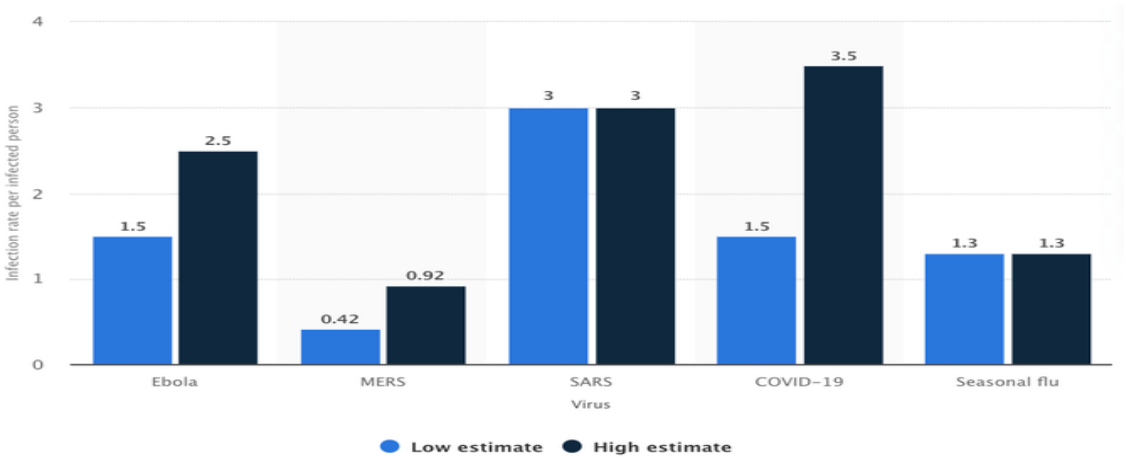

FIGURE-13

SARS-CoV-2 has affected millions and killed over one million worldwide. This unprecedented challenge has prompted widespread efforts to develop new vaccines and antiviral strategies against this virus.

Due to alarming nature of this disaster world-wide and to contain its spread at an early stage, a country wide Lock down was implemented for two months by the Indian Authorities starting from March 25 2020. In earlier studies, we have observed that evaluating percent change in progression of the disease was a better monitor to assess the progression of COVID-19 (1-2). It was also observed from our previous studies on progression and control of COVID-19 after implementation of Lockdown that a) percent alteration in COVID-19 cases, accurately reflected the progression and abrupt changes, if any, occurring due to any change b) With the implementation of complete Lockdown, there was an increase in doubling time of COVID-19 in the population; c) Lockdown had a negative impact on the rate of growth of COVID-19 cases & d) A significant recovery of patients from COVID-19 reflected existence of protective Immunity against SARS-CoV-2 (3-6). In this article we have taken up studies to further elucidate whether protective immunity was actually present/developing in the Indian population against COVID-19 and the plausible implication of moving towards 'Herd Immunity' to eradicate COVID-19 completely from the population.

II. **METHODS:** The present study was carried out on the data collected from different sources that include the Ministry of Health (Health bulletin) Government of India and from other National and International News outlets

starting from March 15, 2020 until date as described previously by us (1-6). The Statistical analysis was performed by Microsoft Excel and power point programs and the correlation studies were done using Pearson Correlation Coefficient program.

III. <u>RESULTS & CONCLUSIONS</u>: Briefly stated that a two month Lockdown was imposed during the end of March 2020 that ended on May 30, 2020. Following which, Lockdown was 'unlocked' in phases of one month starting from 01 June, 2020. In this study, as the focus was on evaluating the extent of protective immunity developed in the population, the data was analysed for the entire month of September (Unlock-4), that is, three months post Lockdown.

The **Figure 1** reflects the percent change in COVID-19 cases during the Month of September, 2020. The graph reflects a volatile nature in percent change of COVID-19 cases at the beginning of September, 2020 due to some untoward events (unpublished data). However, the trend line stabilised with time and positively registered a downward trend until 30 September, 2020. Another interesting finding from this graph is the trend line was until October 30, reflect that the rate of COVID-19 could be under full control provided there is no sudden 'spurt' in cases of COVID-19 as observed earlier due to contribution from a 'single source' for which the entire graph was disturbed during the month of April, 2020 (4). The trend line appears to be weak with the R^2 value at 0.311 suggesting future 2 to 3 months may be crucial. However, the positive feature of this study is the rate of recovery from COVID-19 has been phenomenal as shown in **Figure-2**. The figure

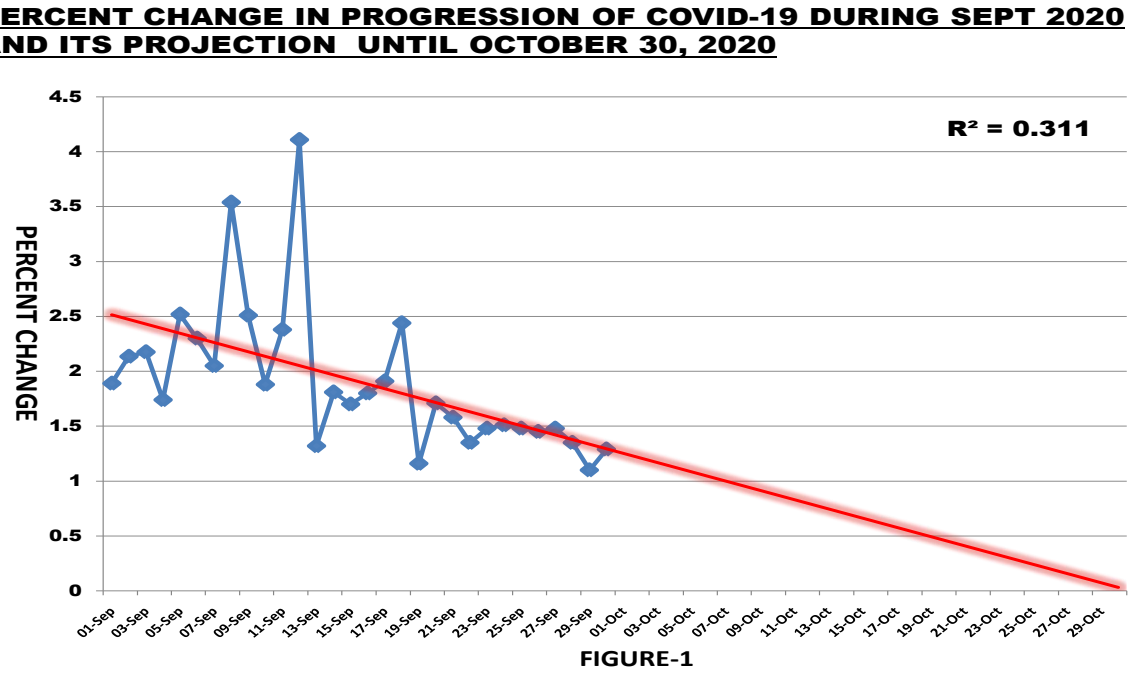

Figure 1: The figure reflects the percent change in COVID-19 during the month of September, 2020 and it projects a possible trend in COVID-19 at the end of October, 2020.

shows that the total number of active cases of COVID-19 and those who recovered completely from COVID-19 during the entire month of September, 2020. The **blue bar** in the graph representing recovered cases show a steady and linear increase in the number of recovered patients from COVID-19 and as on September 30, 2020 the recovery was at 83.3% with R^2 value of 0.995. However, there was not much change in the number of active cases of COVID-19, which is represented by **red bar** in the graph (15.1%). The same outcome is also clearly demonstrated in **Figure: 3**, which shows that the active cases of COVID-19 maintained a flat curve for the entire period of September 2020 and the weak R^2 value 0.419 suggests that there could be improvement in the near future. However, the total number of recovered individuals showed a linear increase in number of patients recovering from

TOTAL RECOVERY AND ACTIVE CASES OF COVID-19 DURING THE MONTH OF SEPTEMBER, 2020

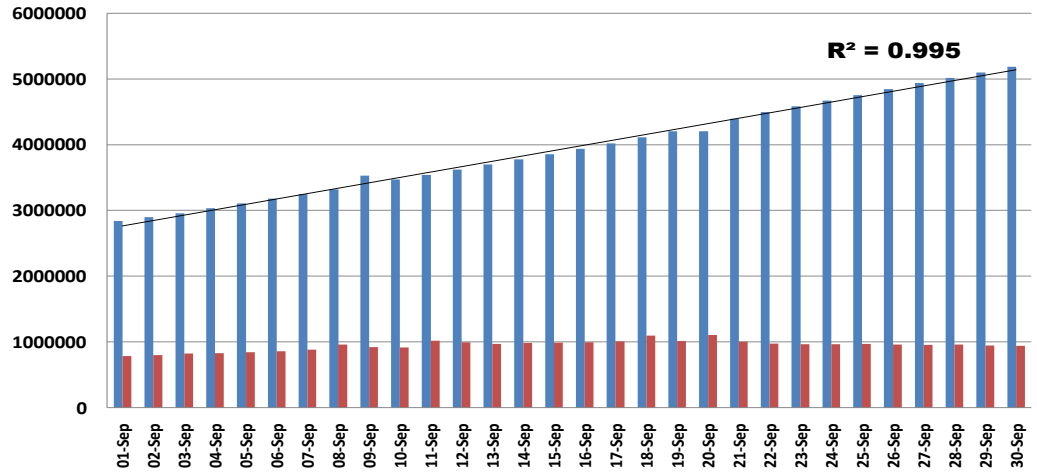

FIGURE:2

Figure 2: The Figure depicts the Active cases suffering from COVID-19 & those individuals who showed recovery from active disease showed a gradual increase in number.

ACTIVE CASES OF COVID-19 COMPARED TO RECOVERD INDIVIDUALS BETWEEN 01 SEPTEMBER 2020 – 30 SEPTEMBER, 2020

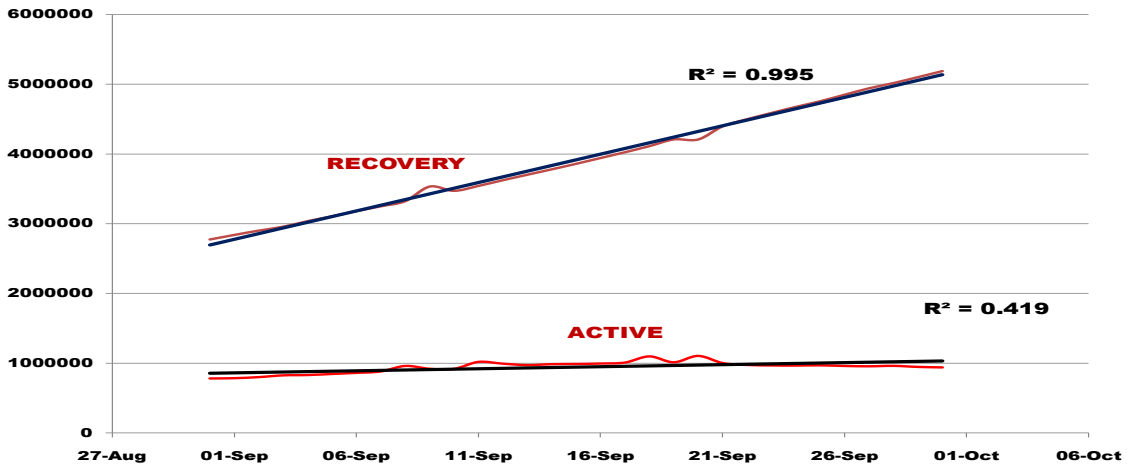

FIGURE-3

Figure 3: The Figure depicts the Active cases suffering from COVID-19 had a flattened curve showing some degree of volatility during month of September, 2020. On the contrary those individuals who showed recovery from active disease showed a gradual increase in number.

from the beginning of September, 2020 with R^2 value being 0.995 (p value ≥ 0.05). Interestingly when the total active cases was considered during the end of September, that is between 24 September and 30 September, 2020, the line graph showed that the number of active cases, after some volatility, gradually decreased from 27 September onwards and the trend line reflected a down ward trend since around the same time as shown in Figure-4.

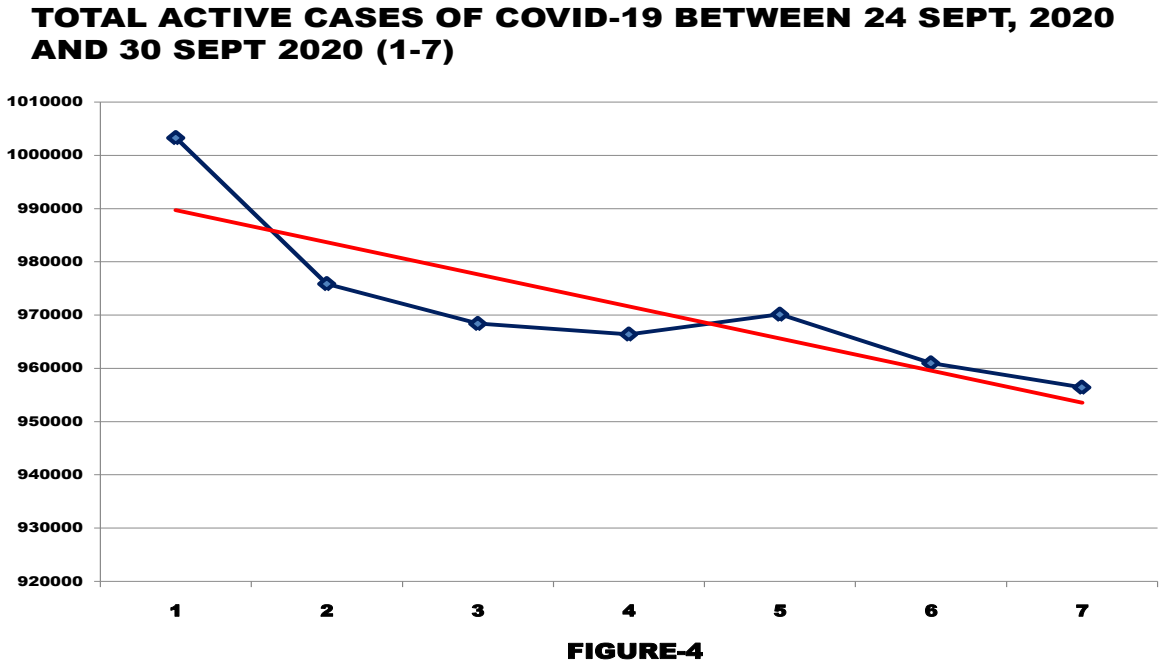

Figure 4: The Figure depicts the Active cases suffering from COVID-19 between 24 September, 2020 and 30 September, 2020 showing a downward trend.

When the total active cases were plotted on a correlation coefficient graph for a period of ten days beginning from 20 September to 30 September, 2020, it reflected that there was a negative correlation though weak with R^2 value of 0.553 as shown in **Figure: 5**. This explains the flatness of the curve observed in Figure-3 representing the entire month of September, 2020. The

pattern shown in Figure 2-5 reflects the actual trend in the active cases of COVID-19 is downward.

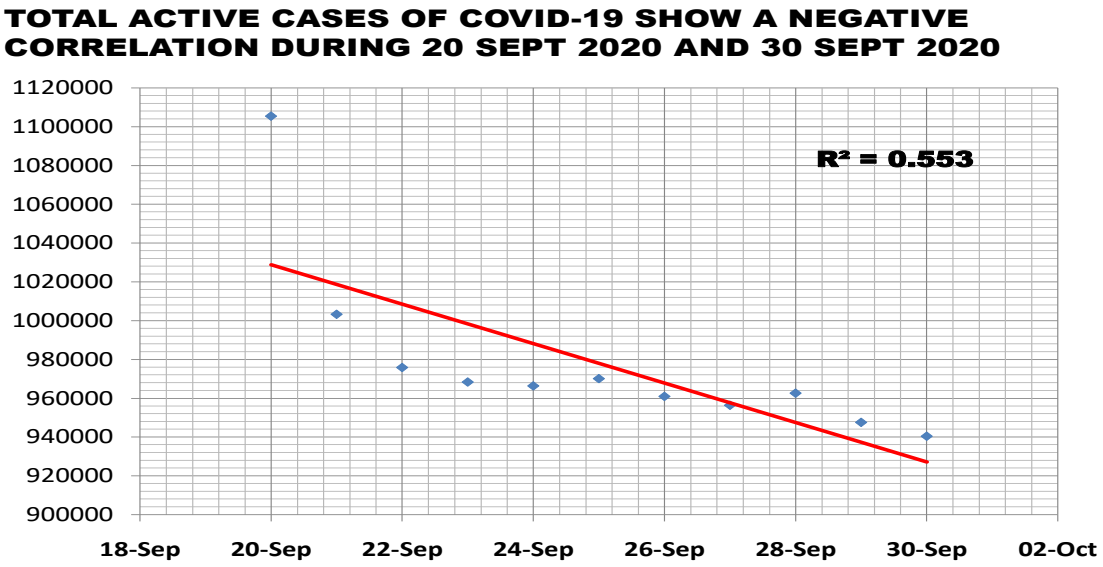

Figure 5: The scatter plot describes a decline in active cases from 20 September until the end of September, though it was a weak correlation with R^2 value of 0.553.

However, when the active cases of the last day of 30 September, 2020 were compared with the last day of August, that is, 31 August, 2020, as shown

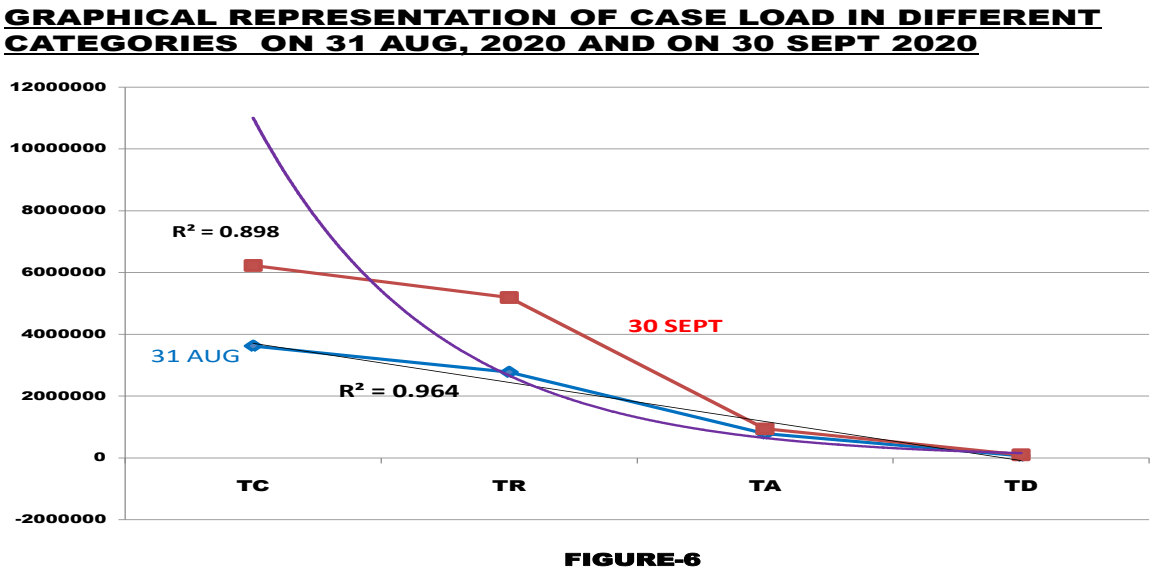

Figure: 6 The graph reflects the confirmed (TC), recovered (TR), active (TA) and Death (TD) due to COVID-19 cases on 31/08/2020 & on 01/09/2020.

in **Figure: 6**, it reflected that there was no change in the number of active cases of COVID-19 between the two dates. The figure shows the distribution of confirmed (TC), recovered (TR), active (TA) and fatal (TD) cases of COVID-19 on 31 August and 30 September, 2020 respectively. The R^2 value of 0.964 on 31 August, 2020 and 0.898 on 30 September, 2020 is consistent in the exponential curve between the two dates. When the case load corresponding to different categories was represented in a dough-nut graph

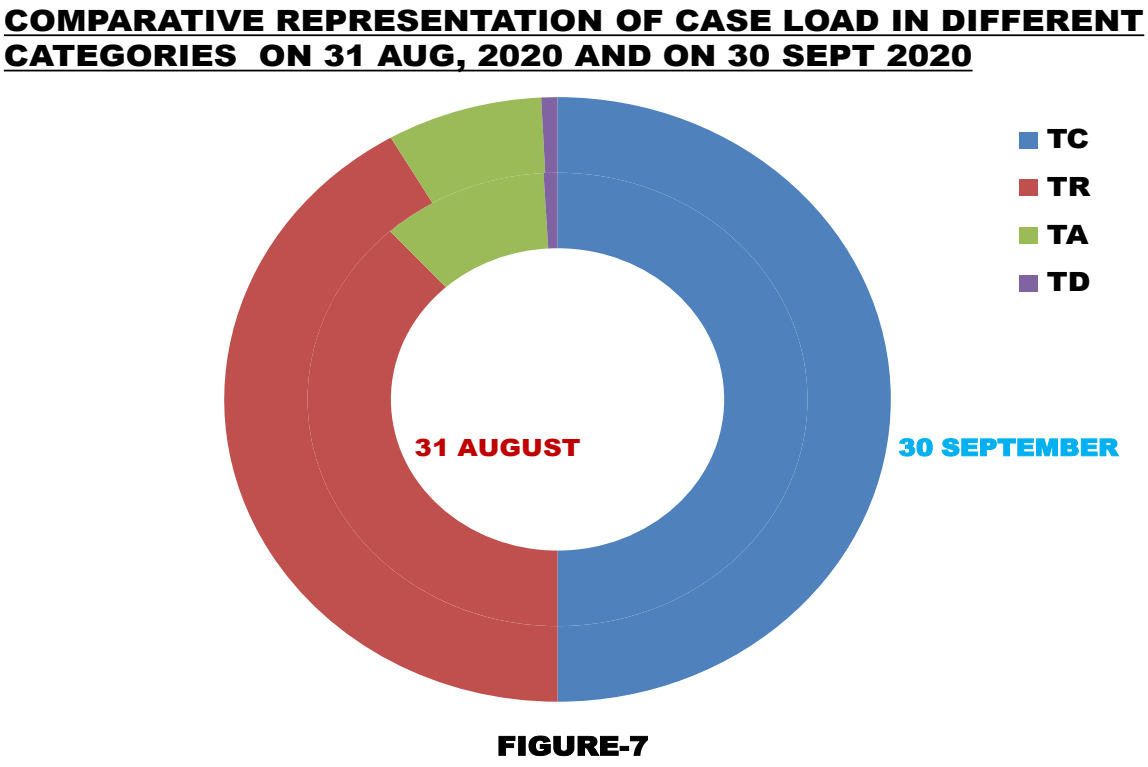

FIGURE-7

Figure 7: The graph represents distribution of the confirmed (TC), recovered (TR), active (TA) and Death (TD) due to COVID-19 as on 31/08/2020 & on 01/09/2020 respectively.

as in **Figure:7,** the data reflected that there was an increase in number of recovered cases and reduction in number of active cases on 30 September, 2020 as compared to that of 31 August, 2020. Whereas, there was no change in fatality between two dates (~1.5%). The point of concern is the

fatality, which has remained consistently the same and appears to remain so as projected until October 30 in the **Figure:8**.

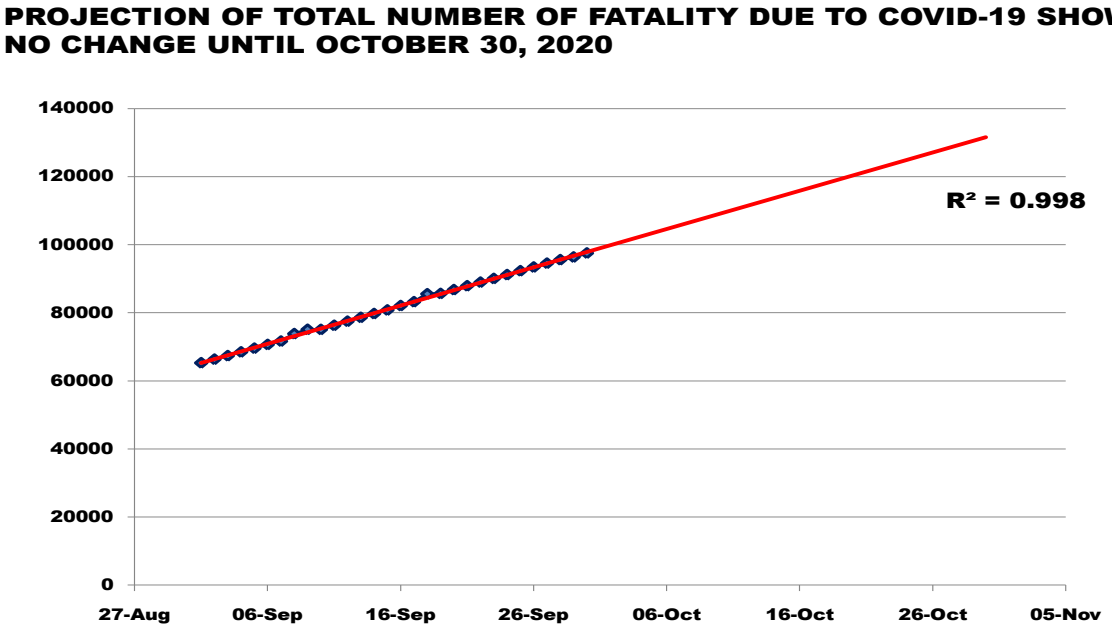

FIGURE-8

Figure 8: The graph represents the projection of fatalities from COVID-19 until 30 October, 2020 (1.5%).

That the percent of fatalities have not come down until now and as projected in the above graph it may not come down until 30 October, 2020 in spite of lower active cases is a matter of concern and requires more attention to be paid for Health care for terminal patients and/or earlier detection of COVID-19 cases by increasing the number of testing for COVID-19 in the population. However, one silvering lining is the gradual decrease in the rate of confirmed cases of COVID-19 were made until November 30, 2020, it reflected a downward trend with a R^2 value of 0.967 suggesting that may be the spread of COVID-19 in the population is gradually coming under control (**Figure:9**).

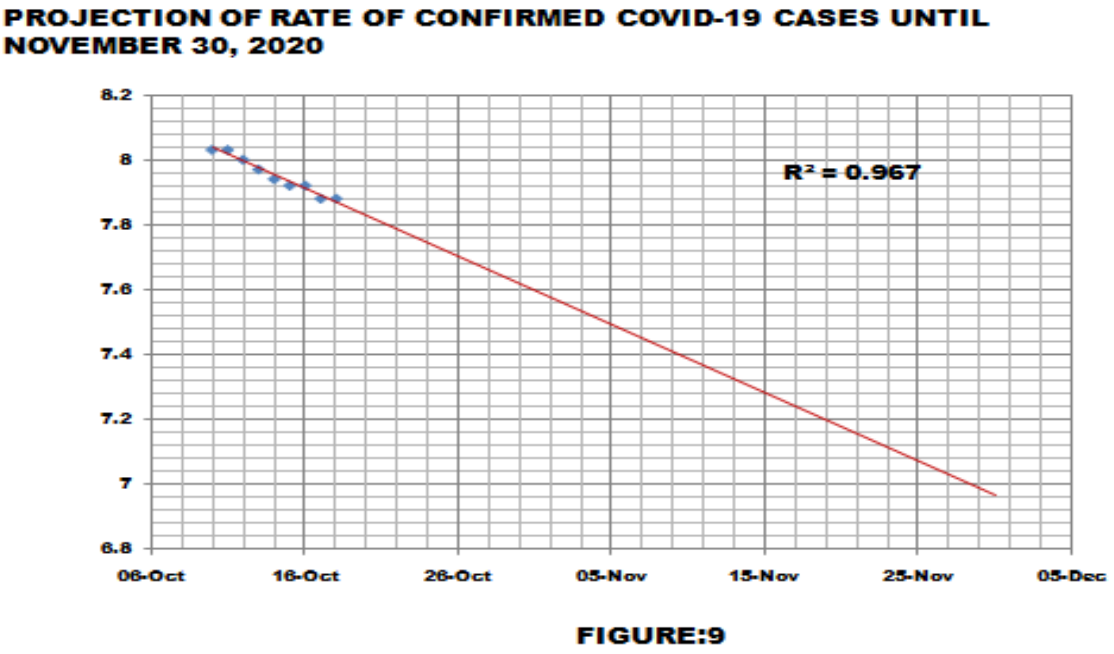

Figure 9: The graph represents the projection in the rate of confirmed cases of COVID-19 until 30 November, 2020.

Another interesting fact which came out from the preliminary data as shown

Figure: 10 depicts the rate of confirmed cases when plotted against

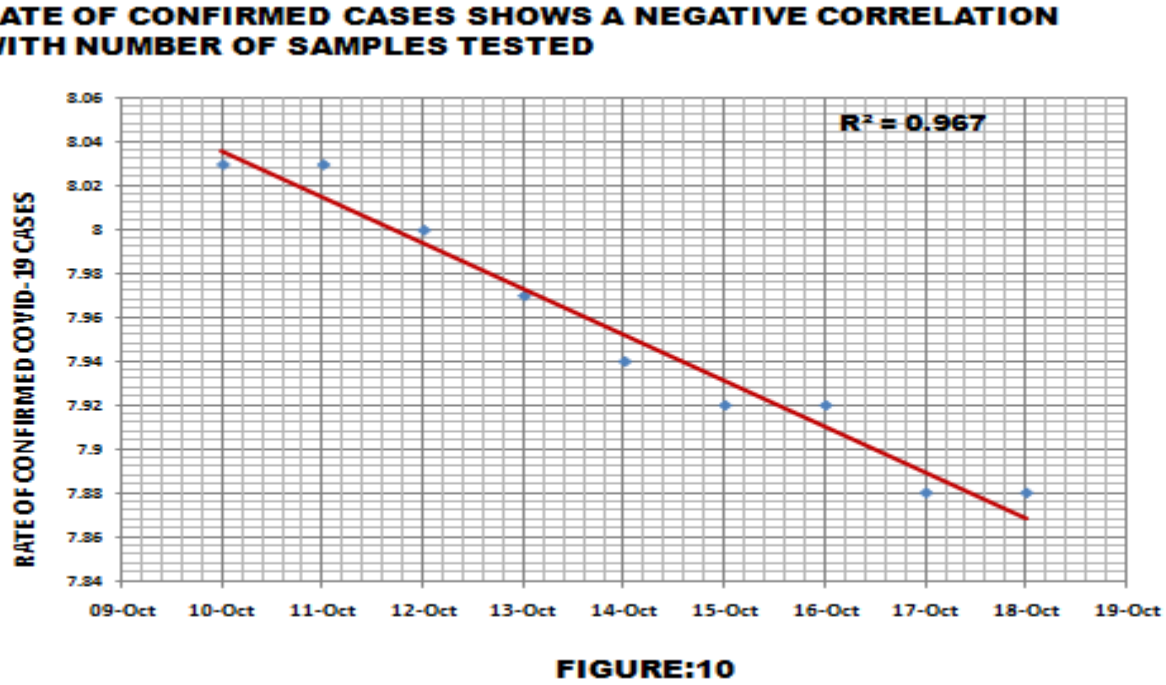

Figure 10: The graph represents rate of confirmed cases of COVID-19 compared to the number of individuals tested for COVID-19.

the number of individuals tested for COVID-19 between 10 October and 18 October, 2020, a negative correlation was observed between the two parameters suggesting that a high number of recovery was taking place among those at an early stage of COVID-19; suggesting some inherent protection against the disease in the recovered individuals.

In our earlier studies, we did observe that following complete Lockdown, implemented at the end of March 25, 2020, in spite of initial volatility the rate of COVID-19 was at around ≤ 4.6% after 25 April, 2020. Thereafter the volatility stabilised and from 11th May, 2020 onwards, the growth rate maintained a flattened nature. The earlier results also suggested that there was a gradual increase in the number of Recovered/disease-free individuals with time (4-6). Considering such observations, concomitant with increase in doubling time of COVID-19 during several Lockdowns, we speculated that the Indian population could be already having protective immunity against COVID-19 and imposing Lockdown only accelerated this process by gradually causing attenuation of SARS-CoV-2 in the population (6).

Immunity and COVID-19: It has been observed that the recovered patients across the world showed presence of antibodies against the novel coronavirus, SARS-CoV-2, and transfer of 'Plasma' taken from such recovered patients were able to cure patients suffering from COVID-19 meaning body's immune response plays a vital role in the cure of COVID-19. Supporting this conjecture, it was demonstrated that specific T cells could be playing a crucial role in fighting the disease at later stage of infection with SARS-CoV-2. A recent study has further corroborated that divergent

SARS-CoV-2-specific T and B cell responses were seen during serious COVID-19 (7). Studies until now have repeatedly demonstrated that a long term memory T-cell mediated response is vital for eradicating the viral infection. Hence there is a scramble for developing a vaccine to fight this pandemic. Therefore, it is reasonable to speculate that an earlier presence/induction of specific T cell response against the SARS-CoV-2 due to earlier exposure may prevent the spread of COVID-19 in a population. The Figure: 11 illustrates the details of T cell response during COVID-19

T cells response in COVID-19

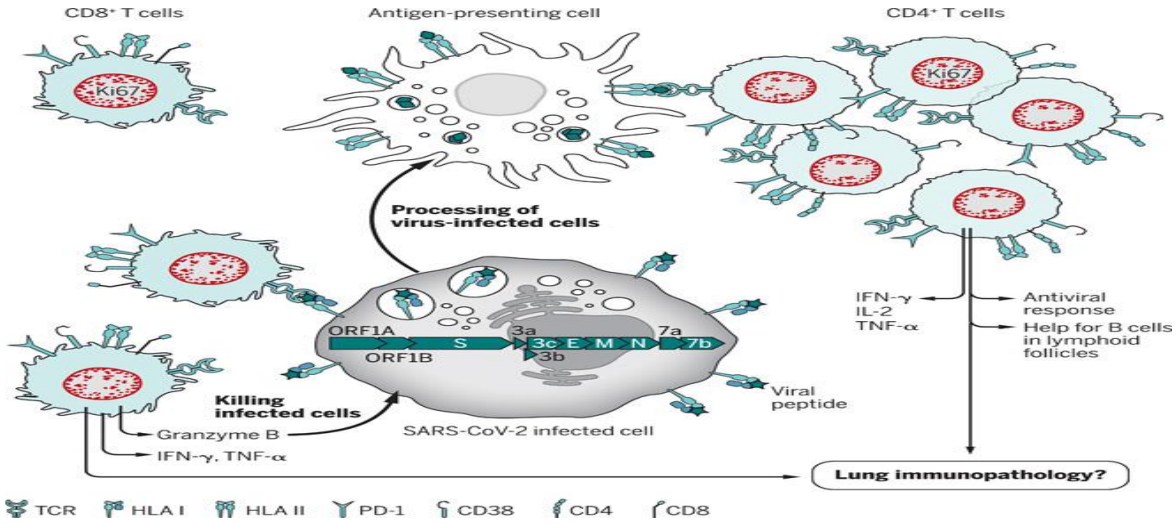

FIGURE-11

Altmann and Boyton, *Sci. Immunol. 10.1126/sciimmunol.abd6160 (2020*

in a SARS-CoV-2 infected cell.

The data presented in this paper is after three months following Lockdown, during the month of September, 2020. The data bolsters our previous claim that a major factor for increased survival from COVID-19 is due to protective immunity and possibly indicates that the entire population is moving

towards achieving 'herd immunity' against COVID-19 with minimum loss of lives.

Protective Immunity moving towards Herd Immunity: Given the importance of immunity in natural control of any viral disease including COVID-19, it is worthwhile to evaluate the existence of prior immunity in the population which could prevent/cure COVID-19. This type of protection could also be achieved either through vaccination or from exposure to previous infections and also by gradually acquiring specific immunity against Lockdown induced weakened (attenuated) SARS-CoV-2.

It is presumed that when the corona virus, SARS-CoV-2, did not meet any substantial resistance (immune response) in a population, it was able to spread quickly and subsequently caused havoc in the population. In India however, the picture was apparently different for various reasons/factors as alluded to in the above paragraphs. Firstly, in the Indian population, due to prior immunization/exposure to related/unrelated infectious agents that protected them against the infection of SARS-CoV-2. The prior immunization could be due to vaccination during early life against TB, diphtheria, influenza etc. as described in **Table-1** that lists the different vaccines used in India since 1893 (8). All the pathogens mentioned in Table-1 could aid in developing a T-cell mediated immune response as described in details in Figure-11. Regarding developing immunity against non-exposed pathogen, a study has demonstrated that blood samples collected from a group of 20 people suffering from Flu in the year 2015, but was never exposed to SARS-CoV-2, had cross-reactive T_h cells that were capable of recognizing &

responding faster to the SARS-CoV-2 (9). Secondly, the SARS-CoV-2 met with stringent resistance by way of physical intervention due to implementation of Lockdown which compelled the virus to be attenuated

HISTORY OF VACCINATION IN INDIA

Year	Milestone
1893	Efficacy trials on cholera vaccine conducted in Agra, India
1897	First plague vaccine discovered by Dr Haffkine
1904/1905	First vaccine research institute established at Kasauli, Himachal Pradesh
1907	Pasteur Institute of India, Coonoor, manufactured neural tissue anti-rabies vaccine
1920-1939	DPT, DT and TT vaccine became available in the country
1940	Drug and Cosmetics Act enacted
1948	BCG vaccine laboratory set up in Guindy, near Madras (Chennai)
1951	Liquid BCG vaccine became available in India as part of mass campaigns
1965	Live attenuated freeze dried smallpox vaccine became available
1967	Freeze dried BCG vaccine became available OPV became available in India
1970	The first time in India indigenous Oral Polio Vaccine Trivalent (Sabin) was developed and produced
1980s	Indigenous measles vaccine production started
1984	Inactivated polio vaccine first produced in India (later on production stopped)
1985/1988	AEFI surveillance system established and initial guidelines were released
1989	Indian Vaccine Company Limited (IVCOL) and Bharat Immunological and Biological Limited (BIBCOL) were set up as public private joint venture companies
1997	First ever recombinant DNA hepatitis B vaccine developed in India
2006	Guidelines for clinical trials by Indian Council of Medical Research (ICMR)
2009	Three Indian manufacturers developed pandemic flu (Novel H1N1: 2009) vaccine
2010	National Pharmacovigilance Programme of India launched Meningitis A vaccine for African Meningitis Belt licensed and successfully used in campaigns in Africa Indigenously researched bivalent oral cholera vaccine developed and licensed in the country
2012	An indigenous 'inactivated JE vaccine' licensed in the country. Indian manufacturer acquired capacity to produce inactivated polio vaccine

Source : Refs 4, 6, 27-30
DPT, Diphtheria, pertussis and tetanus; DT, diphtheria and tetanus; TT, tetanus toxid; OPV, oral polio vaccine

TABLE-1

Table-1: The table gives a list of pathogens against which Indians were immunized at different times that could provide immunity against SARS-CoV-2 infection.

leading to abrupt slow down in the mobility of the virus and aid in development of 'passive immunization' to the virus. Now considering the data furnished and analyzed for a period between 1st September and 30th September, 2020, three months post Lockdown reconfirms that there is protective immunity among the population against the SARS-CoV-2 virus. The high rate of recovery from COVID-19 (~69%) during this period and

swiftly reaching to 90% while making this submission, along gradual waning of active cases of COVID-19 to about 15.1% on September 30, 2020 and to about 9.29% as on 22 October, 2020 re-establishes the concept of prior immunization which works for preventing COVID-19.

Herd immunity, also called herd protection, is the resistance to the spread of a contagious disease within a population that results if a sufficiently high proportion of individuals become immune to the disease. It basically serves as an indirect protection to those who are not immune to the disease. In our study: a) the swift increase in recovery from COVID-19; b) decline in number of active COVID-19 cases and c) negative correlation of total confirmed cases with increase in number of tests detection of COVID-19 clearly indicated that there has been a gradual progression from protective immunity to herd immunity without increase in fatality which has consistently remained at ~1.5%.

Another important factor being the poor maintenance of social distencing in transports and local places has not derailed the rate of recovery from COVID-19. Some earlier instances of abrupt spurt in the number of COVID-19 cases especially on two occasions; once on 1st April, 2020 from a 'single source' as described earlier (3,5) and on 1st May, 2020 onwards, due to mobility of large number of migrant labourers (~6.3 million) returning to their respective home states, in trains, buses & on foot from across India during Lockdown-3/Lockdown-4, without maintaining 'social distancing', should have caused havoc and taken many lives. However, such unprecedented event of mass infection did not happen. It is plausible to

assume that a large number of these people in the population were previously immunized against many of the deadly microbe borne diseases like TB, small pox, diphtheria tetanus etc that generated the required immune response against SARS-CoV-2. For the same reason the efficacy of BCG is being tested for curing unrelated pathological conditions (10).

In classical scenario of herd protection requires significant percentage of people to be immune against the virus in a population. In this study, until now 10 million individuals have been tested for the presence of antibody as the Figure-10 reflects that there is a negative correlation between the rate of COVID-19 with the total number of samples tested in the population. This is complementary to the projection made in Figure-9 about the number of COVID-19 cases until November 30, 2020. Further, the data in Figure: 12

INDIA RECOVERIES AMONG HIGHEST IN THE WORLD

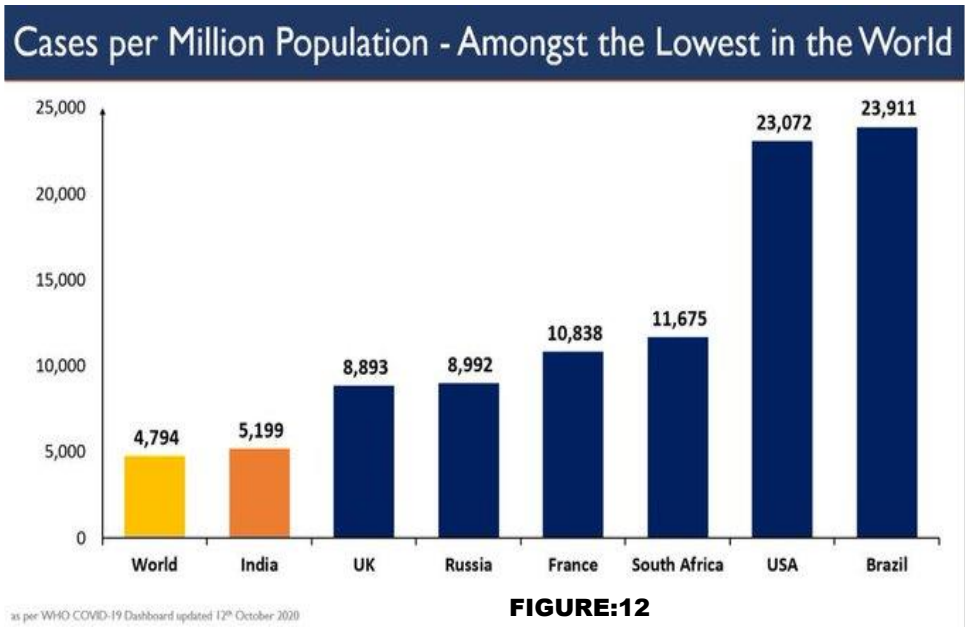

FIGURE:12

corroborated with the finding that India recorded lowest number of cases/million in the world signifying that the recovery from COVID-19 is very high.

Contrary to the present belief that as long as there are susceptible and infected people in the population, the virus could spread, the data presented here demonstrated that the protective immunity prevailing in the population is gradually moving towards attaining 'Herd Immunity' without too many fatalities; a concern voiced by WHO of losing lives if there is an attempt to reach 'herd immunity'.

IV. ACKNOWLEDGEMENTS :

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