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Review Article

Feasibility of Developing Herd Immunity in the Absence of Licensed Vaccines in the Regime of COVID-19 Pandemic

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Abstract

Novel coronavirus disease (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is posing considerable economic and public health concerns worldwide due to high transmissibility it causes many morbidity and mortality in the main parts of the world.

It is urgent to design and develop safe and efficacious vaccines and to establish herd immunity to stop further spread of the COVID-19 pandemic. Even though the global COVID-19 vaccine pipeline is currently expanding daily and many clinical trials to evaluate novel vaccine candidates and drug repurposing strategies for the prevention and treatment of SARS CoV-2 infection up-to-date not effective, due to the nature of the virus. Even no one sure whether these trials will produce effective interventions, and it is unclear how long these studies will take to establish efficacy and safety. Hence alternative approach would be to allow the causal virus SARS-CoV-2 to spread to increase the population herd immunity.

In the absence of a vaccine, building up herd immunity through natural infection is theoretically possible. However, there is no straightforward and not always possible and effective. Therefore, in this review, we try to address the history, concept and feasibility of herd immunity in the absence of a licensed vaccine in the COVID-19 regime.

Keywords: *Herd Immunity; COVID-19; SARS CoV-2; Vaccine*

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, has spread worldwide triggering a pandemic [1]. The ongoing SARS-CoV-2 pandemic has caused over 32.1 million clinically confirmed cases of COVID-19 and has claimed more than 982,047 lives worldwide (as of September 24, 2020). There are no licensed vaccines and medications that are specifically target SARS-CoV-2 [2]. Numerous clinical trials to evaluate novel vaccine candidates and drug repurposing strategies for the prevention and treatment of SARS-CoV-2 infection are currently ongoing. However, it is unknown whether these trials will produce effective interventions, and it is unclear how long these studies will take to establish efficacy and safety, although an optimistic estimate for any vaccine trial is at least 12 - 18 months [3]. In the absence of a vaccine, building up SARS-CoV-2 herd immunity through natural infection is theoretically possible. However, there is no straightforward ethical path to reach this goal, as the societal consequences of achieving are devastating.

Herd immunity has to do with the protection of populations from infection which is brought about by the presence of immune individuals [4]. The concept has a special aura, in its implication of an extension of the protection imparted by an immunization program beyond vaccinated to unvaccinated individuals and in its apparent provision of a means to eliminate some infectious diseases [5]. It is a recurrent theme in the medical literature and has been discussed frequently during the past decade. This new popularity comes as a consequence of several recent major achievements of vaccination programs, i.e. the historic success of the global smallpox eradication program; dramatic increases in vaccination coverage stimulated by national programs and by the expanded Programme on Immunization; the commitment of several countries to eradicate measles ,and international dedication to eliminate neonatal tetanus and to eradicate poliomyelitis from the world by the year 2000 [6]. Along with the growth of interest in herd immunity, there has been a proliferation of views of what it means or even of whether it exists at all. Several authors have written data on COVID-19 which "challenge" the principle of herd immunity [3,7-9]. In this review we pretense the question of "Is it Feasible to develop herd immunity in the absence of licensed vaccines in the regime of COVID-19 pandemic?"

Methods

According to the literature retrieval strategies recommended by Cochrane Collaboration databases such as PubMed, Cochrane Library ,open access, Google scholar, Medline, Embase and Cochrane library were used comprehensively searched using the keywords natural immunity, Herd Immunity, Vaccine, COVID-19, SARS CoV-2 and basic reproductive number.

History and understanding of herd immunity

Herd immunity is a recognized epidemiological concept regarding the population-level effect of individual immunity to prevent the transmission of infectious diseases [10,11]. The first published use of the term "herd immunity" appears to have been in a paper published in 1923 by Topley and Wilson titled "The spread of bacterial infection: the problem of herd immunity" [12]. This was one of a classic series of studies by these authors on epidemics of various infections in closely monitored populations of laboratory mice and which was first to articulate a fundamental problem in infectious disease research and control came to a conclusion by firstly coining the term 'Herd Immunity' [13]. Herd Immunity is also called as Community Immunity, Population Immunity or Social Immunity, and referred to as the population-level consequence of acquired immunity among some individuals that can reduce the risk of acquiring infection among susceptible individuals [14]. The Immunity can be tested for, as the presence of antibody, or as skin test or lymphocyte response to stimulation, against the chosen antigen. Herd immunity is quantifiable by testing a sample of the population for the presence of the selected immune parameter [15]. It is not dependent on the ease or difficulty of circulation of neither an infectious agent nor its elimination. It may be due to natural infection, or immunization or a combination of both [16]. The term "herd immunity" was not widely used until recent decades, its use stimulated by the increasing use of vaccines, discussions of disease eradication, and analyses of the costs and benefits of vaccination programs [17]. Herd immunity has been used by various authors to conform to different definitions [16] and is essentially a simple concept describing the totality of naturally acquired and vaccine-based immunity to a given infectious agent as a proportion of the whole population. While the individual objective of vaccination is clearly to prevent or reduce the risk of infection for the individual concerned, the public health objective of vaccination is to increase the level of herd immunity to that required for control or elimination of the infection from the population and in the longer term on a regional or global scale to eradicate the infection altogether [18].

In the modern concept, the idea of herd immunity was first adopted in 1923 to represent the pre-immunity of a given total population, examining the rate of disease fatality among population at various degrees of immunity in experimental research [19]. The study recognized herd immunity as a naturally occurring phenomenon [12]. During the mid-1930s, A.W. Hedrich's epidemiological study of measles in Baltimore noticed a substantial decline in new infections after several children had been conscientiously exposed and immune to measles [19]. Based on this idea, mass vaccination is performed to develop pre-immunity among the masses; this process is called herd immunity in our modern medical sciences, as everybody of us naturally develops immunity after a due course of time [19]. The thought of herd immunity requires a deeper understanding of disease transmission and vaccination; understanding of the fact that the vaccine reduces not only the probability of infection but also the likelihood of spreading the disease to others. The more individuals who are vaccinated, the higher chances the indirect protection for non-vaccinated individuals in the community [20]. It indicated that indirect protection from infection conferred to susceptible individuals when a sufficiently large proportion of immune individuals exist in a population [3]. This population-level effect is often considered in the context of vaccination programs, which aim to establish herd immunity so that those who cannot be vaccinated, including the very young and immunocompromised, are still protected against disease [3].

As describe by Herd immunity has been demonstrated for infectious diseases of viral and bacterial etiology [21]. The term herd immunity is rarely used to explain the level of population immunity that will result in the elimination of a specific infection from the population [18]. It has to do with the protection of populations from infection which is brought about by the presence of immune individuals. This is because successful immunization reduces the number of susceptible in the population and this effectively reduces the efficiency with which the microbe is transmitted from one person to the other [16]. Herd immunity is achieved if the fraction of population with a high level of protection is equal to or greater than a certain critical fraction of population with a high level of Susceptibility [14,22,23].

Feasibility of herd immunity without vaccine for COVID-19 protection

The concept of herd immunity is commonly used in relation to vaccines. In fact, herd immunity has so far been the fundamental basis and the foundation of any public health vaccination program [24] and levels of herd immunity may be manipulated by the choice of the vaccine [11,25]. The rationality of vaccination is to expose a person to disease causing microorganisms or virus in a weaked, live or killed state or toxins from the organism as vaccines to boost a strong immune response providing a long protection from infectious diseases [11,26] and have a benefit to unvaccinated individual by reducing transmission and thereby lowering the risk of infection through the effect of herd immunity [27] since unvaccinated individual have less opportunity to expose the disease causing organisms [28]. However, to achieved effective herd immunity, we need upward of 70% of protective immunity in a population to prevent large-scale spread [11]. All these indicated that herd immunity comes into true only if the majority of a population has been vaccinated against an infectious diseases [11]. The percentage of people that are required to be immune through vaccination to develop herd immunity to protect infections is differ from infection to infection [11,29]. Depends on multiple factors including the mode of transmission, prevalence, nature of the infection agents, the contact pattern of the infectious person and how easily and quickly a given disease spreads [1,30]. A major advantageous of increasing the level of herd immunity through vaccination is that it may result in the elimination of the infectious agent from the population [30]. However, this is not always true because, archiving of herd immunity alone is not sufficient to accomplish infection elimination without effective and licensed vaccine. Besides herd immunity is not a guaranty to against all vaccine-preventable diseases. The best example of this is tetanus caused by a toxin produced by the bacterium *Clostridium tetani,* whose spores are commonly found in soil, dust and manure that can enter the body through any skin injury, not from other people who have the diseases. No matter how many people closed each other are vaccinated against tetanus, it will not protect people from tetanus [31]. Herd immunity only works if most people in the population are vaccinated (for example, 19 out of every 20 people need to be vaccinated against measles to protect people who are not vaccinated). If people are not vaccinated, herd immunity is not guaranteed to protect them [32].

Herd immunity is the indirect effect of vaccination [33] that occurs in a population where vaccinated individuals reduce the transmission rate of a virus and therefore lower the force of infection in unvaccinated ones [5]. For most infectious diseases, this assumption is correct. However, rarely herd immunity may have negative consequences for those who remain susceptible. Individuals may remain susceptible, either because they did not receive vaccination or because they did not mount an adequate immune response after receiving vaccination. In some circumstances, higher vaccine uptake and thus a lower circulation of a virus may worsen instead of improving this group's prospects. If a vaccination program reduces the transmission of a pathogen, the average time to acquiring infection of those remaining susceptible will increase (though not beyond life expectancy, unless vaccine uptake is very high). Thus, at suboptimal levels of uptake (suboptimal in the sense that elimination does not occur) those who remain susceptible will on average become infected at older age [22,34]. Vaccination creates herd immunity but the effects are not always positive and reaching herd immunity through vaccination is not always possible [34]. Some people may object to vaccines because of religious objections, fears about the possible risks, or skepticism about the benefits [35]. If the proportion of vaccinated people in a community falls below the herd immunity threshold, exposure to a contagious disease could result in the disease quickly spreading [36]. These come true in the present scenario from ongoing covid-19 pandemic disease.

COVID-19 is a very contagious disease and one of the most devastating in recent history [37]. In order to conclude how much herd immunity will be required to alleviate the subsequent outbreak of COVID-19 pandemic several determinant factors needs to be considered [38] including reproduction number (R_0). The basic reproductive number also called the basic reproductive ratio or rate or the basic reproductive rate is an epidemiological metric used to describe the contagiousness or transmissibility of Infection agents [39]. The basic reproduction number, R_0, is the number of secondary infections resulting from a single primary infection into an otherwise susceptible population. It is the most widely used estimator of how severe an epidemic outbreak can be [11,40,41]. Ro is value is affected by different factors such as Socio-behavioral factors, duration of the infectiousness in the host, the lifespan of infectiousness agent in the environment and whether or not infectiousness precedes infection symptoms [30,39]. An R_0 for an infectious disease event is generally reported as a single numeric value or low-high range, and the interpretation is typically presented as clear-cut [39,42]. If $R_0 < 1$, on average an infectious individual infects less than one person and the contagion is expected to stop spreading [40], if $R_o = 1$, the disease is maintained at a baseline level, whereas, if $R_0 > 1$, the infection will be able to start spreading in a population [17]. The larger the value of R_0 the harder, it is to control the epidemic R_0 often serves as a threshold parameter that predicts whether an infection will potentially spread among a completely susceptible population [43].

The R_0 value for SARS-CoV-2 is varying from country to country, from time to time based on the existing data. Current estimates of the mean R_0 range from 1.5 to 6.68 based on twelve studies published from the 1st of January to the 7th of February 2020 [44,45] (For example, the estimation value of R_0 in India pre-lockdown 2.6, post lockdown 1.57, and the estimated herd immunity is 61% and 36% respectively [46], in Italian between February 25-March 12, 2020 range from 2.43 to 3.10 [40], in Iran pre lockdown 4.86 to 4.5, post lockdown decreasing from 4.29 to 2.1 [47] in china 3.58 [48], in USA 5.30 ± 0.95 [49], in Sweden 2.5 [50], in Japan 2.86 [51] and in Africa 2.37 [52]). All R_0 estimates are significantly larger than 1, which indicates the potential of 2019-nCoV to cause outbreaks. We note that WHO reported the basic reproduction number for the human-to-human (direct) transmission ranged from 1.4 to 2.5 [53] this supported by the study done in China [54-57]. However, R_0 value of SARS-CoV-2, is estimated from 2.43 to 3.10 [40]. It is quite likely that some cases are not detected and the actual reproductive number is much higher than what has been stated so far.

A large percentage of the population will need to develop immunity against the disease through infection before herd immunity will be achieved. For COVID-19, the percentage of the population that needs to be infected to achieve herd immunity is estimated to be between 70% and 90%, and this is assuming lasting immunity is possible [58]. However, relying on community infection to create herd immunity to SARS-CoV-2 has faced some major problems. This might be due to several factors; (1) it isn't yet clear if infection with the COVID-19 virus makes a person immune to future infection, (2) the details of corona virus is not yet full studied, (3) there is no finite treatment for SARS-CoV-2, (4) selective severity of disease (COVID-19) in some people are not known, and (5) the emergence of a new strain of SARS CoV-2 due to mutation [11,17,59]. Therefore, other interventions have to be taken to reduce the transmission potential of the COVID-19 pandemic. Since it is not known when that will happen, but it will depend on how many people develop immunity after COVID-19 infection, how soon a COVID-19 vaccine is available, how many vaccine doses will be available for distribution, and how many people get vaccinated. Unfortunately, there is no vaccine for the Coronavirus disease (COVID-19) in the world yet [3].

In the absence of vaccines, it is seen that the best interventions to paused the spread of infection is prevention the hand hygiene comprises the use of alcohol-based hand rubs before as well as after contact with each and every patient. It is also suggested that to follow hand hygiene before as well as after food preparation, before eating, even after removing the face masks as well as hand gloves, not coughing or sneezing into the hands, cleaning the homes, staying indoors or reduce the probability of transmission [14,60,61].

Conclusion and Future Course of Action

In this Review, we try to address history, concept and feasibility of Herd immunity in the absent of licensed vaccine in the regime of the COVID-19 pandemic. Developing herd immunity in a short duration is impossible. To establish herd immunity an effective, safe, and licensed vaccine is a must. Therefore, each country must continue to reimplement national action plans to pause the pandemic till developing a finite vaccine and treatment drug for SARS-CoV-2.

Ethical Approval

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Competing Interests

The authors declare that they have no competing interest.

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