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Review

Impact of covid-19 on mental health and aging

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ABSTRACT

The potential ramifications of the COVID-19 pandemic on the population's mental health are a rising global concern. Both at the individual and community level, the erratic and uncertain COVID-19 outbreak has the prospective to exhibit a detrimental effect on psychological health and aging. At present, various measures are dedicated to the parameters like awareness of epidemiology, clinical aspects, mode of transmission, counteracting the spread of the infection, and public health problems, although this initiative has neglected critical mental health concerns. This study is to investigate the outbreak to study the level of harmful effects on mental health and its crosstalk with aging. Global execution of preventive, control measures and resilience establishment are challenging factors whereas reformed lifestyle such as lockdown, coping with self-isolation, quarantine, social distancing, and post-traumatic stress disorders are alarming. Hallmarks of aging which interact with each other, have been suggested to affect the healthspan in aged adults, possibly due to attenuated immunity. Among various hallmarks, we concentrated on those that show direct or indirect interaction with viral infections, comprising inflammation, genomic instability, impaired mitochondrial function, epigenetic modification, telomere attrition, and damaged autophagy. These hallmarks possibly contribute to the elicited pathophysiological responses to SARS-CoV-2 and may add an additive risk of accelerated aging post-recovery among aged adults. Here, the role of antiaging drug candidates that require main consideration in COVID-19 research is discussed briefly. In the later future, it can emerge as a potential therapeutic approach in the treatment of patients with severe infection.

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1. Introduction

The anomalous impact of COVID-19 does not only affects physical health and well-being of the population but mental health too, which harms the health system. Whereas compared to physical health, the concern on mental health issues always takes a backseat. Mental well-being is a condition in which individuals can cope up well with multiple pressures of life, appreciate their potential, work productively and contribute to their communities (Pfefferbaum and North, 2020). For the overall response and recovery from COVID-19, good mental health is as crucial as the attention on physical health. The most important mental health disorders identified that have been correlated with the outbreak of COVID-19 are stress, symptoms of depression, anxiety, insomnia, outrage, and fright throughout the globe (Torales et al., 2020). A recent report in psychiatry advocates that COVID-19 can lead to an augmented risk of suicide (Liu et al., 2020). Another recent study conducted in China recorded 16.5% of average to severe symptoms of depression, 28.8% of average to severe symptoms of anxiety, 8.1% of moderate to severe levels of stress because of COVID-19 (Wang et al., 2020), and a high prevalence of mental health issues correlated with regular exposure to social media in the course of pandemic (Gao et al., 2020). Organizations and people may build cognitive, sentimental, and interpersonal capabilities that facilitate responses to adaptive managing and contribute to both an organizational and a self- resilience plan (Albott et al., 2020). Based on this, the distress responses to the COVID-19 contagion and strategies for improving organizational and personal resilience have been compiled in (Table 1).

1.1. Effects of contagion on mental health of healthcare experts

Health professionals who are actively involved in the diagnosis, treatment, and care of COVID-19 patients are at risk of psychological distress and other signs of mental health. The elicited number of confirmed and suspected cases, excessive workload, lack of personal protection facilities, lack of specific medicines, and feelings of insufficient support can cause mental problems to health workers (Lai, et al., 2019).

1.2. Impact of contagion on mental health of elderly people

There is a common concern that social restrictions to control the spread of COVID-19 would disproportionately affect older people, especially those who live alone (Armitage and Nellums, 2020). The only study showed the effect of social isolation and self-confinement among older people during health crises focused on jobs after the MERS outbreak in South Korea (Yoon et al., 2016). Social distance has become a major factor for increased incidences of depression, anxiety disorders, and suicide, especially in old-age homes, because of greater biological, physical, psychological, and physiological vulnerability, social isolation of the elderly age group is a significant public health concern. The study has proposed 15 smartphone applications that are thought to be beneficial during isolation for the elderly with cognitive, visual, and hearing impairments (Banskota et al., 2020). The case fatality rate (CFR) of COVID-19, that is the death to confirmed infections ratio, was shown to be lower in patients under 60 years of age (1.4 percent) relative to those 60 years of age or older (4.5 percent) (Verity et al., 2020).

1.3. Impact of COVID 19 on young population

The most productive class of any country are the young individuals who have been severely impacted by the outbreak. People may use different unhealthy ways to cope with stressors, including alcohol consumption, opioids, cigarettes, or wasting maximum time on possibly addictive chores including virtual gaming. Statistical study in Canada shows that during the pandemic, 20 percent of the population which are between 15 and 49 years old have surged their alcohol consumption (Dozois, 2020). According to the studies by Italian and Spanish parents, many children's emotional status and actions have been impacted during quarantine. The most vulnerable are differently challenged children, those who stay and labor on the streets. To combat the issue, the book

Table 1
Psychological stress responses to the pandemic of COVID-19 and preventive measures for the establishment organizational and individual resilience.

General COVID-19 psychological stress outcomes	At individual level	At institutional level
Physical and cognitive/sentimental exhaustion	Practice self-care for sleep, rest, diet, and exercise for physiological wellbeing	Actively convey the value of sufficient rest and self-care to employees
Fear, anxiety, and anger related to self, family, and coworker safety threats	Practice compassion for oneself, altruism, and compassion for others	Provide simple guidelines on PPE, problems with practice, preventing virus transmission
Hyperarousal, fear, and a feeling of lack of control	Maximize self-efficacy practices, establish a customized resilience strategy for hyperarousal control, reduce media and intoxicant intake and pursue individual therapy.	Recognizing doubt and change, fostering optimism and restricting communications
Depression in the context of personal identity, sorrow and disturbance	Practice self-compassion and hope, actively participate where possible in constructive assertive control	Recognizing losses and minimizing the use of unessential words
Loneliness and loneliness due to alienation from society	Foster mutual effectiveness, experience and share personal stories, share optimistic feelings	Encourage mutual effectiveness
Reactions from post-stress and occupational burnout	Using peer help and preventing further repercussions by finding clinical assistance	Encourage ongoing support initiatives for peers and access to mental health resources

'My Hero is You' has been written by a committee of UN and non-UN organizations to assist children with an age of 6–11 years to come up with their difficulties of pandemic (Ghebreyesus, 2020).

1.4. Psychological resilience among population during the pandemic

Psychological resilience is a progressive mechanism confining what is interpreted and understood while confronted with realities (Basim and Çetin, 2011). Psychological resilience improves the capacity to combat and withstand challenges that can make it easier for health care staff to recover from the pandemic. People with a sound mental state are less affected by the consequences of the pressures they encounter and could be more involved in crisis management. By fighting, resisting, and demonstrating the right attitudes, individuals with psychological resilience can easily overcome stressful circumstances (Bahar et al., 2020).

1.5. The psychological effect on quarantine and self-isolation and coping mechanism

Quarantine may be a required preventive measure during major infectious disease outbreaks. This study, however, indicates that adverse psychological effect is frequently correlated with quarantine. Quarantine refers to the isolation and prohibition of the movement of individuals who have been manifested to infectious disease and have a probability to be ailing, thus diminishing the chance of spreading infecting. Whereas isolation is the separation of those people who have been diagnosed with a contagious disease from healthy people but are sometimes termed interchangeably. The psychological effect of quarantine is wide-ranging and can be long-lasting. The psychological effects of not using quarantine and allowing disease to spread might be worse than the suggestions for non-implementation of quarantine. Depriving people of their rights for the broader public benefit, however, is always controversial and needs to be treated carefully. If quarantine is essential, then our findings indicate that officials should take every step to ensure that this experience is as tolerable for individuals as possible. This can be done by: reminding people what is going on and why, explaining how long it will last, providing them with meaningful things to do while in quarantine, providing consistent communication, ensuring that essential resources are available, and strengthening the sense of altruism that people can feel rightfully (Brooks et al., 2020).

1.6. Extensive accessibility of mental health and psychosocial support

In case of emergency, accessibility of mental well-being and psychosocial help becomes a prime concern. These include supporting the actions of community that sustain social solidity and decrease loneliness. Implementation of quality-ensured telecounselling to the frontiers, health care employees and people suffering with depression and anxiety at home (Nations, 2020). Strategies for strengthening and collective resilience, intensive clinical monitoring at the level of patients and populations. In addition, detection and referral of individuals were at increased risk of psychiatric issues. Providing the population with accurate and credible knowledge about the epidemic and the preventive measures. Combating stigmatization and social isolation of those who have lost someone close due to infection, promoting the initiation and maintenance of appropriate psychiatric and psychological therapies, and introducing effective psychosocial measures are key factors that increase the probability of a stable psychiatric response from the COVID-19 pandemic (Bao et al., 2020). To bring together the various determinants effecting the mental health and, a diagram is shown (Fig. 1).

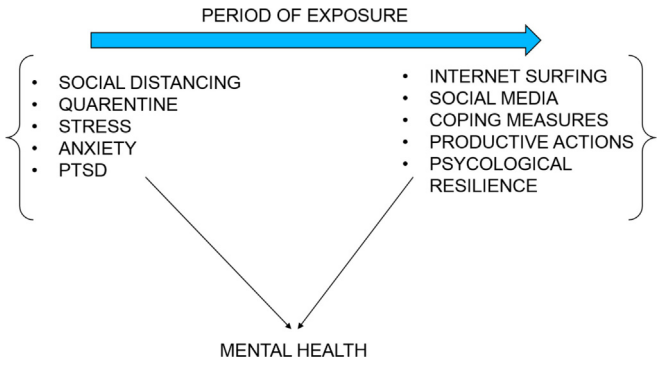

Fig. 1. Mental wellbeing determinants during the COVID-19 Pandemic. The various risk factors and preventive factors affect the mental wellbeing. PSTD (Post-Traumatic Stress Disorder).

1.7. Crosstalk between COVID19 fatality rate and aging

Since the aged individuals are amongst the most vulnerable group, it becomes important to understand the various cellular processes causing aging and its correlation with the pandemic fatality at biological level. Normal ageing involves changes in the marks of aging such as in the cells, tissues, and organs that lead to the aged population's morbidity and deaths. The various hallmarks of aging interact with each other and are key players in chronic diseases in various facets of cellular and system functions (Santesmasses et al., 2020) and associate with viral infection directly or indirectly. Some of the listed characteristics are immunosenescence, inflammation, instability of genome, dysfunction of mitochondrial system, telomere attrition, and damaged autophagy, resulting in the potential variability and adaptation in response to stress. These characteristics are taken into consideration for the treatment of COVID 19 infected elderly people (Salami, 2020).

COVID-19 severe manifestations increase with age, with older patients having the highest fatality rate, implying that aging-related molecular pathways contribute to COVID-19 severity. The continual shortening of telomeres, which are protective structures at the ends of chromosomes, is one cause of aging. Tissues with critically short telomeres have a lower regeneration ability, which leads to a loss of tissue homeostasis and illness. Tissues with critically short telomeres have a lower regeneration ability, which leads to a loss of tissue homeostasis and illness. We measure telomere length in peripheral blood lymphocytes COVID-19 patients with ages between 29 and 85 years-old. We discovered that shorter telomeres are linked to greater disease severity. Individuals with telomere lengths in the lower percentiles and telomere lengths in the upper percentiles are more likely to acquire severe COVID-19 diseases (Sanchez-Vazquez et al., 2021).

Spermidine, a natural polyamine with anti-aging characteristics, has been discovered. Supplementing with this medicine extends life and reduces the occurrence of age-related diseases. Spermidine levels decline with age in the human population, and a possible link between decreased endogenous spermidine levels and age-related declination has been investigated. Spermidine supplements in the diet help to lengthen telomeres. The proposed hypothesis also identifies genes involved in telomere preservation and aging that are altered differently after spermidine therapy. Understanding the role of spermidine in telomere maintenance will aid in deciphering the molecular mechanism behind spermidine's anti-aging effects (Sharma and Jaiswal, 2021).

The analysis shows a close correlation between the fatality rate of COVID-19 and aging with the fatal respiratory diseases should be taken into consideration along with latest emerging aging dis-

eases. Aged individuals are more prone to infection, therefore approaches to address the aging process, along with antiviral approaches and those that increase the human immune system of the aged individuals can be effectively taken for treatment strategy. The points which are to be highlighted for the study encircle the mechanisms which facilitates the COVID-19 virus to target individuals especially with higher chronological age. To understand this two host receptors such as CD26 (Raha et al., 2020) and the other protein is ACE-2 (angiotensin converting enzyme 2) (Ni et al., 2020) have been known. ACE-2 is also known to inhibit cell proliferation and upregulates both chronological and replicative senescence (Gheblawi et al., 2020).

The cell undergone to senescence shows production of high levels of inflammatory cytokines because of senescence-linked secretory phenotype (SASP) and IL-6 leading to the hypothesis that the COVID-19 virus is related to increased mortality in aged patients. Chloroquine and its derivatives like Hydroxychloroquine aggregate in senescent cells. Azithromycin play a vital role in senescence (Arason et al., 2019). Similarly, Rapamycin is well studied for the inhibition of replication in of HIV-1 (Nicoletti et al., 2009) and displays significant anti-aging properties (Blagosklony, 2019). In line, the efficacy of Doxycycline to blocks replication of Dengue virus is significant and acts an anti-aging drug (Sargiacomo et al., 2020).

Therefore, Rapamycin and Doxycycline can be potent inexpensive agents for the treatment as well as prevention of infection caused COVID-19 virus. Lastly, a new analysis based on silico-based supercomputer drug docking to the viral spike protein COVID-19 lead to the identification Quercetin as a possible binding partner with ACE-2 to decrease interaction between virus and host. Quercetin also shows senolytic properties as the dietary supplement (Puttaswamy et al., 2020). Therefore, a hypothesis can be proposed on the progressive chronological age along with mortality from COVID-19 could recommend the application of senolytic or anti-aging agents/drugs in the prevention of COVID-19 disease is represented in Fig. 2. Therefore, clinical trials comes to an important approach to evaluate this alluring, but theoretical hypothesis with lab experiments.

Though few viruses are known to rescue the direct autophagy-mediated cascade, autophagy's immune-mediated effects can also regulate viral infection and tissue damage due to inflammation. Impaired autophagy, a hallmark of aging, can thus lead to the severity of COVID-19 and adversely affect older patients. The two drugs which have been approved by FDA are Niclosamide and valinomycin induce autophagy and attenuates viral replication (Gassen et al., 2019) illustrated in Fig. 3. However, the polyamines show anti-viral affect, one of them is spermidine, an inducer of autophagy is yet to be studied (Li et al, 2016). Despite rapamycin as an immunosuppressive drug, it inhibits mTORC1 and ameliorates immunity in older adults and elicits the outcomes to vaccines as few clinical trials show no severe side effects in population (Stallone et al., 2019). Therefore, rapamycin is anticipated to show better results in older individuals with COVID-19.

COVID-19 Aging Mitigation Interventions The severity of COVID-19 has been linked to host–virus interactions such as cytokine storm and coagulopathy, underlying comorbidities, and possibly polypharmacy. To combat both acute and chronic COVID-19-related disorders, drugs that boost immune system response and increase body system health are required, as well as enhancing vaccine and antiviral therapy responsiveness. Older people who have a poor response to immunizations or antiviral medications could push the pandemic to epidemic proportions among the elderly. As a result, when antiaging treatments become available, they may assist to minimize the severity of COVID-19 and boost vaccine response. As a result, treating SARS-CoV-2 needs measures that go beyond direct virus targeting to increase bodily system performance through improved immunity, which is especially important in the elderly. As a result, interfering with aging mechanisms has the potential to boost the responsiveness of antiviral medications (Barzilai et al., 2016). Medications that minimize mitochondrial ROS production and improve the immune system are among the possibilities. Rapamycin has been shown to improve immune function in the elderly while also enhancing influenza vaccination immune response (Mannick et al., 2018). Metformin, a long-used anti-diabetic drug that may also be used as an anti-aging treatment, prevents viral replication and interactions between the host and the virus (Moser et al., 2012). The enzyme Sirt6, which regulates multiple age-related signaling pathways, has been demonstrated to reduce the massive inflammatory response to the deadly dengue virus infection (Li et al., 2018). We propose a more quick understanding of COVID-19′s interactions with host aging hallmarks in order to find biomarkers that can be utilized to identify people at higher risk. Understanding the processes of COVID-19 will most likely come from comparing

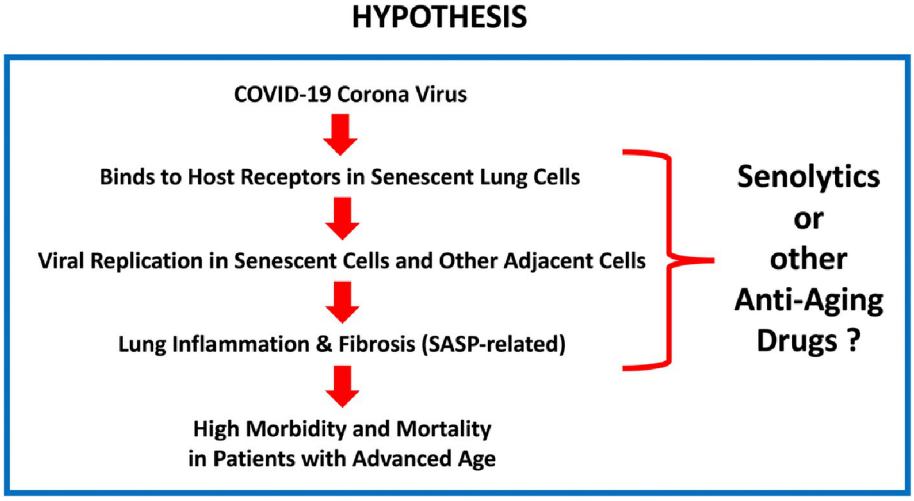

Fig. 2. COVID-19′s relationship with advanced chronological age. The diagram suggests the COVID-19 virus attacks senescent lung cells contributing to increased morbidity and mortality in the aging population. Usage of senolytics or other antiaging medications will be one potential option for prevention/treatment (). adopted from Sargiacomo et al., 2020

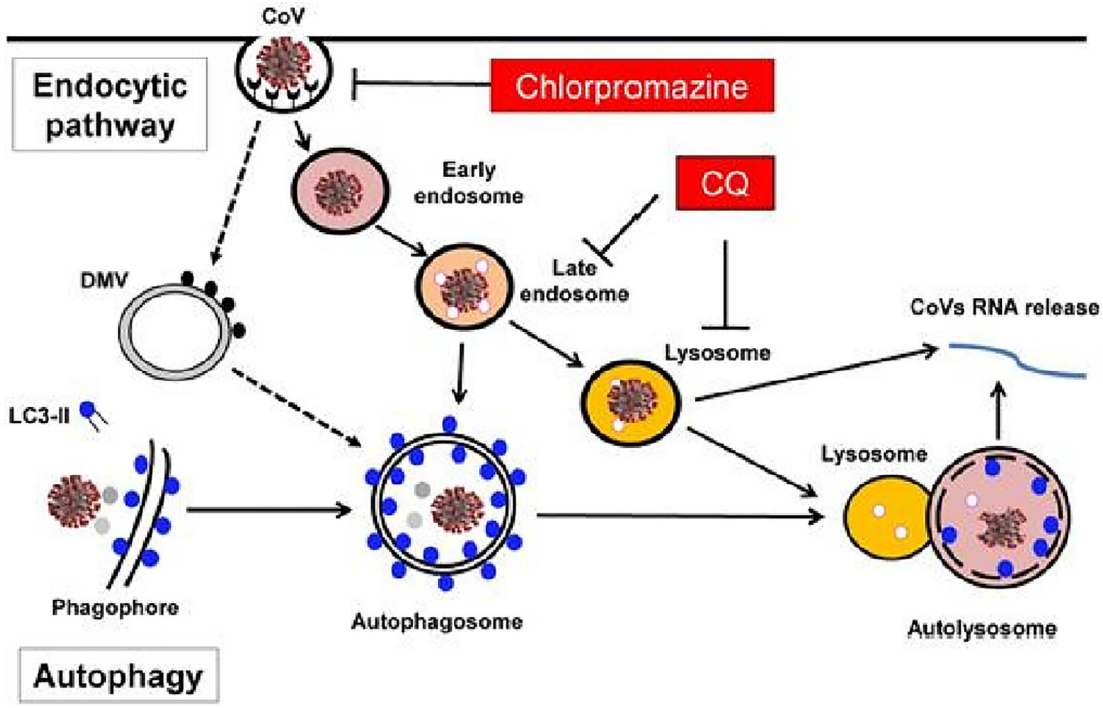

Fig. 3. Autophagic participation in the entry and replication of CoVs in the host system. The entry into the host system of CoVs is primarily mediated by the endocytic pathway, and autophagy has also been associated with the replication of viral cells, a process linked to the formation of DMV in the host cells**.** The entry into the host system of CoVs is primarily mediated by the endocytic pathway, and autophagy has also been associated with the replication of viral cells, a process associated to the formation of DMV in the host cells (adopted from Yang and Shen, 2020).

the illness risks and treatment responses in young men and women with COVID-19 vs older patients—to do so, older adults must be included in clinical studies.

1.8. Impact on brain health

To understand the mental health deeply, the neurological aspect could not be overlooked. The scope of the mental health in addition to the effect of neurological and drug administration in COVID-19 must be acknowledged. The infection can also cause neurological complications like headache, diminished sense of olfaction and taste, hysteria, delirium, stroke and meningo-encephalitis (Mao et al., 2020). The neurological disorders elicit the risk of COVID-19 infection particularly in elderly adults (Garg, et al., 2020). Social isolation, lack of physical activity and decreased cerebral stimulation up shoots the risk of cognitive deterioration and dementia in aged individuals. Older adults and individuals suffering from pre-existing physiological complications are at potential risk of fatality from COVID-19 infection

1.9. Effects of the COVID 19 virus on nervous system

The effect of infection with SARS-CoV-2 on the nervous system of human being is almost unknown. SARS-CoV-2 is a zoonotic virus and almost fifty percent of the epidemics of zoonotic viruses have been affected by neurotropic viruses entering the central nervous system (CNS) (Olival, et al., 2020). One of such closely related coronaviruses known for the severe acute respiratory syndrome outbreak and therefore named Middle East respiratory syndrome are neurotropic on biological aspect and neurotoxic on clinical aspect, which possibly share their neurotropism and neurotoxicity leading to mental health and neurological disorders. The hypothesis is supported by the study that the structure of SARS-Cov-2 receptor-binding domain is identical to SARS-CoV (Lu, et al., 2019)

There are general, complex and often extreme neurological signs of infection with COVID-19. A population study conducted in Wuhan, China shows that 36 percent had CNS symptoms or disabilities in a retrospective sample of 214 patients, and a group of 88 patients suffering with severe respiratory disease had a considerably higher rate (45 percent) of CNS problems) (Mao, et al., 2019). Till date there is no report regarding whether SARS-CoV-2 infection have the potency to activate harmful effects on mental health or neurodegenerative complications instantly or post-acute respiratory phase of COVID- 19 infection, but urgent action is required to construct research capacity in the neuropsychological database, such as the development of COVID-19 case studies, to combine standardized tests of these potentially important biological causes (Desforges et al., 2020).

2. Methodology and hypothetical approach

2.1. Research is a vital aspect of recovery efforts

It is crucial to monitor and assess any measures generated by the pandemic to alleviate or address mental health problems. Again, it is demand of situation to understand the level of the effects of COVID-19 on mental wellbeing and the socio- economic effects of the outbreak, and to consult on a personal level with the affected mass. Such research will strengthen the ongoing efforts for mental health. Procurement of Expeditious knowledge required to the institution of research priorities (Holmes, et al., 2020a). Collaborative research, open-data sharing and funding are some of the ways to strengthen the machinary. Therapeutic targeting of ageing processes has the ability to improve resistance to ageing and consequently to age-related diseases including agents of infectious diseases, thereby enhancing and expanding healthy living with chronological age.

2.2. Implication of autophagy in COVID 19 infection and as a therapeutic strategy

Understanding the overwhelming picture that COVID-19 already has, a variety of potential approaches to SARS-CoV-2 have been established and thus autophagy is one of the potential cellular process to be explored. The consequence of autophagic processes in CoV infection has gained considerable attention in the last one and a half decades. Autophagy invokes to an evolutionary preserved mechanism in which intracellular constituents such as protein aggregates and weakened organelles are submerged in a double-membrane structure called autophagosomes, which gradually merges with lysosomes to form autolysosomes for degradation (Mizushima, 2018., Levine and Kroemer, 2019). At present, two critical issues have been addressed in various reports, is CoV induces autophagy via autophagy apparatus or (Autophagy Related) ATG proteins indulged in CoV infection along with replication. Mouse Human Virus (MHV) was the basis of the first study showing the role of autophagy in viral replication, where several important observations were identified. This include from the induction of construction of double-membrane vesicles (DMVs) as autophagosome, which is a hallmark of putative autophagy. Secondly, the viral replication complexes at DMVs co-localized with the autophagy proteins, LC3 and ATG12. Thirdly, MHV replication was dysfunction in ATG5 deficient embryonic stem cells. Thus, the group came to a conclusion that autophagy is associated in the construction of DMV in addition to the replication of MHV (Prentice et al, 2004), proposing a common function of autophagy in the SARS-CoVs replication. Therefore, there appears to be a certain form of interaction between the machinery of autophagy and CoVs, and it remains to be further explained the entire picture of such interaction.

2.3. Anti-aging drugs as potential candidates for COVID-19 prevention and treatment

Moreover, recommending the known FDA-approved drugs could provide a welcome opportunity for the rapid development of COVID-19 treatments. Certainly, the efficacy and none side effects of anti-COVID-19 therapy need to be demonstrated in clinical trials subject to novel scientific review. Interestingly, another recent in vitro study shows that SARS-CoV-2 infection resists autophagy and inhibits viral propagation by pro-autophagic compounds, including spermidine (Gassen et al., 2020). Spermidine has numerous physiological roles, including controlling the translation of RNA, as well as increases the stability of RNA and DNA (Pegg, 2016), and these effects need to be explored further, especially in relation to potential autophagy induction. Possibly, during infection, the function of spermidine can be pleiotropic. Spermidine, on the one hand, is an inducer of autophagy that lead to endosomal pH buffering, thus blocking viral entry (Madeo et al., 2018, Yang and Shen, 2020) illustrated in Fig. 4. Polyamines are important for viral replication and host overexpression of spermidine/spermine-N (1)-acetyltransferase leads to depletion of spermidine, which is a typical cellular process to viral pathogenesis along with RNA viruses (Mounce et al., 2016). This underlines that any pharmacological contestant contrary to SARS-CoV-2 during infection should be investigated for its potential pleiotropy. On the basis of earlier and ongoing research, a hypothetical approach has been illustrated in Fig. 4, where the role of anti-

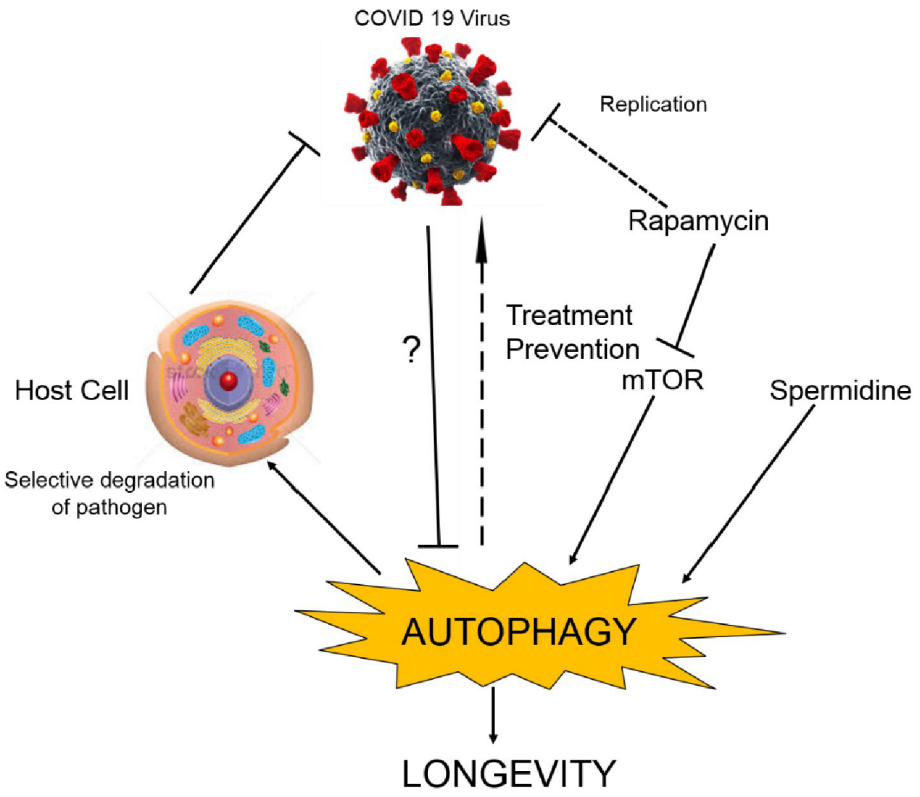

Fig. 4. Proposed hypothetical model illustrating the autophagy defense pathway against coronaviruses and a therapeutic approach. By executing and supporting various antiviral pathways in infected host cells and fostering the role of autophagy can counteract viral infection. CoVs may therefore have evolved strategies to minimize cellular and organismal immunity by avoiding autophagy. Various drugs rapamycin and spermidine elicits autophagy and thus activates longevity. The solid lines represents the well-studied functions whereas the broken lines represent the hypothetical function yet to be proved experimentally.

aging drugs can be a potential candidate for pharmacological interventions and therapeutic strategies.

3. Conclusions

Mental wellbeing and psychosocial support are essential for health, safety and social security, nutrition, labor, education, justice. The government should ensure that mental wellbeing is thoroughly considered in the health, socio-economic reactions, and recovery plans of governments. In addition, humanitarian coordinators should ensure that preparation and planning can provide mental health and psychosocial support. Mental well-being will persist as a primary problem even as countries emerge from the pandemic and focus on economic and social recovery.

Existing evidence makes it possible to speculate that activation of autophagy may offset CoV infection at various levels, although much detailed information is certainly needed. Many biogenic or synthetic compounds having the potential to induce autophagy can resolve the concern. The prevailing outbreak is a startling indication that evolving infectious pathogens are major challenge regardless of whether modulation of autophagy will ultimately be part of COVID-19 strategies. In view of limitations of our medical systems and socio-economic well-being, this pandemic highlights the importance of further developing and safeguarding global healthcare, as well as supporting and extending comprehensive infectious disease research. On the basis of the various studies of the therapeutic interventions a hypothetical model has been proposed in Fig. 4. Along with delivering medical treatment, extensive health care experts have a major role to play in following psychosocial essentials and providing their patients, health care workers and the population particularly aged individuals with psychosocial support and activities should be incorporated into common pandemic health care

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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