Learning from the COVID-19 pandemic: Concepts for good decision-making

Aprendiendo de la pandemia COVID-19: Conceptos para una buena toma de decisiones

To the Editor:

1) Recognizing the enemy

COVID-19 is caused by the SARS-CoV-2 virus, which due to its phylogenetic relationships shows a clear relationship with SARS-CoV-1 (SARS agent) and therefore with a very probable origin in bat reservoir (Macrochiroptera)[1-3]. Bats have more than 76 viruses with human pathogenic potential, such as Rabia, Marburg, Hendra, Nipah, Menangle, Tioman, Ebola, and the SARS and MERS coronaviruses[4]. Therefore this is probably an emerging zoonosis as a consequence of the transgression of the specific barrier, a phenomenon known as spillover.

After advanced studies on the subject, a case fatality of 1.38% (95% CrI: 1.23-1.53%)[5-7] has been determined, which is not so high compared to other diseases. Although it has caused a large number of deaths, it is not comparable to the number of deaths that TBC or

others. For example, COVID-19 reports 175,694 deaths today in 3 months, seasonal influenza 290,000-650,000 in one year, HIV 570,000-1,100,000, Malaria 450,000, TBC 1,300,000-1,500,000 a year[8,9].

So what is the problem? The problem is the large number of cases in a short period of time, that is, what we call an epidemic (a pandemic if it involves the entire world). This produces saturation of health systems and increases case fatality due to lack of adequate treatment, reaching values up to 7.7%[10] as the tragic Italian example. This is potentiated by the saturation of the health system with other respiratory diseases (seasonal influenza, SRV, adenovirus, etc.) and produces a "domino effect" on other serious diseases that need intensive treatment units (ICU).

The consequence of this is that the enemy is not the SARS CoV-2 virus. It is the accelerated transmission of this: the COVID-19 epidemic.

2) Estimating the transmission capacity of the virus.

The natural transmission capacity of the virus can be estimated through the basic reproductive number (R_0) of COVID-19: the number of new cases produced on average by each case, in a serial interval, in a completely population susceptible. The serial interval (τ) corresponds to the average time that passes between contagion and contagion. It is equivalent to the population concept of generational time. For example, the human life expectancy is about 80 years and their generation time is 30 years, in the same way the infective life expectancy of COVID-19 is 14 days but its serial interval is τ = 5 days). Although there is controversy in this regard [11], an approximate and reasonable value for COVID-19 is R_0 = 2.35.

However, during an epidemic, the size of susceptible population decreases, and as a consequence, the probability of transmission decreases until at some point the effect known as herd immunity occurs. That is the transmission slows down and finally stops. This generally occurs at a prevalence level p = 1-1 / R_0, which in the case of COVID-19 is approximately 60%[12] (57.4% for R_0 = 2.35). When epidemiological and disease control measures are taken, R_0 is not the best measure of transmission during the epidemic. A better parameter is the effective reproductive number *Re(t)*, which corresponds to the same concept as R_0, but under the effects of control and mitigation interventions during the epidemic, and can be expressed as $Re(t) = q(t)R_0$, where $q(t)$ represents the proportion of susceptible over time[13].

Therefore, it is clear that if the problem is the transmission and the overload of the health system, it is necessary to decrease *Re(t)*.

3) Estimating the burden of the health system

Since the most severe cases need to be admitted to the ICU, it is adequate to measure the ICU and compare it with the ICU availability of the ICU.

Let us look at two ways:

a) Maximum daily tolerance of patients (*MT*): if we have an availability of X ICUs and each ICU is used on average 14 days[5-7] then the system will only tolerate X / 14 patients per day. Since 5% of patients require an ICU, the system has a maximum daily tolerance of MT = (X / 14) /0.05 = 20 (X / 14) patients each day. Example: if we have 500 ICUs, 36 daily admissions will be tolerated or equivalently 714 new cases/day.
b) Expected ICU burden (*E (ICU)*): The number of new patients occurring in a serial interval (5 days) can be calculated by multiplying the number of "active" infected people ($I(t)$) by *Re(t)*. The active infected people can be estimated as the new cases accumulated in the last 2 weeks (14 days). Thus, the new cases generated in a serial interval ($C(t+\tau)$) will be $C(t+\tau) = Re(t)I(t)$. Since 5% of them will need an ICU with a delay of one week[5,6], it can be estimated that $E(ICU) = 0.05C(t+\tau)$ in approximately two weeks. This value can then be compared with the number of ICUs available. Example: if there are 5,000 active infected people and $Re(t)$ = 1.1, 5,500 cases will be generated in 5 days and we will need 275 ICUs available in 2 weeks.

4) Decreasing Re(t) with epidemiological interventions

Since $Re(t) = q(t)R_0$ and $q(t)$ represents the proportion of susceptible population over time and decreases throughout the epidemic, there will be a natural reduction in *Re(t)* due to herd immunity. However, unless a vaccine is created this takes a long time and would necessarily result in a large number of deaths and a saturation of health systems. Then we must decrease R_0.

The reproductive number can be expressed as:

$$R_0 = \frac{\beta Xo}{(\gamma+\mu)},$$

where β is the transmission coefficient, *Xo* is the initial density of susceptibles, γ is the recovery rate and μ the mortality rate. That is, R_0 is the product of the reproductive potential (βXo) and the infective life expectancy ($1 / (\gamma + \mu)$) [14]. A first idea then is to increase γ, finding a treatment, which until now has not been possible. Since we cannot modify *Xo*, we have to decrease the transmissibility coefficient.

The transmission coefficient can be expressed as: $\beta = bP(I/C)P(C)$, where b is the contact rate between people, $P(C)$, the probability of infectious contact and $P(I/C)$ is the probability that this infective contact yields an infection[15,16]. It follows, that epidemiological interventions must be aimed at reducing one or more of these three factors:

a) Probability of an infectious contact resulting in an infection *P(I/C)*: personal hygiene measures, use of disinfectants such as alcohol-gel, hand washing, use of masks.
b) Contact rate *b*: measures of immobility and social distancing.
c) Probability of infectious contact *P(C)*: traceability and isolation of infected and contacts, closure of schools and universities, quarantines, sanitary cords and lockdowns

These interventions have succeeded in reducing the initial $R_0 = 2.38$ to current *Re(t)* values of 1.1 (personal calculations) in Chile. But it should be noted that as long as there is no vaccine (which directly affects *P(I/C)* and *q(t)*), the virus retains the potential ability to return to values close to R_0 when epidemiological interventions are relaxed, since that the herd immunity is not occurred yet. The de-escalation of the interventions should consider at least four aspects: Load of active infected (*I(t)*), effective reproductive number (*Re(t)*), load of the health system and diagnostic effort, which is what allows the identification of cases, their traceability and isolation. The de-escalation measures will be more risky the more burden of active infected, the higher the effective reproductive number and the greater the burden on the health system. The risk will be lower the greater the diagnostic effort and associated traceability.

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References

1. Andersen KV, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Nature Medicine 2020; 26: 450-5.
2. Zhang YZ, Holmes EC. A Genomic Perspective on the Origin and Emergence of SARS-CoV-2. Cell. 2020. Doi: https://doi.org/10.1016/j.cell.2020.03.035
3. Lam TTY, Shum MH, Zhu HC, Tong YG, Ni XB, Liao YS, et al. Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins. Nature. 2020. DOI: 10.1038/s41586-020-2169-0
4. Callisher CH, Childs JE, Field HE, Holmes KV, Schountz T. Bats: important reservoir hosts of emerging viruses. Clin Microbiol Rev 2006; 19(3): 531-45.
5. Russell TW, Hellewell J, Jarvis CI, van Zandvoort K, Abbott S, Ratnayake R, et al. Estimating the infection and case fatality ratio for coronavirus disease (COVID-19) using age-adjusted data from the outbreak on the Diamond Princess cruise ship, February 2020. Euro Surveill 2020 Mar; 25(12): 2000256. Doi: 10.2807/1560-7917.ES.2020.25.12.2000256.
6. Russell T, Hellewell J, Abbott S, Golding N, Gibbs H, Jarvis CI, et al. Using a delay-adjusted case fatality ratio to estimate under-reporting. CMMID; London School of Hygiene & Tropical Medicine. CMMID Repository. April 2020; cmmid.github.io/topics/covid19/global_crf_estimates.html.
7. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of Coronadisease. 2019 in China. NEJM March 6, 2020, at NEJM.org. DOI: 10.1056/NEJMoa2002032.
8. WHO. World health report. Infectious diseases kill over 17 million people a year: WHO warns of global crisis. https://www.who.int/whr/1996/media_centre/press_release/en/ (consultado en abril de 2020).
9. Roth GA, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018; 392 (10159): 1736-88.
10. Lazzerini M, Putoto G. COVID-19 in Italy: momentous decisions and many uncertainties. Lancet Glob Health 2020; https://doi.org/10.1016/S2214-109X(20)30110-8.
11. Sanche S, Lin YT, Xu C, Romero-Severson E, Hengartner N, Ke R. High Contagiousness and Rapid Spread of Severe Acute Respiratory Syndrome Coronavirus 2. Emerg Infect Dis. 2020 Jul 4. https://doi.org/103201/eid2607.200282.
12. Anderson RM. How will country-based mitigation measures influence the course of the COVID-19 epidemic?. The lancet.com Vol 395 March 21, 2020 Published Online March 6, 2020 https://doi.org/10.1016/ S01406736(20)305675.
13. Chowell G, Hyman JM, Bettencourt LMA, Castillo-Chavez C. Mathematical and statistical estimation approaches in epidemiology. Heidelberg: Springer; 2009.
14. Anderson RM. Epidemiology. In Modern parasitology (Cox FEG ed.). Oxford: Blacwell Scientific Publications; 1993. 75-117 pp.
15. Canals M, Bustamante RO, Ehrenfeld M, Cattan PE. Assesing the impact of insect vectors on animal populations. Acta Biotheoretica 1999; 46: 337-45.
16. Canals M. Introducción a la epidemiología matemática. Santiago: Edicion Sociedad Chilena de Parasitología, Chile ISBN: 978-956-368-734-7; 2017.

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