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Analyzing The Possibility of Quorum Sensing in SARS COV-II

Manaal Tariq

The Shri Ram School, Moulsari, Delhi, India

ABSTRACT

COVID-19, a disease caused by the SARS COV-II virus has had alarmingly high transmission rates and cases in the past. In most places, they have reached up to a certain high value and then fallen back down. In this paper, we analyze some trends in the number of COVID cases in different countries (India and Thailand as examples) to contrast the transmission with the process of quorum sensing in bacteria wherein bacteria alter their gene expression in response to a signal on reaching a particular population density. Although quorum sensing is exclusively a bacterial phenomenon, here we analyze some potential similarities and substances that could serve as the link and could justify the idea of quorum sensing in viruses. Do note that this is simply an untested idea which I have researched thoroughly to provide an insight into the possibility of merging two disparate systems.

***KEYWORDS**: Quorum sensing, COVID-19, Bacteria*

1. Introduction

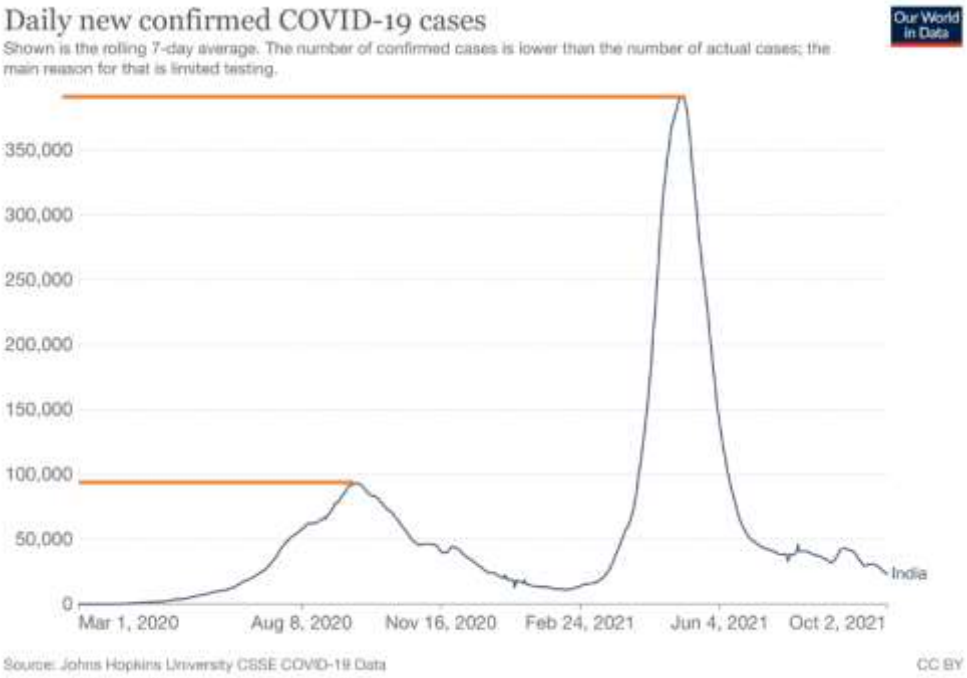
Cells, the fundamental blocks of the human body, communicate with each other through direct contact and chemical signaling to maintain a balance and coordinate activities. Living organisms- be it plants, animals, or bacteria- have all evolved their own method of sending and receiving signals to interact with their community members. Unicellular organisms also need to do so in order to perform a required task. While organisms like yeast use chemicals like the mating factor to initiate a signaling cascade, others like bacteria depend on a method called quorum sensing to use chemical signals, detect their population density and adjust certain associated behaviors subsequently.

As a part of their reproductive cycle, bacteria produce chemical molecules called autoinducers (in gram positive bacteria) and homoserine lactones (in gram negative bacteria) which are released into the environment. The continuous reproduction of autoinducers by a bacterial community increases their concentration which reaches a certain threshold limit. It is at this limit that the bacteria respond by changing their gene expression and producing an effect. This process is called quorum sensing and is responsible for multiple commonly observed phenomena like bioluminescence and biofilm formation. Analyzing the trends of the coronavirus pandemic across the globe reveals the analogous nature of a critical upper limit on the spread of the virus.

2. Abbreviations:
COVID-19/COVID: Coronavirus pandemic
SARS COV-II: Severe Acquired Respiratory Syndrome Coronavirus II
P. *aeruginosa: Pseudomonas aeruginosa*
QS: Quorum sensing
AI: Autoinducers
HSL: Homoserine Lactones
CRP: C-Reactive Protein
CF: Cystic Fibrosis
QSI- Quorum Sensing Inhibitors
QQE- Quorum Quenching Enzymes

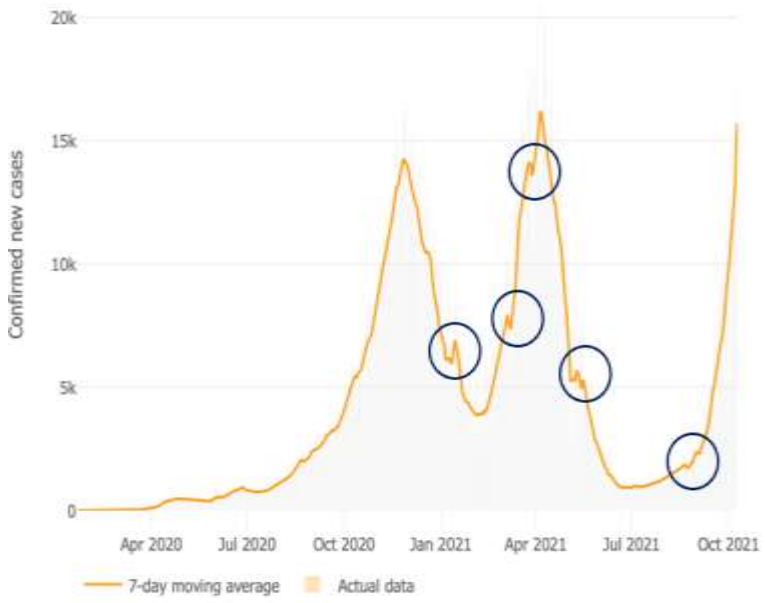
3. Analyzing India's COVID trends

The COVID pandemic, caused by the SARS COV-II virus, was a new type of virus from a previously existing group called the coronavirus. Its new abilities included moving from one species to another and between people. The transmission rates first peaked in China and soon augmented across the globe.



Above is a chart representing the trends in India from March of 2020 to October of 2021. A quick glance at it showcases the two major peaks in daily confirmed COVID-19 cases at two points (September 2020 and May 2021). After a high record of 93198.57 cases on September 16, the number of cases almost consistently went down. Similarly, on May 9 after a record high of 391008.29, the cases yet again went down consistently. This *general* observable trend in infection rates across the globes signals some mechanism that regulates a decline in the spread of the virus. Now while this can be attributed to improved management and characteristics of a virus, it can be compared to quorum sensing in bacteria wherein a change in gene expression is noted after a critical threshold is reached.

Although even a single SARS-II virus can spread the disease within a community, the spread cannot be as much as that in the case of a large viral presence. This indicates how the transmission can also be regarded as a process- not entirely but- dependent on the population density.



4. Thailand's Graph and Some Debateable Inconsistencies

Although India's graph was more convincing for the overall hypothesis being tested, when we look at the adjoining chart for Thailand we are able to see certain irregularities marked by the blue circles. Such inconsistencies in the graph suggest that the decline in cases was in fact not governed by an upper threshold value but was a matter of chance. However keeping in with the discussion in our paper, we can attribute such a irregularity to a commonly observed limitation of quorum sensing. In a study on acyl-HSL based cell signalling

in gram-negative bacterial species where interspecies communication was discussed, it was considered likely that one bacterial species could produce acyl HSL's that inhibited the results produced by quorum sensing of another species. [i] Co-infections with COVID have been noticed a large number of times and could potentially indicate some communication that hindered the decline.

In some studies concerning the coronavirus, certain inflammatory serological markers such as raised C-reactive protein and procalcitonin, that are commonly linked with bacterial infections, are observed even without a bacterial co-infection occurring. The increase in the levels of CRP is one that raises questions. In infections due to P. aeruginosa, the CRP value is also seen raised and is also used to monitor respiratory exacerbations.

Quorum sensing in P. *aeruginosa* may be linked back to the coronavirus. According to a study, N-3-oxododecanoyl-homoserine lactone and N-butyryl-homoserine lactone are two P. *aeruginosa* HSLs that can produce transcriptional results in mammalian eukaryotic cells. They can interact with and activate certain undetected endogenous proteins. What if a chemical like these HSLs are also present in the body of a COVID infected individual? The CRP, an acute phase protein, has already been noticed in increased concentration in some individuals with COVID. The presence of the HSLs can activate the CRP and get it detected in tests. They can also explain the hypothesis and prove the critical upper thresholds that we have elaborated upon.

5. Proposed Scope

The hypothesis and written matter is simply an analogy drawn from the process of quorum sensing. In a case where the above proposed idea holds true or where quorum sensing can be linked to the spread of COVID or another similar viral infection, it can be used in context of the variability of the virus. The coronavirus has approximately 12700 identified mutations and 12 main virus types. This high mutation ability can be attributed to being RNA viruses and having high virulence and evolvability however if one can prove that certain viruses use quorum sensing as a means to depend on population density and accordingly alter their gene expression then by simulating the population using a similar AI or HSL we can mimic the critical threshold and prevent the virus from infecting further. (By bringing an alteration in gene expression earlier)

In case of P. *aeruginosa* two QS systems are involved in virulence gene expression- the las system and Rhl. These two have transcriptional activator and putative transcriptional activator LasR, LasI and RhlI, RhlR respectively. If in fact the similarity we identified between a bacteria such as P. aeruginosa and SARS COV-II (or one close to it) holds true then virulence in viruses can also be controlled using QSI's that are directly affecting the aforementioned transcriptional activators. QS disruption through the use of QQE and QSI has been observed to reduce siderophore, protease, and rhamnolipid secretion. It has also been documented in inhibiting biofilm formation. Reducing rhamnolipid secretion and inhibiting biofilm formation are activities that can directly be associated with reducing virulence of these bacteria.

Viral genes affect viral virulence in a number of ways. Out of these, two include those that affect transmissibility and another than encodes for proteins that prove harmful to the hosts. Whether the same QSIs and QQEs can be used to prevent the spread of COVID is a matter of research and requires satisfactory data.

Another limitation however if we use this approach is related to the drug azithromycin. A gram-negative bacterium, *Pseudomonas aeruginosa* has been associated with infections in the blood, lung and other parts post-surgery in humans. CF patients have a high susceptibility to chronic P. Aeruginosa and have used antibiotic therapy to improve their life expectancy in the past however due to the presence of several encoded antibiotic resistance genes, the promise of this approach is limited. Azithromycin is also used in CF patients where it reduced the number of pulmonary exacerbations. According to a study published in the Lancet, using Azithromycin does not show any benefits in treating COVID-19 especially in the absence of any additional indicators. This showcases little possibility of the presence of P. Aeruginosa in the body of a COVID infected individual. On the contrary, certain studies have noted the presence of dental biofilms in people infected with SARS COV-II. Knowing that biofilm formation is associated with QS, we reach back to the same idea of them being linked.

6. Conclusion

The possibility of the occurrence of QS in the case of infection with SARS COV-II, a coronavirus is a matter of debate and deliberation. While one can make note of many similar agents between the two (P. *aeruginosa* and SARS COV-II), the possibility is hindered by certain studies and results. Nevertheless, it is evident that in the event of a confirmation of the presence of QS in viruses like the COVID-19 will allow us to reason a large number of facts about it ranging from biofilm formation to potential thresholds and associated complications.

The extension of a bacterial phenomenon to the world of viruses can also provide us with cues about overwhelming questions and leaves us pondering over ideas about critical upper thresholds even in other diseases.

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AUTHOR:

Manaal Tariq is a high school senior at The Shri Ram School Moulsari. She is an avid public speaker and advocate for health equity. She is intrigued by the idea of using technology and basic biological principles to find solutions to health issues and intends to pursue medicine at college.