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EPIDEMIOLOGICAL STUDIES OF CORONA VIRUS DISEASE IN THE STATE OF GUJARAT, INDIA

Epidemiology

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ABSTRACT

COVID-19 pandemic has left world aghast over the large number of incidences within a short span There are 56,11,597 confirmed cases and 3,48,330 deaths reported globally due to corona virus infection as on 21 June 2020. India is now on the fourth position amongst the worst affected countries with 4,25,827 confirmed cases and a R_0 of 1.13. Gujarat which has one of the highest Mortality Rate (6.09%) is among the top four states of India with a total of 27,317 confirmed cases and 1,664 reported deaths. In order to contain the surge in infections, it is important to devise an effective strategy which aims at reducing the rate of transmission and preventing its spread, specifically when there is no vaccine and/or treatment available. The present review is focused on the epidemiological study of COVID-19 in the state of Gujarat and suggestive strategies for management of disease.

KEYWORDS

Corona Virus, Epidemiology, Fatality Rate, Basic Reproduction Number

INTRODUCTION

Novel corona viruses belongs to the family Coronaviridae of order Nidovirales, comprises of positive sense, single stranded RNA. It has been named as SARS-CoV-2 by the International Committee on Taxonomy of Viruses (ICTV) while the disease is named as COVID-19.[1] The corona virus can lead to death due to respiratory failure, which is mainly caused due to the clinical conditions, viz. Severe Acute Respiratory Syndrome (SARS) and acute lung injury (ALI).[1]

CORONAVIRUS LINEAGE

Corona virus belongs to four subgroups namely alpha-α, beta-β, gamma-γ and delta-δ, and amongst these alpha-α, beta-β can cause infection in mammals only.[2] The etiological agent involved in the present outbreak belongs to β-group of corona virus. This is the same group of virus that was involved in SARS in Guangdong province of China in 2003, with increased infectivity and mortality probably due to genetic recombination at S protein in the receptor-binding domain (RBD) region. The population genetic analysis has suggested prevalence of 2 major lineages of the virus viz. L and S types of which the former is more prevalent.[3]

It requires an in-depth investigation and comprehensive genomic analysis to test the rates of transmission and virulence in the two lineages.[3]

Genomic Organization of SARS-COV-2

Studies on the genome organization of SARS-CoV-2 have shown that it has four structural proteins, S (spike), E (envelope), M (membrane) and N (nucleocapsid) proteins (Figure 1).

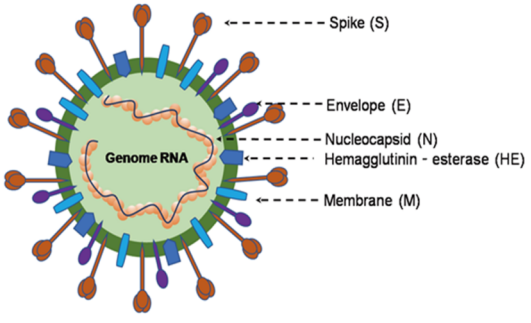

Figure 1: Structure of SARS-CoV-2 (Source: Jin et al)[4]: The SARS-CoV-2 virion has a genome size of 29.9 kb. It possesses a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid (N) protein. SARS-CoV-2 has surface viral proteins, namely, spike glycoprotein (S), which mediates interaction with cell surface receptor ACE2. The viral membrane glycoprotein (M) and envelope (E) of SARS-CoV-2 are embedded in host membrane-derived lipid bilayer encapsulating the helical nucleocapsid comprising viral RNA.

The spike protein is responsible for allowing the virus to attach to the membrane of a host cell. It has affinity to human angiotensin converting enzyme 2 (ACE2) receptor of human cells to use them as a mechanism of cell entry. Two-thirds of viral RNA, mainly located in the first ORF (ORF1a/b) translates two polyproteins, pp1a and pp1ab, and encodes 16 non-structural proteins (NSP), while the remaining ORFs encode accessory and structural proteins. The rest part of virus genome encodes four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and also several accessory proteins, that interfere with the host innate immune response (Figure 2).

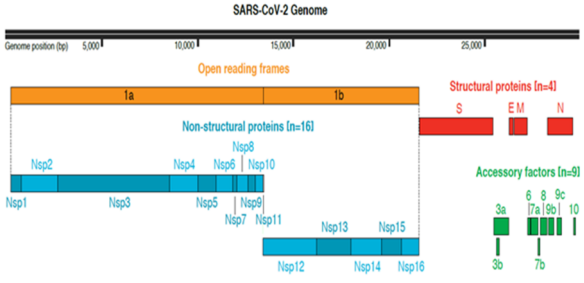

Figure 2: Genomic organization of SARS-CoV-2 (Source: Gordan et al, 2020)[5]. The ORF 1a and 1b comprises of approximately 67% of the genome that encodes 16 nonstructural proteins (nsps), whereas the remaining ORFs encode for accessory and structural proteins. The nsps includes two viral cysteine proteases, including papain-like protease (nsp3), chymotrypsin-like, 3C-like, or main protease (nsp5), RNA-dependent RNA polymerase (nsp12), helicase (nsp13), and others likely to be involved in the transcription and replication of SARS-CoV- 2. In addition to nsps, the genome encodes for four major structural proteins including spike surface glycoprotein (S), membrane, nucleocapsid protein (N), envelope (E) and accessory proteins like ORFs.[6,7]

ORIGIN AND TRANSMISSION-SARS-COV-2

Reservoirs and transmission

Occurrence of severe pneumonia caused by an unknown causative

agent[8,9] with concurrent radiological findings of lung opacities led the Chinese government to inform National Health Commission, China CDC and WHO about the disease on 31st December 2019. The origin was considered to be the human seafood market in Wuhan city of China where live animals like bats, frogs, birds, rabbits, marmots, snakes etc. were sold[10]. On January 12, 2020, the National Health Commission of China declared it as epidemic[10] and the logarithmic expansion in the number of cases globally led to the declaration of COVID-19 as a pandemic by WHO on 11th March 2020.[11,9] It was presumed that people who visited seafood market and/or consumed infected birds or animals got pneumonia due to the novel etiological agent. Later the same was transmitted from human to human through respiratory activities viz. coughing, sneezing i.e. by droplet transmission.[12] The other transmission modes reported in various studies are through conjunctiva, fomites, fecal oral route, body fluids.[13,14]

Based on the history and data collected from infected people at the starting point of outbreak at China it was confirmed that the disease is of zoonotic origin. The SARS-CoV-2 is linked to the bats and the phylogenetic and genomic analysis suggests that pangolins are the intermediate host[15] but still it requires further studies to establish that it emerged directly from pangolin-CoV-2020.[16]

SYMPTOMS AND PATHOGENESIS

The most common symptoms are fever[17], cough, sore throat, swollen adenoids[18], pneumonia, bronchitis, fatigue, headache, sputum production, haemoptysis, diarrhoea, dyspnoea and lymphopenia[19]. Its unique pathogenesis and manifestations of abnormal features such as RNAaemia, Acute Respiratory Distress Syndrome (ARDS), are mainly attributed to the upper and lower respiratory tract infections[20] and together with other clinical symptoms like cardiac injury, grand glass opacities that can lead to death[21]. The signs and symptoms[17] for COVID-19 infections can be seen with the percentage manifestation in the Table 01. The other common symptoms are decreased sense of smell which may be accompanied by change in taste[22].

Table-1 Prevalence of Signs and Symptoms in Covid-19 Infection

Signs and Symptoms	Percentage
Fever	87.9
Dry Cough	67.7
Fatigue	38.1
Sputum production	33.4
Shortness of breath	18.6
Sore throat	13.9
Headache	13.6
Myalgia/arthralgia	14.8
Chills	11.4
Nausea/vomiting	5.0
Nasal congestion	4.8
Diarrhea	3.7
Hemoptysis	0.9
Conjunctival congestion	0.8

The patients develop these symptoms with varied intensities and in different proportions, but most of the patients have mild to moderate disease (80%) while a few develop severe disease (13.8%) and only few are critical (6.1%).[17] In fact, many are asymptomatic in the initial phase but gradually develop symptoms in a few days. The severity of COVID-19 infection can be established with the logarithmic increase in morbidity and mortality.

Started in Wuhan, China, on December 29, 2019, with 05 cases and 01 death the number reached to 51174 with 1666 (3.25%) death by February 16, 2020, in China alone. The median age in these cases was 75 year (range 48-89 years). All the persons infected showed higher leukocyte counts i.e. $2.9x10^9$ cells/L of blood of which 70% are neutrophils. Blood C reactive protein was increased up to 16 mg/L of blood. High erythrocyte sedimentation rate and D dimer were also observed along with abnormal respiratory findings, increased level of plasma pro-inflammatory cytokines. The patient's sputum showed positive real time polymerase chain reaction that confirm COVID-19 infection.

IMPORTANT EPIDEMIOLOGICAL PARAMETERS FOR RISK ASSESSMENT

The contagiousness of disease can be estimated by reviewing the Basic Reproduction Number (R_0), Case Fatality Rate (CFR) and the incubation period.

Transmission Rate and Severity

In order to understand the magnitude of infection it is important to take into consideration the rate of transmission of disease which is best depicted from the basic reproduction number (R_0)[23]. The R_0 number represents the average number of people to which a single infected person can transmit the virus. A value of 1 or less than 1 indicates that the infection would be self-containing while a higher value indicates its contagiousness. The R_0 for SARS-CoV-2 as estimated by WHO is between 1.4-2.5[24] but as it depends on various other variables (containment measures, treatment etc.) hence the values keep changing. It has been ranging between 2.24- 3.38[25] in many other studies and can be best estimated for a particular geographical location to plan an implementation strategy[19] to limit the spread of infection. The R_0 number varies with time and factors and is mainly dependent on the behaviour change with respect to control measures-quarantine and isolation protocols, travel restrictions, school closures, physical distancing, the use of face mask etc. and development of immunity. This variability makes it necessary to constantly update the R_0 number. A R_0 number is the most trusted value in the making of a strategic plan, it helps the government, healthcare authorities and other agencies in taking decision for efficient resource allocation. and institutions.

Case Fatality Rate (CFR)

It is calculated by no. of deaths by total number of cases infected by the disease (includes the active and the recovered cases). It is critical to get the accurate estimates for CFR during an outbreak of a disease and can be improved by vigorous testing and surveillance and data collection. The CFR for COVID-19 is 3.4% as per the WHO projection[26,27] while the estimated CFR for world is 5.3% based on the European CDC data[28].

Incubation period

Incubation period helps in designing mitigation strategies specifically the quarantine period. Symptoms of novel corona virus (COVID-19) appear between 02 to 14 days with differing mean values obtained from various studies which are- 4.0[29] days, 5.2[30] days, and 6.4[31] days. The incubation period depends on many factors like age, sex, patient's immune status, environmental conditions, etc.

PREVENTION AND CONTROL

There is no potential therapeutic treatment or vaccine available for COVID-19 as of now and hence the only control measure which can be undertaken is 'prevention'. The primary mode of entry in the human body is through respiratory tract but it also gets transmitted through fomites, conjunctiva, fecal-oral route, and body fluids. The human-human transmission can be prevented at the first stage if effective screening and isolation is practiced. The screening and detection of disease at the earlier stage has helped in reducing the morbidity and mortality in various countries. The PCR based testing is considered to be the gold standard[32] for screening COVID-19 being a sensitive, specific, and rapid detection qualitative assay which can help in early detection at onset of infection. The other important ways to prevent COVID-19 is maintaining social distancing (1-3 meters) and following hygiene practices as per the WHO guidelines. As far as the treatment is concerned, the patients are given symptomatic treatment or are provided and tested for compassionate treatment. Present strategy of treatment of COVID-19 cases involves the use of broad spectrum antiviral drugs[33] like Favipiravir,[34,35] Remdesivir,[36,37] Ribavirin, Oseltamivir, Ganciclovir etc. The other existing drugs used for the treatment are Dexamethasone,[38] Tocilizumab[39] and Camostat mesylate[40]. It is clear that urgent research is needed to identify new chemotherapeutic drug for the treatment, currently there are more than 80 clinical trials[41] under process for testing the efficacy and effectivity of new drugs. Similarly, there are around 128 vaccines in preclinical evaluation phase and around 13 are under the clinical trial phase as on 18th June 2020.[42] A most effective yet simple treatment modality is use of convalescent plasma[43] but this has a limitation of its own in case of an outbreak situation due to limiting availability[2].

GUJARAT-DEMOGRAPHIC PROFILE

India is the second most populous country and a most populous democracy in the world. Gujarat is a state on western coast of India with a population of 60.3 million (4.99% of Indian Population). It is the fifth largest state by area and ninth largest state by population having third largest economy in the country. The state has 33 districts, with Ahmedabad being the largest city with a population of 7.20 million which makes it the fifth most populous city of India. The other cities of Gujarat with higher population density are Surat, Vadodara, and

Rajkot. It has a female: male population ratio of 0.918: 1,[44] which is one of the lowest in country as per 2011 census.

COVID-19: SPREAD IN INDIA AND GUJARAT

The present epidemic started during December 2019 and within a short time of three months, converted into a pandemic affecting 213 countries across the globe. In India, the first case of COVID-19 was reported in Kerala on January 30, 2020. Only three cases were reported till March 2nd. However, cases rapidly increased and reached to 29 by March 5th, mostly in Delhi, Jaipur, and Agra. COVID-19 cases in India reached to a total of 4,26,910 with 13,703 deaths and 2,37,252 recoveries on June 21, 2020 (worldometers.info/coronavirus)[28]. The ten most affected states with higher number of confirmed cases registered are presented in the Table 2.

Table-2 Top 10 States of India with higher number of confirmed Covid-19 Cases

No.	State/UT	Confirmed Cases	Active Cases	Patients Recovered	Total Deaths
1	Maharashtra	132075	60147	65744	6170
2	Delhi	59746	24558	33013	2175
3	Tamil Nadu	59377	25866	32754	757
4	Gujarat	27317	6296	19357	1664
5	Uttar Pradesh	17731	6186	10995	550
6	Rajasthan	14997	2996	11652	349
7	West Bengal	13945	5093	8297	555
8	Madhya Pradesh	11903	2373	9015	515
9	Haryana	10635	4918	5557	160
10	Karnataka	9150	3391	5618	137

Source : COVID-19 Dashboard as on 21 June 2020, https:// www. mygov. in/covid-19

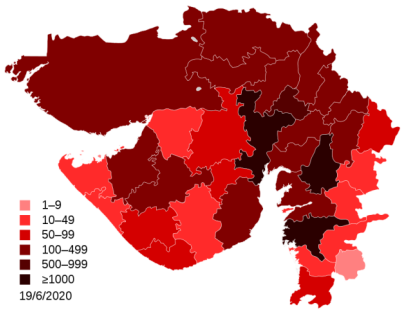

Figure 3: District map of Gujarat with profiling on basis of number of confirmed cases of COVID-19 (Source: By Timbaaa and Shanze1 - This file was derived from: India Gujarat location map.svg: CC BY-SA 4.0, https:// commons. wikimedia. org/ w/ index. php? curid=89251238)

COVID-19: Gujarat Scenario

After the detection of first case of corona in Gujarat State on March 19, 2020, it took only nine days to reach to 50 cases. In close to about a month time (29 days) number of positive cases reached 1000 mark in the state which was doubled in four days i.e. by April 21, 2020. Fortunately, the next doubling took 08 days (2000-4000) and 11 days (4000-8000), the trajectory of number of confirmed cases of COVID-19 are presented in Figure 4.

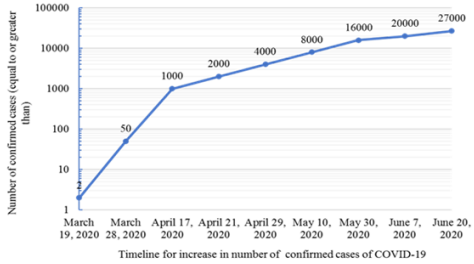

Figure 4: Time line of number of confirmed cases of COVID-19 in the state of Gujarat (Source: Prediction and Assessment of Corona Infections and Transmission in India Updated on 21 June 2020 (http://pracriti.iitd.ac.in/ and https://www.covid19india.org/state/GJ))

The worst affected top 10 districts of Gujarat with confirmed number of cases are enlisted in the Table 3.

Table-3 Top 10 Districts of Gujarat with higher number of confirmed Covid-19 Cases

No.	District	R_0	Confirmed Cases	Patients Recovered	Total Deaths
1	Ahmedabad	0.3	18564	13185	1312
2	Surat	0.41	3057	2190	120
3	Vadodara	0.39	1813	1155	47
4	Gandhinagar	0.32	548	331	23
5	Mehsana	0.28	209	124	11
6	Bhavnagar	0.29	189	128	13
7	Rajkot	0.42	181	95	5
8	Aravalli	0.35	167	129	14
9	Banaskantha	0.03	163	139	8
10	Sabarkantha	0.14	148	98	7

Source: COVID-19 Dashboard as on 21 June 2020- Gujarat (https:// gujcovid19.gujarat.gov.in/ and http://pracriti.iitd.ac.in/).

Table no. 3 highlights one important parameter, i.e. the R_0 number, although some districts have higher number of confirmed cases, they have significantly lower R_0. Five districts which have higher estimated values R_0 are represented in the Figure 5 along with the total number of confirmed cases to understand if there is any correlation between the two values. It is the R_0 value which helps in deciding the strategy for control of the spread of disease in a particular geographical location.

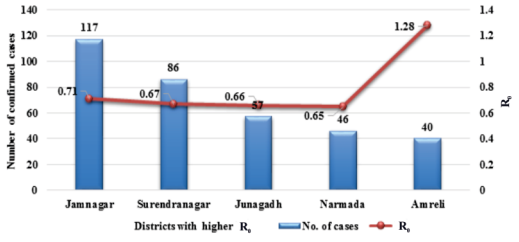

Figure 5: Districts of Gujarat with Higher R_0 values Source: COVID-19 Dashboard as on 21 June 2020- Gujarat (https:// gujcovid19. gujarat.gov.in/ and http://pracriti.iitd.ac.in/).

Considering the R_0 values, the present trajectory, and the high mortality rates in Gujarat, it is suggested to have a Level 2 Lockdown within district as per the 'An Adaptive, Interacting, Cluster-Based SEIR Model' (AICSEIR), which is the modification of Susceptible–Exposed–Infected–Removed (SEIR) model (Figure 6). The similar prediction is also presented for the districts with higher transmission rates (Table 4). The predicted number of cases are tabulated for varying scenarios of lockdown, viz. Level 0, Level 1 and Level 2 which are implemented 'within districts' or 'across district borders'. The term "District border" means managing or controlling the traffic across the borders of the district and it helps in controlling the transmission of infection between the districts. Level 0 refers to normal traffic or no restriction across the borders of district. The option Level 1 refers to partially allowing traffic across the borders, which falls under the essential category. The Level 2 refers to minimum or completely restricted movement across the borders.

Similarly, the term "Within the district" mentions about the restriction or controlling of movement of people outside their owns residence but within a district. Level 0 does not confer any constraints in movement while, Level 1 refers to permitting the movement for people outside their residence for wing essential goods and services and allowing essential services to work. Level 2 lockdown restricts the movement of people from their houses even for essential items.

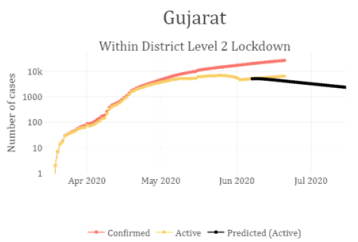

Figure 6: Suggested lockdown strategy for Gujarat (Source: PRediction and Assesment of CoRona Infections and Transmission in India (Updated on 21 June 2020))

Table-4 Suggested Lockdown Strategy For Districts of Gujarat with Higher R_0

Suggested Lockdown strategy							
No.	**District**	**No. of cases**	**R_0**	**With lockdown at District border**	**With lockdown within district**	**Remarks**	
				0 level/ level 1/ level 2	**0 level/ level 1/ level 2**	**No. of predicted cases by 15th July 2020 in best scenario**	
1	Amreli	40	1.28	125/117/115	494/117/48	**48**	Level 2 Lockdown within district
2	Jamnagar	117	0.71	163/156/154	311/156/106	**106**	
3	Surendranagar	86	0.67	123/117/115	221/117/81	**81**	
4	Junagadh	57	0.66	95/83/79	156/83/57	**57**	
5	Narmada	46	0.65	53/51/51	95/51/36	**36**	

A Level 2 lockdown within the districts is suggested to be implemented for the districts with higher R_0 to control and prevent exponential increase in the number of cases in Gujarat.

Lockdown-Gujarat

Gujarat in general followed a similar pattern as in other parts of the country. The state authorities follow all the instructions given by the central government. On March 22, 2020, the state observed 14 hours voluntary curfew at the instance of Prime Minister of the country. Further on March 24, Prime minister ordered a nationwide lockdown for 21 days which was extended till May 03, 2020. Looking to the situation in the country the lock down was further extended with minor exemptions till May 17, 2020, and now up to May 31, 2020. The result of lock down was visible in the state of Gujarat as the doubling time increased from four days to eight days and further to eleven days. The results are almost parallel to the country results. The Oxford COVID 19 Government Response Tracker (OxCGRT), in its report based on the data from 73 countries, reports that the Indian Government has responded more stringently than other countries in tackling the pandemic.

It noted the government's swift action, emergency policy making, emergency investment in health care, fiscal measures, investment in vaccine research and active response to the situation. During the period from its inception the state carried 324,874 tests which is 0.47% of the population of state. This data matches with the testing percentage of country. The coronavirus illness in 70% of the cases is associated with other diseases like hypertension, asthma, thyroid, diabetes, cancer, heart, and kidney related illness. For this reason, experts are putting weightage on immune status of individual particularly of the health workers, old age people and children, which is very essential to fight with the coronavirus. The major rise in the positive cases experienced during the month of April, probably by the people who returned from Tablighi Jamaat religious congregation took place in Delhi. Over 9000 missionaries may have attended the congregation, with majority being from various states of India and 960 attendees from 40 foreign countries. According to Ministry of Health and Family welfare, 4291 out of 14378 confirmed cases were linked to this event in 23 Indian states and union territories till 18th April 2020. The male female ratio in cases of death is roughly 60:40 in Gujarat. If we see the death rate over confirmed positive cases in India, the country has a death rate 3.23% and the global death rate is 5.3%,[45] while it is higher in state of Gujarat 6.13% and is increasing with an average growth rate of 2% per day.

In India, it took 64 days to reach to the number of positive cases to one lakh, while the rates were much higher in USA, Spain, and Germany with 25, 30 and 35 days respectively. The number of death per 10 lakh population is much lower in India (10) as compared to United Kingdom (628), Spain (606) and Italy (573)[28]. The higher death and infection rate has put Gujarat on second position in the country.

Gujarat has a total of 33 districts, of which the highest number of cases have been reported from Ahmedabad district (69.58%) followed by Surat (11.45%) and Vadodara (6.79%). The state has 402.1 Confirmed per million (CPM) cases as compared to the 320.11 CPM for India, this is when the tests per million count is 4702 for Gujarat[46]. This clearly indicates that the number of tests per million needs to be increased significantly in order to reduce the mortality rate as has been in other States/UTs where better control has been observed with increasing the screening like Delhi, Tamil Nadu and Rajasthan (Table 5).

The increase in number of cases in Ahmedabad is related to several factors, of which a high population density, presence of international airport and high travel history are the prime reasons.

Table- 5 States and UTs with Higher Number of Tests Per Million along with an Overview of other Indicator Parameters

No.	State/UTs	R_0	Av. Growth Rate/ day (%)	CPM	Tests per Million	Mortality Rate (%)	Recovery Rate (%)
1	Maharashtra	1.18	3	1081.23	6352	4.67	49.78
2	Delhi	0.82	6	3015.34	18674	3.64	55.26
3	Tamil Nadu	1.39	4	784.42	11792	1.27	55.16
4	Gujarat	1.17	2	402.1	4782	6.09	70.86
5	Uttar Pradesh	1.35	4	78.81	2413	3.1	62.01
6	Rajasthan	1.05	2	193.23	9049	2.34	77.68
7	West Bengal	0.99	3	143.9	4143	3.98	59.5
8	Madhya Pradesh	0.81	1	144.75	3611	4.33	75.74
9	Haryana	1.37	5	370.92	7596	1.5	52.25
10	Karnataka	0.87	4	139.06	7702	1.5	61.4

(Source: https://www.covid19india.org/)

CONCLUSION

The Lockdown measures undertaken (Phase 1.0-Phase 4.0) in the country have helped in containing the exponential rise in the number of confirmed cases. The relaxations in the Lockdown phase 5.0, have led to a surge in the COVID-19 cases. Considering the present scenario, where resuming economic activities have had an obvious impact in spreading of disease, it is imperative to apply a combination strategy[47] to contain this spread when physical distancing measures are not stringently followed. The combined strategy is essentially multipronged in approach with major emphasis on the surveillance [48,49] (the ILI and SARI surveillance through Integrated Disease Surveillance Program (IDSP) network), contact tracing, quarantine and moderate social distancing following all precautionary measures as per the Public Health Guidelines for the civilians which have been frequently reiterated.

The screening-(Test Per Million-TPM) needs to be significantly increased as it very important to identify the infected people, so that they and their immediate suspected contacts can be quarantined and provided treatment at earlier stages which would help in reducing the incidences of high fatality[50]. Many a time, due to the existing social stigma resulting because of lack of awareness, or lack of trust on the healthcare facilities, the symptomatic patients do not undergo screening[51] and hence remain unidentified, spreading the disease; also there are large number of asymptomatic patients making it difficult to contain the spread. Under such conditions where the number of unidentified persons exceeds 20%,[52] there is a dire need for Level 2 lockdown within district.

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