Review Article

Understanding the COVID-19 prevention and control strategies and their appropriate applicability through the basics of epidemiology

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ABSTRACT

The current article is about the background knowledge of corona, various epidemiological definitions and different strategies adopted to prevent and control corona infection. How the preventive measures are applied and what is epidemiological basis behind these measures is the core of the article. The article also mentioned the variations in mortality pattern and goes on defining important indicators as case-fatality ratio, deaths/1 lakh population and the relevance of both in the current situation of corona infection. In the article, important terms such as different types of cases in corona infection, basic reproduction number, effective reproduction number, and their epidemiological significance in corona infection, herd immunity, and herd immunity threshold are discussed. The importance of lockdown as a preventive measure, enforcement of epidemic disease act 1897 and its amendment, disaster management act 2005, social distancing, cough etiquette, and others are highlighted.

KEY WORDS: Herd Immunity; Herd Immunity Threshold; Basic Reproduction Number; Effective Reproduction Number; Preventive measures

BACKGROUND: CORONA VIRUS DISEASE

The viral disease "COVID-19" started from Wuhan city in Hubei province in China from late December 20. It was declared as PHEIC, that is, Public Health Emergency of International Concern on January 30, 2020 by the WHO. The rate at which the cases has increased and the spread of cases in different countries across the world has alarmed both the developed and developing nations. Countries adopted different strategies to control the epidemic. Due to the vastness of the spread across the nations and in the nations, law and order situation has also seen a twisting mode in many nations. Even though the administration is managing the situation and trying to control and simultaneously helping and reaching out to the public at large, but still until today, nothing can be said conclusively. If we see the figures across the World and in India, the total number of cases across the world in 216 countries as on June 27, 2020, is 9,653,048 confirmed cases of Coronavirus (CoV) Disease (COVID)-19, including 491,128 deaths which are reported to WHO.[1]

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By different regions of the WHO, the cases are
America: 4,816,794
Europe: 2,638,903
Eastern Mediterranean: 1,006,279
Southeast Asia: 710,455
Africa: 268,102
Western Pacific: 211,774

In India, the cases reported till June 27, 20 are
Active cases: 197387
Cured/discharged: 295880
Deaths: 15685[2]

CoVs cause respiratory infections of mild to severe forms.[3] CoV-2 is one of seven types of CoV. Earlier types have

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caused severe diseases such as the Middle East respiratory syndrome and sudden acute respiratory syndrome (SARS).[4] Before the outbreak, this new virus was unknown. Fever, dry cough, and tiredness are the most common symptoms of COVID-19. Nasal congestion, headache, sore throat, diarrhea, and other symptoms are less common.[3] Older people and people with medical comorbidities are at higher risk of developing a serious illness. The disease is seen as a spectrum. Mild illness is seen in almost 81%, severe illness in 14% and critical disease is reported in 5%. Reported case-fatality ratio is between 2.3 and 5%. Incubation period ranges from 2 days to 14 days and median incubation period as 5.5 days.[5]

CERTAIN EPIDEMIOLOGICAL TERMS AND DEFINITIONS

In Corona Positive Case

Asymptomatic case

Found out only by testing and remain without symptoms throughout.

If not tested – status can never be known

The WHO in its report has mentioned that 25% remained as asymptomatic out of those who tested positive without symptoms during the follow-up exams.[6]

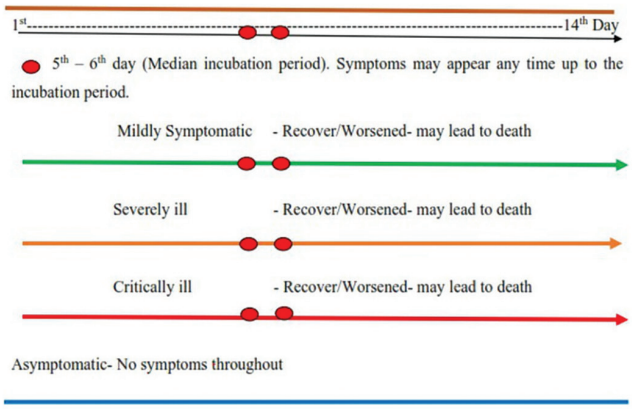
Pre-symptomatic case

These are the cases harboring virus in them and within the incubation period will develop signs and symptoms and will test as positive. Scientific studies suggested that pre-symptomatic case can definitely transmit this virus before symptoms manifestation.[6] Transmission of the virus through the shedding of virus can occur in the absence of symptoms and before symptoms onset as evident from pre-symptomatic transmission.[7] This evidence is also supported from the study by Wang *et al*.[8] and Hu *et al*.[9] Asadi *et al*. in their study found the role of generated respiratory droplets and indirect transmission as a possibility in pre-symptomatic transmission. Various different forms of vocal activities generate air particles, as they found in their study. They also found that the vowel content in a phrase and the rate of emission were positively correlated.[10] According to Wang *et al*., young people who had close contact with infected family members seldom become asymptomatic. They also found that in the majority of patients, the outcome was mild COVID during hospitalization.[8] Screening for asymptomatic infections is very difficult and thus prevention and control of this disease at national level becomes tough.[11] Kerkhove has mentioned that about three fourth of asymptomatic people turn out to be pre-symptomatic in follow-up exam, thereby making pre-symptomatic a much more common category than asymptomatic.[6] About 80% COVID-19 cases remain asymptomatic or mildly symptomatic as mentioned by Indian Council of Medical Research.[12] The challenge remains with the purely asymptomatic cases and with the pre-symptomatic till manifestation of the disease is there because by this time, they might have spread the disease.

The overall concept can be explained by such a timeline diagram.

Diagram showing the asymptomatic and pre-symptomatic cases based on the incubation period.

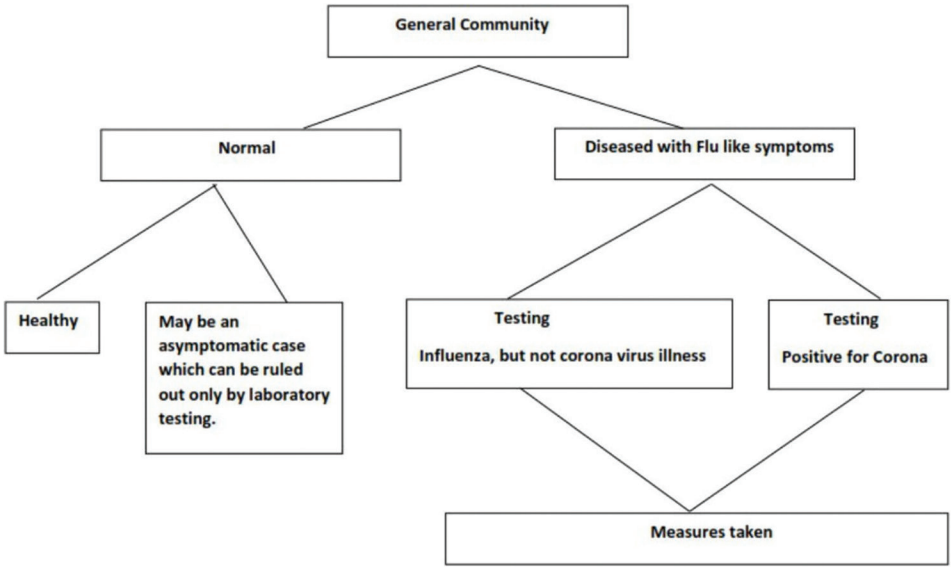
Pre symptomatic



Testing Strategies

The testing which is done in India is on symptomatic people and high-risk contacts of confirmed cases.[13] Time to time, the strategies have changed according to suitability and seeing to the resources and other feasibility conditions. Here, in the contact, these can be asymptomatic initially and may then be further categorized into pre-symptomatic who may develop symptoms within 3 days and may be longer; but within incubation period and then further may be mild, severe or critical based on the initiation of symptoms, and worsening of the symptoms. The idea of positive asymptomatic can only be got by laboratory testing. Based on reports from places where testing was done on a wide and extensive scale like in a medical facility in Washington state, it was found that more than half of those who were tested positive were found to be asymptomatic. This fact was strengthened from the testing done in Japan where they found 50% as having no symptoms, but tested positive and 18% remained asymptomatic.

Flowchart showing the situation of cases identification and healthy person in the community.



Situations

In contact list of cases

a. Asymptomatic, coming as positive on laboratory examination; but remain without symptoms throughout the incubation period
b. Asymptomatic initially, turned out to be a pre-symptomatic case, later on, with manifestation of signs and symptoms
c. Asymptomatic, if tested and coming as negative, person not having corona illness.

Without any contact list and in the community

a. Asymptomatic, status unknown as not tested, not in the contact list of any, if is positive, will act as a carrier in the community and is transmitting the infection
b. Asymptomatic, status unknown, as a pre-symptomatic case develops symptoms later on, if positive when diagnosed, then further workup can be done with contact tracing of this person.

Any asymptomatic or pre-symptomatic case till diagnosis and without being in contact history of anyone is a real potential carrier and will be a real challenge in the control of this pandemic.

VARIATIONS IN MORTALITY ACROSS COUNTRIES

There are various different indicators to see the impact of a disease. Apart from morbidity, mortality remains an important demographic factor. The different case-fatality ratio was reported across different nations. If we see the deaths/1 lakh population, it is not high as compared to other diseases like road traffic accidents. The case-fatality ratio is the number of deaths attributed to a particular cause to the total number of confirmed cases of that particular disease. Differences can be visualized based on the overall number of people tested. All the people are not tested and those who are tested are identified as a case or not diseased, if negative and out of the diseased how many deaths took place. Hence, it is not actually the real picture due to the lack of testing. More is the testing, a greater number of milder forms will be identified who may not die, so lowering the numerator and increasing the denominator which reduces the ratio. Gender wise and age group wise, there can be variation in the mortality ratio, which needs to be seen carefully. The availability of appropriate health-care infrastructure to take care of the serious patients, who will otherwise die, may reduce the mortality. Many factors may remain unexplained and unknown.[14] Positive health behavior of the people may prevent the disease, so overall the rate of infection becomes less. Deaths due to COVID-19 in India per/lakh population are 1.10 whereas the case-fatality ratio is 3.1%.[14]

BASIC REPRODUCTION NUMBER AND EFFECTIVE REPRODUCTION NUMBER

What is the Relationship between these Two?

Basic reproduction number

The potential to transmit disease is measured by the basic reproduction number (R_0). It is the average number of secondary infections from a case in a population considering that everyone in the population is susceptible.[15] The rates at which the disease spread in the community differs with the type of infectious disease as R_0 differs from disease to disease. Here, the entire population is considered as a population which is susceptible for infection. Further, in this understanding, if a disease is having a R_0 of 1, then the infected person is likely to infect one person, who can then spread this infection to one more person and so on, this chain will continue. One person is infecting only one is seen when R_0 is 1 and that's

why the spread is seen in the form of linear rate, that is, one is to one. If R_0 is more than or equal to 2, the rate of spread will be exponential, that means a single person will infect 2 persons, and then these 2 will give infection to other 2 and so on, 1–2, from these 2–4 then from 4 to 8 and so on. Three possibilities exist for the potential transmission or decline of disease, depending on its R_0 value and whether it is <1, equal to 1 or >1, which corresponds to decline, being stable and a chance of an outbreak or epidemic, respectively.[16]

Effective reproduction number

In some situations, due to the immunity gained through vaccination, natural infection or by taking chemoprophylaxis for a period, the entire population is not susceptible for infection. Susceptibility can be reduced to a greater extent by following certain special means like in case of COVID by doing the social distancing, so this population is rendered as not susceptible till the measures are adopted correctly. A population is rendered as not susceptible by the previous infection where immunity develops after the infection or by vaccine. The average number of secondary cases by a case in a population where the entire population is not susceptible is termed as the effective reproductive number (R). Social distancing is one of the ways by which the population is made lesser susceptible and not susceptible in case, it is properly followed. Seeing to the role of fomites in transmission, the preventive measures are to be more stringently followed and troublesome and act as a loophole in the chain of transmission. Hence, there are 3 situations when R is more than 1, <1 and equals to 1. The number of cases will increase if R>1, the disease will be seen in endemic form when R=1 and decline in the number of cases will be seen when R<1.[17]

Relationship between R and R_0

The relation is $R = sR_0$

R is Effective reproduction number
s is the susceptible population
R_0= Basic reproduction number

Importance of this relationship

Even though if R_0 is higher which is a biological inference where nothing can be done much, but if we want R as <1, the onus now lies on "*s*" which is the proportion of the susceptible population. If this **s** is made less by any intervention, the final R will be less.

R_0	s	R
1	1	1
2	0.5	1
4	0.25	1
5	0.20	1

Hence, here in this table, we can see that even if R_0 is more than 1 such as 2, 4 or 5 or any higher number, if the susceptible population which is a proportion can be lessened, can modify R to be finally as 1 and in this case when R is 1, the infectious disease is not a problem, that is, not seen in an epidemic form as the rate of spread will follow a linear rate. The ideal aim of any intervention, be it vaccination, chemoprophylaxis, or social distancing, is to get the effective reproduction number down to 1 and lesser by reducing the proportion of s.

So, we have seen that the ultimate aim of interventions which are deployed should ideally make R as <1.

HERD IMMUNITY

Herd immunity is a response of the immunity derived from the people who are immune by any means, may be by getting a natural infection or by vaccine. Hence, the people who are surrounded by such persons are protected from infection as this group of surrounding people which is termed as "herd" is protecting the persons who are not vaccinated or did not get the infection. Herd immunity is the protection given indirectly to unvaccinated individuals by others who are protected from the infection either by vaccination, natural infection, or other means like chemoprophylaxis during the epidemic. It varies according to many factors. These factors are multiple and depend on the infectious agent, routes of transmission, immunization effectiveness, and its coverage in the population.[18] The mechanisms of herd immunity are multiple and illustrated in a study by Fine.[19] The remaining susceptible persons are protected by a group of people now immune, so the exponential growth of the disease flattens out and with a final decay.[20] In herd immunity, there are two things to ponder upon, one is a natural infection and the other is through vaccine. Here, in this case of corona epidemic, still, vaccine is in trial. The vaccine usually takes 2 weeks for antibody response, so in between this period, the person is susceptible.[21]

Measurement of Herd Immunity

Herd immunity can be measured directly by the assessments of immunity in a defined population group. It can be done by antibody surveys or skin tests. Herd immunity can also be measured indirectly from the incidence pattern of the disease and how the disease is distributed among different age groups. This can be done only when the disease is easy to identify clinically and relatively common. For subclinical infection, this is an insensitive and inadequate method.[22] Hence, this method will not be a feasible method to measure herd immunity in corona, as it is a novel disease and majority cases are asymptomatic and in milder forms for which investigation is not done, so cannot be identified as a corona patient.

Herd Immunity Threshold (HIT)

It is the percentage of the population which requires to be vaccinated to make R <1. It is known that R=s R_0. There are two conditions. 1st is when R and R_0 are same that means when the entire population is susceptible and s is 1. 2nd is when "s" susceptible is the proportion of the population, so <1. If total susceptibles are s in a given population and 1 is taken as the universe, so immune will be 1-s. If R< 1, the epidemic will not occur. Replacing R by s R_0, that is, s R_0 <1. s<1/ R_0. Deducing the immunized person from the universe will be 1-s. Hence, 1-s >1-1/ R_0. The total population which needs to be immunized of the pool of susceptibles is 1-1/R_0. When the entire population is susceptible, 1-1/ R_0 is a proportion from the entire population and when s is a fraction of the population, 1-1/R_0 is a proportion of the susceptibles to be immunized. When the susceptibles are 100%, R and R_0 are same. Overall spread of infection depends on s and R_0 and the relationship, as shown in the table above. If susceptibles are less, even though the R_0 of the disease is more and the product that is s R_0, that is, R is <1, the epidemic potential of the disease will not be evident. Diseases having a basic reproduction number greater than 1, the epidemic threat is there, but if the susceptible population is less, the disease will not be seen in epidemic proportions. Interventional play is to keep the effective reproduction number <1, then the epidemic potential of the disease remains no more.[23,24] If the threshold for herd immunity is reached and further crossed, then the value of R reduces from 1 and the cases will decrease. Here, in the case of COVID-19, "s" can be considered as 1 or 100% as this infection is by a novel strain, so its but natural that there is no previous exposure to this virus, so no one is immune by infection and when this disease was introduced, the disease eventually reached an epidemic form in no time and also as reinfection has been reported in many cases of the previously infected cases, so again the immunity achieved by infection is a question. As per an article by the WHO released on April 24, 2020, enough evidence about antibodies to prevent reinfection in those who have recovered from COVID-19 is not there to issue a risk-free certificate.[25] If enough people are vaccinated against a disease, its R_0 can be effectively reduced to 1, ensuring that a disease will only spread at a linear rate.[24] Hence, if R_0 is 2, then the people who need to be vaccinated are 50%, this is by putting R_0 as 2 in the formula 1–1/R_0, that is, 1–1/2=.5, that is, 50%. According to the Oxford textbook of Public Health, at equilibrium, when R is on average unity, the proportion susceptible represents a threshold and below this infection rates would decline. At equilibrium, this proportion of susceptible is equal to the reciprocal of the basic reproductive rate. As per the literature from the Oxford textbook of Public Health, as the incidence and density of susceptible changes, the R fluctuates below and above unity. When the interventions are not applied or because of change in the demographics of the population structure, over a series of incidence cycles, the average value of R will approximate to one.[26] Hence, this is important that over a few cycles of incidence, the equilibrium is attained and the epidemic potential of the disease reduces and the disease becomes more of endemic nature. Prevention of infections and control of infections remain the mainstay measures. Isolation of symptomatic individuals and contact tracing with the quarantine of susceptible contacts is the main strategy. Fraser *et al*., in their study, showed that the success of the control measures such as isolation, contact tracing, and quarantine is determined much by the proportion of pre-symptomatic and asymptomatic transmission. During an outbreak of a novel infectious agent, contact tracing should be a priority to estimate the proportion of asymptomatic and pre-symptomatic.[27] Isolation of symptomatic individuals was a very effective control measure during the SARS outbreak and it reduces the effective reproductive number.[28] The effective reproduction number R can be reduced by intervention measures whereas R_0 remains unaffected, as it is the rate of infections.[29]

Reproduction number of some respiratory diseases is

- Measles 12–18
- Smallpox 3.5–6
- Mumps 10–12
- Influenza (1918 pandemic strain) 1.4–2.8.[30]

In the initial period of the epidemic in Wuhan, the doubling time was found to be 2.3–3.3 days by Sanche *et al*. They authors calculated a median R_0 value of 5.7 with 95% confidence interval as 3.8–8.9.[31] Based on this, HIT comes to 82.5%.

INTERVENTIONS

Interventions are directed to:[32]

1. Control or eliminate the agent as a transmission source
2. Protect entry in the host
3. Increase the defense mechanism of the host.

Susceptible are all and the only way out to reduce getting infection is avoiding the infection. Avoiding getting infection can be by multiple means. Lockdown remains as a measure for restricted movement and by this way, infections among susceptibles can be reduced to a great extent as the natural chain of transmission is interrupted. If properly applied in a planned way and seeing to the needs of all the sectors, it may bring out wonderful results. Again, relaxing of lockdown should be in a controlled way, so that it does not result in a multitude of cases over a quick period of time. Lockdown is a legislative measure and an attempt over successive periods to control the situation by avoiding being infected, whereas herd immunity is protecting the unprotected by reducing their susceptibility because of immune people in the vicinity. The thing of contrast is that lockdown means that many of those who are not infected will be susceptible post lockdown if the population HIT is not achieved. Hence, a greater number of peaks of the epidemic may be envisaged at this level, once such measures are completely uplifted and taken off. The community is advised to eat healthy and nutritious food, take good sleep, and doing yoga and meditation. AYUSH ministry suggested the use of homeopathy

as it is effective in the prevention of virus infections,[33] but contrasting reports are also available which says the guidance as irresponsible because the users feel prevented which may be a false security sense.[34] Zhang *et al*. in their study concluded that wearing of face masks in public is the most effective means to prevent human to human transmission. When simultaneously applied with measures such as social distancing, quarantine, and contact tracing represents the best efforts to stop the COVID-19 pandemic.[35] Medicines for corona have started coming,[36] but again it is suitable for mild or moderate cases. Vaccine is still in the trial phase. It will also come in the market sooner or later, but effectiveness should be much for widespread use in the community. However, still, amidst a high level of uncertainty, "Prevention" remains the main strategy for containment of this corona spread.

Intervention	Methods in place
Control or eliminate the agent as transmission source	• Avoiding crowded places • Avoiding unnecessary gatherings/meetings in person and such similar activities • Avoiding unnecessary travel • Lock Down measure to stop unnecessary movements • Strict Enforcement of Epidemic act 1897[37] nationwide and under individual states with their regulations in a strict manner with an amendment passed on April 22, 2020[38] • Strict enforcement of Disaster Management Act 2005.[39] Putting penalties under sections 51–60 of the act and section 188 in the IPC, 1860 • Division of areas in different zones and containment areas[40] • Use of Aarogya Setu app.[41] An alert system • Identification of pre-symptomatic, asymptomatic, and contact persons of confirmed cases and putting them on treatment and appropriate measures such as quarantine or isolation as per the Government rules and regulations • Washing the surfaces, cleaning of vegetables and fruits and other eatables[3]
Protect entry in the host	• Self-protection by use of face mask, whenever going out or meeting someone • By regular practice of hand hygiene • Maintaining a distance of 1 m
Increase the defense mechanism of the host	• Eating healthy and nutritious food • Taking good sleep • Doing yoga and meditation • Using immunity boosters[42]

According to Russell K, the words, "self-isolation," "social distancing," and "abundance of caution," were never seen together as in a pair before this year and are now spelled everywhere universally.[43]

CONCLUSION

Public understanding has to be there and this will play a major interventional role as overall, it reduces the transmission by blocking the transmission pathways through the use of interventions. Health education through mass media methods is already going on a very regular basis. Every citizen of this nation must perform and act in a sensible way as this will be very crucial for the development of this country, by not becoming a victim of corona disease on the context of being relaxed and not following the preventive measures as this is ultimately related to the economy by reducing the burden of the disease. One should live with a positive attitude in this current situation. The patients who are suffering from corona and those after the treatment should not be stigmatized. The support to the health system with due respect to the health functionaries and the overall system to maintain law and order is much needed and is the demand of the hour.

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