The Danse Macabre: Autobiography of COVID-19, the mysterious me!

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The year 2020 has faced one of history's worst pandemics, especially in terms of economic disruption. Every individual is universally confronting the worst contagion since the post-1918 Spanish flu pandemic caused by the H1N1 virus [1]. Some analysis in relation to the Spanish flu has shown that the virus was deadly, as it triggered a "cytokine storm" which ravaged the immune system in all age groups, especially young adults [2]. Paradoxically, in COVID-19 infection, it is the elderly with co-morbidity who are at greater risk! With continuously rising numbers of confirmed cases, the COVID-19 pandemic is creating havoc amidst the entire human clan. Currently, it represents the pandemic of the century, with a mind-blowing number of confirmed cases of COVID-19, including infinite deaths [3]. Moreover, global healthcare professionals are clueless about any specific therapy or cure.

The current essay/opinion piece narrates a sequence of events in context to the emergence of COVID-19 in India, intermixed with the autobiography of the causative and the mysterious pathogen "SARS-CoV-2" (Severe acute respiratory syndrome-Coronavirus 2). The peculiarity of this piece is that the entire script has been flavoured with "Shakespearean quotes," mimicking the plot, poetry, and wit in Shakespearean writings. Blending Shakespearean quotes into the text gives the entire manuscript a dialogical feel, thereby emulating the liveliness of Shakespearean plays along with the crux of the problem.

Act I Scene I

First, as healthcare professionals, we need to unravel the mysteries of SARS-CoV-2. How should we do it? "Let us decode the structure of this sinner."

Beware the ides of March! -William Shakespeare, Julius Caesar (Act 1, Scene 2, Page 2) [4]

India is currently witnessing a spurt of COVID-positive cases! The major events of the COVID-19 pandemic in India started with an upsurge of cases commencing, especially from March 2020, with 100 COVID-19 positive cases confirmed on the "Ides of March," i.e., March 15th, 2020. [5] Subsequently, a cascade of events followed, as international passenger screening was initiated in March, while the first confirmed death in India occurred on the 12th of March 2020. The Indian government announced a countrywide lockdown starting at midnight on March 24th, 2020, to control the spread of COVID-19. By the 28th of March 2020, 1000 confirmed cases were reported, and on the 31st of March, the capital of India identified clusters of COVID-19 infection at one of the religious congregation events. Since then, the number of people testing positive in the country has reached more than eight lakhs.

Thus, March may be noted as one of the major occurrences of infection outbreaks in the pandemic timeline in India. To fight the contagion, several reactive measures were initiated in March 2020. Presently, everyone in the country is highly strained by the COVID-19 disaster. Emotional events such as grief following the loss of a loved one or some other traumatic event and the anxiety due to lockdown have taken a toll on everyone's lives. What is uniquely stressful about COVID-19 is that it is exacerbated by its duration and by its mysterious nature.

Act II Scene I Autobiography of SARS-CoV-2

The Coronas enter the world with a big bang. SARS-CoV-2 narrates the world about itself.

All the world's a stage, and all the men and women are merely players; They have their exits and their entrances -William Shakespeare, As you like it (Act II, Scene VII, Page 6) [6]

Look, folks — the world despises me right now as if I were some terrorist organization holding the entire world hostage. People are scared, petrified beyond their wits. And I am the one responsible for it. Yes, it is not a typing error. I am a viral disease and do not commit typing errors like humans. Yes, that is how you humans decided to spell me in capitals, as if the mere mention of my name wasn't frightening enough!

Based on the large number of infected people who were exposed to the wet animal market in Wuhan City, Hubei Province, China, it is suggested that I am likely to be zoonotic in origin [7] (Lu, Stratton and Tang, 2020). Unfortunately, I do not have any memories of my parents. So, folks, what do you know about me? How do I look? What am I made of? Who am I? It would be quite intriguing to identify me from a medical professional's point of view.

Microbiologically, I am SARS-CoV2, a severe acute respiratory syndrome coronavirus-2, known to the layman as the Novel Coronavirus or the Wuhan Virus. I come from a family of viruses called Coronaviridiae. Oh boy, we are a huge family. There are just so many of us. Me? I belong to one of the many lineages in this family.

My ancestry goes back to the sub-family of Orthocoronavirinae. There are four divisions in this sub-family, namely Alphacoronavirus (AlphaCoV), Betacoronavirus (BetaCoV), Deltacoronavirus (DeltaCov) and Gammacoronavirus (GammaCov) [8] (Ziebuhr et al., 2019).

Me? I am a proud member of the Betacoronavirus family.

You know who else is from the BetaCoV family? You know it... Come on. No? Okay, I will tell you. They are SARS-CoV and MERS-CoV. My cousin's man! Of course, you know them. They terrorised the world just like I am doing right now. SARS-CoV in 2002-03 and MERS-CoV in 2012. Damn the legends, I tell you. Soon, I will become a legend as well. [9]

Act II Scene II 3.1

You know why they call me the "Corona" virus? Ha! Ha!

"What's in a name? A rose by any name would smell as sweet."

-William Shakespeare, Romeo and Juliet (Act 2, Scene 2, Page 2) [4, 10]

Any guesses? It is a simple matter of linguistics. "*Corona*" or "*Coronam*" in Latin means "Crown". Because of the glycoprotein spikes we have in our envelope. And no, we have no relationship whatsoever with Corona Beer. [11, 12] It is just that we share the same name. Ha! Ha!

Furthermore, let me reveal more about my naming ceremony. It is quite intriguing, you see. I was nominated as SARS-COV-2 by W. H. O. on 11th February 2020, which stands for severe acute respiratory syndrome-Coronavirus 2. This name was chosen because I am genetically related to the coronavirus responsible for the SARS outbreak 2003. Although we are cousins as:

"We came into the world like brother and brother, And now let's go hand in hand, not one before another"

- William Shakespeare, Comedy of errors (Act V, Scene 1, Page 18) [4, 13]

But please do not be confused; both of us stand in sharp contrast to each other, befitting the popular saying "No two of us are alike—even identical twins." So you see, mine is a perfect example of a "Tragedy of errors" and not a "Comedy of errors". I seem to display higher levels of transmissibility and pandemic risk. Following this, WHO announced "COVID-19" (Corona Virus Disease-2019) as the name of the disease caused by me on February 11th, 2020. [14] Although from a risk communication perspective, using SARS as my name can have unintended consequences in terms of creating unnecessary fear for some populations, especially in Asia, which was worst affected by my cousin's outbreak in 2003. [15] So, as a result, WHO re-designated me as "the virus responsible for COVID-19" or "the COVID-19 virus" when communicating with the public. But remember that none of these designations are intended as replacements for the official name of the virus as agreed by the International Committee on Taxonomy of the virus.

Basically, we are a family of large, enveloped, positive-sense single-stranded RNA viruses. I can proudly say that we have the largest genome amongst all RNA viruses. You simply cannot imagine!!! And we protect this very valuable RNA inside a helical capsid of nucleocapsid protein and an extra layer of the envelope. On this envelope, we adorn our glycoprotein spikes, which give us the appearance of a crown under a microscope. Apart from that, we also have two other kinds of protein in our envelope – membrane protein and envelope protein. [16] I am zoonotic in nature and liable to cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms [17, 18]

It is difficult to imagine that, isn't it? Well, picture your favorite chocolate, the one and only "Ferrero Rocher" and his brother, "Ferrero Rondnoir". The innermost nut is my positive-stranded RNA. A nice gooey chocolaty mess covers the nut, the nucleocapsid layer. The crunchy, wafery layer is my envelope; on that layer, you'll find the small pieces of nuts, my surface proteins. Gorgeous and elegant, I must say. You see, I am pretty! Look at me. Isn't it hard to believe that something so destructive can be so beautiful?

Even though I am the reason for causing havoc on a global scale, I am so tiny that you can't see my details under a microscope. Experts have divided my infection into three main phases. Phase 1 is an asymptomatic or mildly symptomatic incubation period that does not necessitate hospitalization, with or without detectable virus; Phase 2 is a non-severely symptomatic period with the virus present; and Phase 3 is a severe respiratory symptomatic phase with a high viral load and a generalised hyperinflammatory state. Phase 3 is the most severe and dangerous; the generalised hyperinflammatory state is caused by a sudden release of cytokines into the circulation, defined as "CytokineStorm" (CS), which can lead to damage to organs and, in some cases, to death [19]. Prospero created the cytokine storm to the ferocious storm of "The Tempest" [4]. Although respiratory symptoms usually dominate clinical presentation, they are also known to cause serious cardiovascular consequences, including myocardial injury, myocarditis, acute coronary syndromes, arrhythmias, heart failure, cardiogenic shock, and respiratory insults like pulmonary embolism, along with gastrointestinal and genitourinary tract infections etc [20, 21].

So, folks that is it regarding my name, nickname, character, and reputation!

Act II Scene III

Corona is all gaga about his good looks. *All that glisters is not gold. -William Shakespeare*, <u>The Merchant of Venice (</u>*Act II, Scene VIII, Page 2)* [22, 4]

Now that we have established that I am quite handsome (thank you!), let me tell you a bit about what my good looks do for me. As you all have seen, I and my brothers (SARS-CoV and MERS-CoV) are respiratory viruses. And we come from animals. SARS-CoV came from civets and MERS-CoV came from dromedary camels. I come from bats. [23] Don't worry, you can still love Batman. He doesn't transmit the disease – because he is socially more distant than any of you can ever aspire to be!

Brother SARS-CoV and I are more alike in terms of our pathophysiology. [24] In fact, I was named SARS-CoV2 after him only. Once I enter the respiratory tract, I infect the ciliated bronchial epithelial cells and the type-II pneumocytes (you know, the ones responsible for surfactant production). And I do this via the Angiotensin-converting enzyme receptor 2 (ACE-2). [23] And as those cells are damaged, respiratory difficulty sets in, eventually leading to SARS. But more on that later. While we may have the same action, I am much more potent than my elder brother. I can be transmitted far more easily. Almost ten to twenty times more. This may be why I have created so much havoc in the world. The smart researchers then studied three monoclonal antibodies from my brother against me. But it was in vain. Those antibodies are not effective against me. [25] So, what makes me different from my brother, SARS-CoV? Why do they call me the novel coronavirus? [26] Humans, I believe, have some mutation. Maybe one, maybe more. Dozens, hundreds, and possibly thousands. And they believe one of these mutations is responsible for creating the pandemic. This mutation could have happened while I was enjoying my sauna in the bats (or supposedly even Pangolins, they can't place my origin), or it could have happened after I left the human bio-world. That is why, you see, I am the mysterious one. They have my entire genome; they have identified so many mutations, but they have yet to isolate that one mutation that makes me what I am today.

Act II Scene IV

Corona to mankind: Though I appear alluring, I am omnipresent. Beware of me! *"The devil can cite scripture for his purpose" -William Shakespeare, The Merchant of Venice (Act I Scene III Page 6) [4]*

Okay, are you still coughing? Uh-oh! If you're still guessing "Who am I?" you're not going to make it. Open your eyes, your ears, and all your senses, and you will see that now I am everywhere. Clinically, as described earlier, I primarily cause fever, sore throat, dry cough, tiredness, and flu like symptoms followed by dyspnoea, diarrhoea, loss of taste, and subsequently watch out! If it is not treated at the earliest, it can lead to acute respiratory distress syndrome and multiorgan failure. On an average, it takes 5–6 days from when someone is infected for symptoms to show, but it can take up to 14 days.

Act III Scene I

Now that I am an established pandemic representing a global public health concern, WHO has declared me a public health emergency! *"Hell is empty and all the devils are here" - William Shakespeare*, <u>The Tempest (Act I Scene II, Page 10) [4]</u> 2020 started off in the worst possible manner for the entire world. First, the seemingly never-ending Australian bushfires, followed by the standoff between the USA and North Korea with social media abuzz with talks of WW3, the assassination of a top military leader in Iran, the incessant torrential rains and flash floods in Australia, which then invited the funnel-web spiders to multiply like anything and envelop Australia in a web of their own. Not to forget, one of the worst locust invasions in Eastern Africa in 70 years, the eruption of Taal volcano in the Philippines, the earthquake in Turkey, an avalanche in Kashmir, flash floods in Jakarta, Indonesia and the tragic death of National Basketball Association (NBA) star Kobe Bryant. Yes, hell was definitely empty, and all the devils had descended on Earth. And while all of this was going on, the coronavirus was silently festering (not that silently either), just waiting to stake its claim to the limelight.

Act III, Scene II

Out, out, brief candle. Life is nothing more than an illusion -William Shakespeare, Macbeth (Act 5, scene 5, Page 2) [4]

This new virus outbreak has challenged the economic, medical, and public health infrastructure of every country globally. Time alone will tell how the virus will impact our lives here in India. More so, future outbreaks of viruses and zoonotic pathogens will likely continue. With no vaccine to protect against influenza infection and no antibiotics to treat secondary bacterial infections that can be associated with influenza infections, control efforts worldwide were limited to <u>non-pharmaceutical interventions</u> such as isolation, quarantine, good personal hygiene, use of disinfectants, and limitations of public gatherings, which were applied unevenly.

Unfortunately, there are no drugs or other therapeutics approved by the US Food and Drug Administration to prevent or treat COVID-19. [27] At times like this, these are words that come out: "The scientists who discovered me should be guilty of the outcome." This Shakespearean quote seems apt here:

"Hell is murky," The pair, in their destructive power, have created their own hell, where they are tormented by guilt and insanity. -William Shakespeare, Macbeth (Act 5, scene 1, Page 2 [4, 28]

Current clinical management includes infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated. [29, 30]

Act IV Scene I

There is nothing either good or bad, but thinking makes it so. ' - William Shakespeare, <u>Hamlet (</u>Act 2, Scene 2, Page 11) [4]

Corona's internal discord now appears reflected in angry defiance of the world and its opinions and beliefs. Its contagious presence has left people with mixed emotions. Some feel life is something to unsettle, while others feel the experience of seeking truths about life. With the national lockdown due to COVID-19 in India, the lives of medical students have been overturned, which is distressful. Pessimism is caused by negative emotions such as stress and worry, which altogether influence students' wellbeing and academic performance in the long run. Although isolation helps reduce infections, reduced access to family, friends, and other social support systems causes loneliness, increasing mental issues like anxiety and depression [31].

During such stressful situations, the concerned governments, hospitals, educational institutions, organizations, and even individuals need to look into psychological intervention and adopt necessary measures. In addition to educating individuals to stay isolated, it is vital to educate and prepare them to face the mental health issues they may endure during the period. Therefore, apart from curbing this outbreak, efforts should be made to

devise comprehensive measures to prevent anxiety and psychological manifestations due to the lockdown. [32, 33]

Hence, the following tips provided below can help overcome the impact of COVID-19 or any health calamity on mental health:

1. Take a break from the news: As we sit at home, we need to consciously minimize ourselves from reading depressing stories and watching videos of people struggling around the globe. Starting today, reduce your news consumption related to COVID-19 to not more than half an hour. People who watch the negative news can have both anxious and sad mood, and also show an increase tendency to catastrophize a personal worry.

2. Learn to work from home: While work from home was a social experiment, the world was thinking for a long time, we never thought that we would be forced into it suddenly and that this will become the new-normal. We have to use this opportunity to develop ways and means on how you can work from home.

3. Use time constructively: Staying at home during this time can be not only protective but also productive as you will never get so much of free time to do the things you always wanted to do and learn. It could be from as simple as learning to make a tea to learning how to play the guitar through a number of online tutorials. Utilize your time for something constructive and creative.

4. Rekindle your passion: So many of us always complain about the shortage of time when we are not able to follow our hobbies like reading, writing, painting, cooking, etc. You can't ask for a better time. Just pick that book up which you wanted to read so badly. Research also suggests that using leisure time enjoyably is associated with positive mental well-being

5. Adopt a minimalist life: People around the globe are beginning to realize the vanity and futility of so many things which we hoard at home only to find them absolutely useless. This is the best time to take control, declutter, and adopt a minimalist life. That pair of shoes you rarely wear; those clothes you have been hoarding all along, etc. There are many such things at home, and you know it. If you still don't know then relax you have three weeks to find out. Minimalism removes clutter and allows you to focus on important things.

6. Fall in love with a healthy diet, a diet full of tryptophan It will perhaps be for the first time that our generation will avoid going out on weekends for dinner. It is the perfect time to fall back in love with your mother's food, and after we come out of this pandemic, we might just not get the need to go out and party all the time. Home cooked and organic food is healthy, and there is a lot of science to back and 21 days is good enough to develop a healthy habit.

7. You can still exercise: Just because the gyms are closed, and you cannot go out and play your sport does not mean you cannot exercise at home. There are hundreds of videos on YouTube on how to exercise even lying in your bed. It is not a bad time to make exercise a part of life. You can also add meditation to your routine.

8. Reconnect with your family: Those who are lucky to have a family at home please understand that you are privileged. Share time with them and reconnect with them over a hot cup tea and some good light music.

9. Remember it is still the best time to be alive: This might appear shocking to many but understand that in the entire history of humanity we were never so equipped to handle the pandemic as we are now. We know the virus, we know how it spreads, and that is the reason why we are isolating ourselves. Our poor forefathers who faced encountered several pandemics couldn't fathom what hit them and would just call it "Black Death". We are privileged to live in this connected world and can still do most of the things, sitting at home. Indulge in exercise at home, gardening, pursue your hobbies, pray, meditate, learn some recipes for food, involve yourself in creativity etc.

10. Remember to breathe and have fun. Do not let the humour die even during these turbulent times. It is okay to joke or enjoy memes, even on coronavirus. We are lucky to have the likes of technology and media services like Netflix as companions during such a crisis. Think of the previous century and compare. Stay happy, stay safe and healthy. Binge-watch old comedies, new web series and have fun at home. So, sing, love, laugh and say to yourself the following Shakespearean quote:

"This too shall pass" -William Shakespeare, Hamlet (Act II, SceneII, Page 4) (Shakespeare, 1914).

Note:

This piece is dedicated to the first author's i.e. Dr. Anuradha Joshi's, Literature teacher in her school days, Mr. Sudarshan Chowdhary, for playing a pivotal role in making Shakespeare plays an interesting read during literature classes. He is currently the Principal of St. Pauls School, situated at eastern part of India. Authors here wish to convey the importance of interdisciplinary education by blending literature with medicine (a pertinent example of Creativity in medical education).. Educators need to impart and foster creativity in medical education and allied subjects.

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