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*Review*

## **Parallel Outbreaks of Deadly Pathogens (SARS-CoV-2, H5N8, EVD, Black fungi) around the World in 2021: Priorities for Achieving Control with Socio-Economic and Public Health Impact**

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**Abstract:** Concurrent waves of Coronavirus disease, Ebola virus disease, avian influenza A and black fungus are jeopardizing the lives in some parts of Africa and Asia. From this point of view, this review aims to summarize both socio-economic and public health implications of these parallel outbreaks along with their best possible management approaches. Various online databases were used to collect the necessary information regarding these outbreaks. Based on the reports published and analyses done so far, the long lasting damages caused by these simultaneous outbreaks on global socio-economical and public health status can be conceived from the past experiences of outbreaks, especially the COVID-19 pandemic. Moreover, prolonged restrictions by the local government may lead to food insecurity, global recession and enormous impact on the mental health of people of all ages, specifically in the developing countries. Such overwhelming effects already have been reported to be declining national growth of the economy as well as increasing political insecurity and shortage of basic needs. Although various actions have already been taken including vaccination, clinical management and further research, social distancing, and lockdown etc. to improve the situation, the emerging variants and associated genetic mutations may make the containment difficult worsening the situation again. Considering the current mutational dynamics of the pathogens and the past experiences, perpetual preparedness along with updated clinical management backed by epidemiological studies and innovating scientific effort are inevitable to combat the simultaneous waves of multiple infectious diseases.

**Keywords:** COVID-19, EVD, HPAI, Socio-economic impact, Public health impact, Measurements

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### **1. Introduction**

The world continues to deal with the COVID-19 pandemic that began in Wuhan, China, in December 2019 [1], which has affected 221 countries and territories causing over 3.5 million deaths by April 2021 [2]. Along with the direct health impact of COVID-19, restrictions (e.g. isolation and social distancing) induced economic instabilities including loss of employment were common in developed and developing/under-developed countries [3, 4]. This not only caused a major economic problem worldwide but also severely affected the other sectors including travel and tourism, catering, leisure etc. [5]. So, it is estimated that the COVID-19

outbreak has reversed the world's economic improvement by 30 years with a surge in the global poverty level [6].

While the present data indicate that there is a global decline in the number of new COVID-19 cases and/or deaths probably due to vaccination and maintaining strict regulations recommended by WHO [7], Unfortunately, the emergence of new variants in different countries (India, Brazil) and territories has been a matter of great concern with the risk of reinfections, lower vaccination efficacy, and increased transmissibility [8]. More alarmingly, amidst this COVID-19 situation, a new outbreak of Avian influenza subtype, Highly Pathogenic Avian Influenza (HPAI) H5N8 hit the poultry farms and wild birds in Saudi Arabia, which later spread to other countries of the Middle East, Eurasia, and Africa [9] (Figure 1). Besides, an EVD outbreak was detected concurrently in rural areas of Guinea according to the report on 14 February 2021, which is threatening to get spread to other countries unless strict regulations are maintained alongside the COVID-19 restrictions and as of 18 February, seven cases with 5 deaths due to Ebola have already been reported [10] (Figure 1). On top of that, the most recent outbreak of black fungus in India is of concern, which is showing a dramatic rise in incidence rates especially among the recently treated COVID-19 patients [11] (<https://www.bbc.com/news/world-asia-india-57027829>). Besides, within only first 15 days, 40 cases were reported and eight patients lost their eyes due to mucormycosis [11]. So, the devastating impact of the combined surge of these deadly infectious diseases to be caused can easily be assumed from this preliminary data. Besides, such catastrophe left a mark in East Africa in 2020, while the combined impact of COVID-19, desert locust, and floods caused 34 million or more people to starve according to WFP projection and only in Ethiopia, GDP might have fallen by 3% in 2019/2020 [12].

So, the present data of the combined effect of these infectious diseases urge immediate attention from the scientific community, international leaders and general people to acknowledge its socio-economic and public health impact especially in low-resource settings and to develop a policy to combat such waves of multiple outbreaks in near future. This article aims to raise awareness by summarizing the detrimental effects of these infectious viral and/or fungal agents observed in the recent times.

## 2. Methodology of the review

The review aimed to focus on the all possible past, present and future socio-economic impacts along with public health impacts and possible managements of "Tetra Threats" of COVID-19, EVD, Black fungi, and H5N8 in East Africa and Asia. To generate a most informative and potentially relevant materials following database were used to collect the information's: PubMed/PMC/Medline, Global Health, ORCID, Publons, Indian citation index, Research gate, Scopus, Google Scholar, Google, ScienceOpen, Chinese Social Science Citation Index, and Science Direct. The terms and keywords including socioeconomic impacts, Public health impacts, Management, Possible destruction have been used for searching in conjunction with SARS-CoV-2 infection, COVID-19 pandemic, Ebola infections, H5N8 outbreaks, Black fungus, Asia, World outbreak, and Africa. All the relevant journals, Book chapters, conference papers, online newspapers, local/international media and organization based news articles were taken into account for this study. A total of more than 100 relevant information's from the initial 431 search results has been used in this review.

## 3. Results & Discussion

### 3.1. Socio-economic impact of each outbreak, morbidity and mortality

Ongoing surge of COVID-19 already have caused the loss of income of approximately 256 million people individuals [13]. In a study by Shammi et al., 2021 [14] had revealed the impact of COVID-19 in Bangladesh on gender discrimination, gender-based violence, business, economy, and education sectors which supported by another study by Singh et al., 2021 [15] in India who reported the 59%, 38%, 28% people losses job, income and food security due to the surge of ongoing COVID-19 at 2021. This socio-economical scenario is

in everywhere around the world [12-15]. Moreover, due to the death of 3,538,764 around the world which already have affected the working manpower number around mainly in food and others basic industrial level [10-15]. While the impact of COVID-19 pandemic is known to all, the other three outbreaks should not be ignored considering their potential impact on health and life standard. Among them, the ongoing outbreaks, the currently circulating HPAI H5N8 strain have been reported from poultry in Russia, Europe, China, the Middle East, and North America in 2020-21 [9] While no human cases of HPAI H5N8 were found in previous outbreaks [9, 16], but on February 19, 2021 cases of 1<sup>st</sup> human infection with H5N8 was reported by the WHO H5 Reference Laboratory of the State Research Centre for Virology and Biotechnology VECTOR (FSRI SRC VB VECTOR) Rospotrebnadzor of the Russian Federation [9,16] However, the cases were reported with mild symptoms [9, 16] and no human-to-human transmission has been observed so far [17]. Interestingly, since its first emergence in Eastern China in 2010, HPAI H5N8 caused a major outbreak into poultry farms of South Korea in 2014-2015 reintroduced by migratory waterfowl and spread throughout Asia, Europe, and the United States [18] causing culling of more than 12 million poultry to control the outbreak in South Korea [19]. Again in 2016-2017, more than 29 European countries along with vast regions of Asia [20] was affected by the outbreak of this virus, which was more devastating than the other outbreaks considering the socio-economic effects. Especially, the world's leading poultry meat producing country France, suffered huge financial loss due to the culling of about 6.8 million poultry [21] and as a whole, approximately 25 million poultry were destroyed in Europe as a part of the preventive measure [17].

On the other hand, previous outbreaks of EVD have a history of causing extreme hardship of poverty, infrastructure breakdown, rise in endemic diseases due to overrun healthcare system, crop abandonment, and economic turmoil [22] (Figure 2 & Table 1). The longest-lasting and most fatal one [23] was in West Africa in 2013-16 which reported 28,646 cases and 11,323 deaths, mostly affecting Sierra Leone, Liberia, and Guinea and spreading across international boundaries of Nigeria, Mali, Senegal, Spain, the UK, the USA and Italy [24]. The World Bank estimated a cost of 2.2 billion to the most affected countries [25], while the intensive study suggests the combined economic and social burden of the outbreak to be at least \$53.19 billion globally [26]. Disruption of agricultural products' market chains and trade [27] reduced the productivity of staple crops and percentage of traders by 12% and 20% respectively which was attributed to severe food insecurity and unemployment (Figure 2 & Table 1). This outbreak had a huge impact on public health taking the lives of over 500 healthcare workers, which forced them to shut off many healthcare facilities [26].

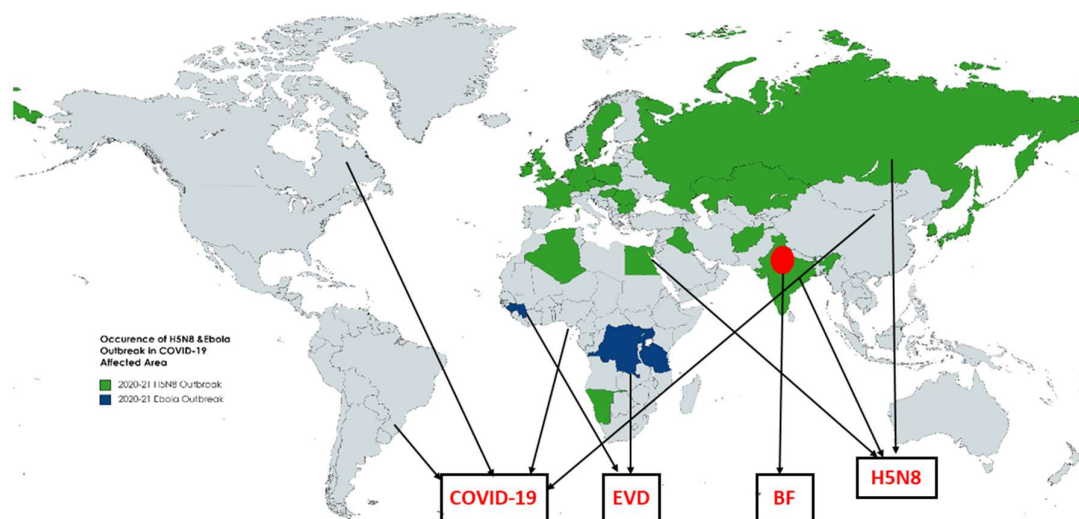


Figure 1: Distribution of H5N8 and Ebola outbreaks in the COVID-19 affected regions across the globe [8, 10, 12].

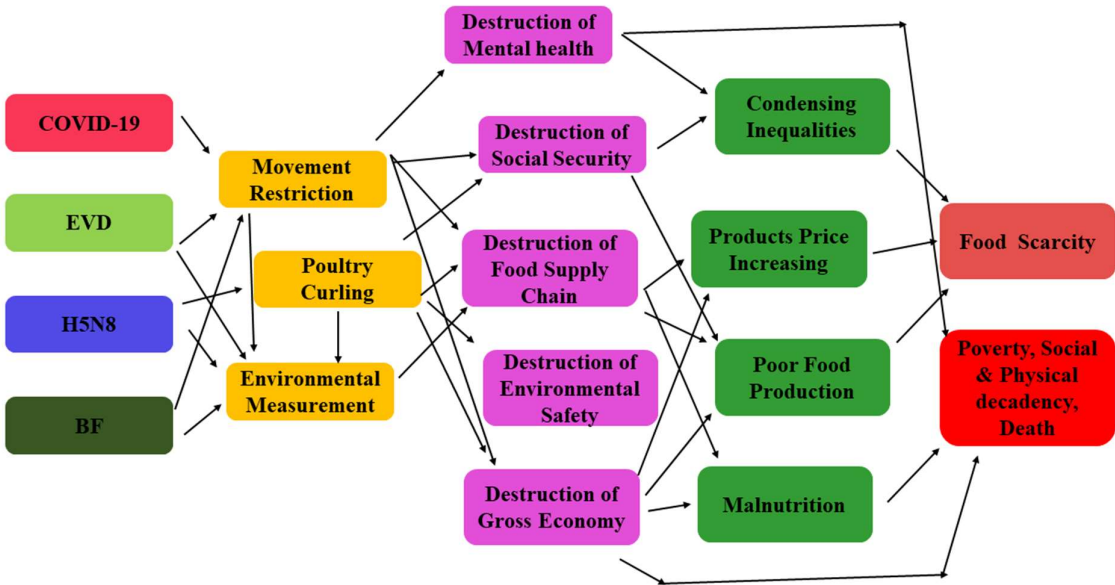


Figure 2: The dynamics of tetra outbreak (COVID-19, H5N8, and Black Fungus) that threaten both the socio-economical and public health sectors. Here, EVD-Ebola Virus, BF- Black Fungus. Each arrow indicating the consequence of each incidence.

Consequently, the simultaneous outbreak of COVID-19 and EVD in April 2020 in North Kivu triggered a massive economic downturn with worsening food insecurity and increasing poverty [28, 29] (Figure 2 & Table 1). Since then, the DCR government along with other African countries have been trying to balance between these two outbreaks, minimizing the greatest obstacles of combined negative economic and socio-political impacts and health impacts of other diseases [30]. However, the most recent reported cases of mucormycosis, commonly known as black fungus outbreak in post COVID-19 patients still do not have a precise data about economic loss, but scientists are predicting its huge impact on socio-economic sectors in near future as it is costing the eyes of patients (Figure 2 & Table 1). So, the outbreak at a larger extent may deprive the affected persons of their productivity and employment making them the burden of society. Furthermore, the cost of COVID-19 has been doubled in India for the treatment of both COVID-19 and mucormycosis, which might lead them in financial debt and to lose their valuable assets. While the mortality rate of mucormycosis is estimated to 50% [31, 32] more alarmingly, this outbreak has already spreader to its neighboring country Bangladesh from India. So far only two patients have been detected in Bangladesh and already reported its first death (<https://www.aa.com.tr/en/asia-pacific/bangladesh-reports-1st-death-by-black-fungus/2253604>). So, such combined outbreaks must have a negative impact on the developing countries with high population load in near future (<https://www.bbc.com/news/world-asia-india-57027829>).

3.2.Possible social complications of these outbreaks in near future

Based on the past experiences with these outbreaks, we can speculate the dire consequences and global impact of combined effects of EVD, COVID-19, black fungi, and HPAI. Social distancing might be necessary to contain these deadly pathogens, but it comes with panic and socio-economic collapse [33]. However, considering vaccination, pandemic control measures and re-emergence of new variants, the global economic activity might reduce to 4% in 2021 and 3.8% in 2022 or to the darker side, might face downfall with below potential growth by 2022 if the situation getting worsen [34, 35]. Besides, due to lockdown and other restrictions, mental health would wither away mainly because of unemployment which may also lead to crime, burglary, fraud business.



Affording medical care would be difficult for low-income people, while avian influenza outbreak would cull domestic birds and disrupt the food supply chain (Figure 2). So, the mortality and morbidity rate would increase not only due to diseases but also due to malnutrition-associated complexities [34, 35]. The World would face severe poverty, which is also currently evident with the COVID-19 outbreak [36].

### **3.3.Impact of Each Outbreak on Public Health**

In February, 7 positive cases of H5N8 infection were detected among the poultry workers in Russia [37]. Among them, 5 (Age 29-60) were female workers involved in response operations to contain the outbreak [38]. Although the relationship between patients' age and H5N8 infection has not proved yet. On the other hand, it was speculated that Ebola incidence increases linearly as age increases up to 35-44 years, after which a plateau is generated for older age group [39]. Another study calculated Ebola Virus Disease risk among different age groups and stated attack rate for children less than 2 years of age, 5-14 years of age and  $\geq 30$  years of age to be 43%, 30%,  $>60\%$  respectively. In contrast, women attending to sick people and health care workers' condition might contribute to the higher risk in middle-aged people [40]. However, risk of acquiring Ebola was similar for both male and female [40]. On the contrary, COVID-19 infection comes with a greater risk rate, severity and mortality rate among elderly people due to immune impairment with increasing age [41]. Children are less infected to COVID-19, or in most cases, they remain asymptomatic [41]. Reportedly, age dependent susceptibility of COVID-19 infection and probability of acquiring clinical symptoms is 20% for young children and 70% in older adults [42]. Meanwhile, among children, infants are reported to be more vulnerable to COVID-19 infections with 10.7% severe cases [43]. According to recent national data of Asia and African countries, with demographic shift [44], COVID-19 infections are largely increasing in younger adults [45]. Among almost 7 million COVID-19 cases, 76% of them are represented by young adults (age below 65 years old and 18-29 years) contributing to largest proportion, though death rate still happens to be greater among older people [41,42]). Possible risk factors for COVID-19 infections being severe in young adults are preexisting health conditions like overweight, heart disease, type 2 diabetes, unhealthy lifestyle, smoking etc. [44] which is also true in case of black fungus attack. However, another study calculated that age does not contribute to COVID-19 susceptibility, rather it might just affect disease severity [46]. In case of pregnancy, Ebola is associated with a high mortality rate being 72% [47] to 100% [48]. But no evidence has been reported if pregnant women are alarmingly susceptible to Ebola infection or not, but it certainly has led to miscarriage and neonatal death in almost every case [48], with one review concluding with speculation of transmission risk of Ebola to baby through pregnancy related fluid and breast milk [47]. However, susceptibility to SARS-CoV-2 infection is reported in pregnant women also in which clinical complications are associated with [49] their first and third trimester and downregulation of immune system [50] (Figure 2 & Table 1). This immune suppression is associated with the black fungi infection during post COVID events, especially in case of steroid treatment and in diabetic patients [51]. On top of that, if these three outbreaks prevail, the public health sector will be the hardest-hit area. Because healthcare facilities and resources are limited in underdeveloped countries [29]. Moreover, less outpatient attendance will be possible for the fear of contracting disease leaving the people with other diseases like malaria, HIV, etc. with no/minimal medical attention [37]. Also, community health and the global economy would be severely disrupted.

### **3.4.Present containment strategies of all outbreaks**

The tendency of frequent re-assortment, genetic mutation, and evolution of emerging pathogens threatens to be evolving in a new strain that might be transmitted to humans and human-to-human even human to animals or animals to human [17]. Each outbreak monitoring is therefore essential in identifying new strains to avoid the risk of the adverse situation and to minimize the pathogenic transmission as much as possible.

Firstly, this is especially a concern for HPAI H5 viruses, as they can transmit silently without any severe clinical symptoms in their wild hosts [52] which forcing to paying attention to the Russian cases to identify and monitor exposed individuals, test suspected cases, and prevent their spread to the community. To

halt the propagation of the virus, millions of birds were mass slaughtered based on previous experiences with the H5N1 outbreak in 2008 [53]. To contain this virus, some 600,000 poultry were killed alone in France [54]. While culling wild birds alone is not an effective way to prevent dissemination, as the virus is highly contagious [53]. Researchers are attempting to make progress in searching for vaccines to treat this infection and many candidate vaccines have shown significant results that give cross-protection against the H5 strains [55]. Still, no vaccine has been approved by the FDA for the treatment of H5N8 alone. Moreover, earlier experiences show that antiviral drugs are 50% to 70% effective in the treatment of reported viruses [55]. Currently available antiviral drugs approved for the treatment of influenza are M2 ion channel blockers and neuraminidase (NA) inhibitors [56]. Along with the human vaccination, vaccination for domestic poultry can be considered. A number of vaccine candidates were developed and, after multiple trials, several vaccines were considered effective against HPAI H5N8 including recombinant H5 and H7 bivalent inactivated vaccines, Modified vaccinia virus Ankara (MVA)-based H5 vaccine, single dose of inactivated oil-emulsion bivalent H5N8/H5N1 vaccine [57, 58, 59] followed by antibody-based therapies [60]. Along with all possible attempt, the global initiative on sharing avian influenza data (GISAID) has set up the platform to gather and share all available sequence data for providing a better understanding of the epidemiology and evolution of the currently circulating viruses including the H5N8. Also, flu surveillance laboratories have been established in more than 50 countries worldwide [61].

However, lately Ebola affected African countries have been trying to adopt control measures and interventions to mitigate the Ebola outbreak [21, 24]. Community engagement with strong international support has been greatly helpful for effective outbreak response. Interventions that helped the 2013-2016 Ebola outbreak to control were effective case management, contact tracing, quick diagnosis and treatment, isolation of suspected and confirmed cases, strong infection control, safe burial, establishing an Ebola treatment centre (ETC) by the United Nations (UN). Also, research on vaccines and therapeutics development and active genomic surveillance helped to make decisions for Ebola response [24]. Moreover, European Union (EU) contributed nearly 1.8 billion to provide more medical and support staff to West Africa during EVD outbreak. In Europe, EU made policies to combat this global health emergency and set up an evacuation system to provide resources to international health workers [62]. Strategies that have helped contain the Ebola virus during the 2018-20 outbreak in Democratic Republic of Congo include deploying a multidisciplinary rapid response team to support Ebola case management, providing patients with equitable access to advanced therapeutics Mab114, REGN-EB3, ZMAPP, vaccinating over 303,000 people with the highly effective rVSV-ZEBOV-GP vaccine [63], introducing novel Ebola diagnostic tools as well as applying new technologies like whole genome sequencing and building community engagement alongside new surveillance programs [64]. Along with the advanced therapeutics and approaches, several vaccines and treatments against Ebola virus are under clinical trial including rVSV-ZEBOV or Ervebo [65] which was proved to be 100% protective against EVD [66]. It can be administered in people of 18 years age or above [66]. In July 2020, another vaccine, a two dose regimen of Ad26.ZEBOV and MVA-BN-Filo under the brand name Zabdeno/Mvabea was approved for medical use by the European Union, developed by Johnson & Johnson [67]. Reverse vaccinology approaches utilizing immunoinformatics are being exploited recently to produce vaccines against Ebola virus strains, conferring good performance in silico [68]. Like vaccines, until 2020, there was no approved drug or therapy for EDV treatment. Treatment mostly focused on supportive care therapy [24]. Supportive care includes oral rehydration that contains electrolytes [69] preventing complications of shock and fluid resuscitation in Ebola infected people [24, 70]. A number of anti-Ebola therapeutics such as anti-viral drugs, monoclonal antibodies, anti-inflammatory agents, convalescent plasma etc were proposed and evaluated during Ebola Virus Outbreak to contain and reduce the risk of the virus [24, 71]. Inmaze, also called REGN-EB3, combination of three monoclonal antibodies and Ebanga (Mab114) – single monoclonal antibody were the only two drugs approved for Ebola treatment by the US Food and Drug Administration (FDA) in the late 2020 [72] which were previously used in a randomized control trial during 2018-2020 Ebola outbreak in Democratic Republic of Congo and resulted in high survival rate [68]. Another therapeutic called ZMapp, cocktail of three monoclonal antibodies also proved to be superior to standard care for Ebola Virus Disease treatment [71].

On the contrary, antiviral drug Remdesivir, though proven to be good in pre-clinical studies, did not manage to reduce Ebola transmission effectively. But on the other hands, some of them like Remdesivir has proved effective against COVID-19 infections [50]. Remdesivir, ZMapp, Mab114, REGN-EB3 were associated with 53.1%, 49.7%, 35.1% and 33.5% of mortality rate respectively in one study [73]. Hopefully, remdesivir, along with ZMapp treatment benefited newborn babies against Ebola infection [71]. Considering all the reports and overall positive effects related to them, MAB114, REGN-EB3, Remdesivir, ZMapp were recommended by WHO and Health authorities in 2018-19 Ebola outbreak in DRC [71, 73]. Notably, TKM-Ebola, intravenous formulation of small interfering RNA (siRNA) which inhibits Ebola L protein, VP24, VP35 proteins, showed in vitro efficacy against Ebola and was authorized by FDA for emergency use [70]. Chloroquine, cationic amphiphiles like Amiadarone are also reported to be good as prophylactic agents for Ebola virus infection, where antivirals or vaccines are not available [70]. For critically ill patients with Ebola infection, oxygen supplementation, mechanical ventilation or renal replacement therapy have been shown to reduce death rates [74]. Also, WHO stated convalescent plasma transfusion can be used to treat Ebola infection [70], as it decreases Ebola viral load by increasing anti-Ebola Virus antibody level [66]. They might be an aid to public health response for both COVID-19 and EVD outbreak in the future and a way to decrease socio-economic impact to already vulnerable citizens right now [30].

Meanwhile, recognizing COVID-19 as a pandemic, all countries are trying to reduce transmission of SARS-CoV-2 by testing and treating infected patients, restricting large gathering, stopping flights and public transport, closing schools, colleges, non-essential workplaces and maintaining lockdown measures [75, 76]. Physical distancing has been reported to have a profound impact with an overall reduction of COVID-19 incidence of 13% globally [77]. Currently, there are several vaccines approved by distinct regulatory bodies for mass vaccination. WHO issued Pfizer, AstraZenca/Oxford and Ad26.CoV2.S vaccines, working with partners for safe and effective vaccine equity for billions of people [78].

But due to widespread circulation, the virus has undergone a significant amount of mutation that has led to the emergence of new variants. These are- UK (VOC 202012/01), South Africa (501Y.V2), Brazil (P.1) etc. Existing vaccines are expected to provide a degree of protection against these variants. But the WHO and other regulators are monitoring the data carefully to suggest changes needed to combat these new variants [79]. Unlike vaccines, there is no specific treatment enlisted for COVID-19. In general, for mild to severe cases of infection, anti-viral drugs, antibiotics, steroids, anti-inflammatory drugs, low molecular weight heparin, biological agents such as hyper immune immunoglobulins, convalescent plasma are used [80]. According to guidelines issued by National Health Commission and State administration of Traditional Chinese medicine, several drugs have been recommended for COVID-19 treatment including lopinavir, ritonavir, arbidol, chloroquine phosphate, ribavirin, remdesivir, tocilizumab and Traditional Chinese Medicines etc. Chloroquine phosphate, a potential antiviral drug, helps inhibit pneumonia exacerbation and reduce disease course during COVID-19 infection [81], although hydroxychloroquine has been proven to be better in fighting the infection than chloroquine in context of dose dependent toxicity profile [82]. Azithromycin, along with hydroxychloroquine is reported to be useful for virus removal in COVID-19 infection [82, 83]. Similarly, combined use of Lopinavir and Ritonavir have been shown to have potent antiviral activity with positive outcome in the treatment of SARS-CoV-2 infected patients [64]. Remdesivir, observed to inhibit SARS-CoV-2 at low concentration, was stated to be the first authorized investigational therapeutic for use in treating SARS-CoV-2 infection [30]. Additionally, WHO has authorized the use of Dexamethasone for anti-inflammatory purposes in critical conditions of COVID-19 patients [84]. For critical condition, tocilizumab, a recombinant monoclonal immunoglobulin G1, also showed satisfactory effect against the infection [85]. Interferon alpha and Janus-kinase inhibitor are also recommended, as they showed a significant decrease in SARS-CoV-2 virus replication [86], mortality rate and ICU admission of COVID-19 patients [87]. Convalescent plasma transfusion might also be a promising treatment against COVID-19 as its use reduces mortality in critically ill patients increasing neutralizing antibody titers and decreasing SARS-

CoV-2 viral RNA [88, 89]. Considering COVID-19 infected patients to have increased risk of venous thromboembolism (VTE), anti coagulative therapy should be given importance in the treatment [86].

Most dramatically, more than 70% of morality rate bearing black fungus have no effective treatment except antifungal, antibiotics, intravenous (IV) medication or through a surgery [87]. Importantly, utilizing its experience of Ebola outbreak, Democratic Republic of Congo has established a multisectoral public health approach for community based screening testing, contact tracing, risk communication, community engagement and case management to fight against COVID-19 and other deadly super contagious pathogens [51]. WHO along with national authorities continuously monitor disease control activities including epidemic and genomic surveillance, strategic testing and sequencing new variants of concern (VOC) and assessing their vaccine efficacy. Infection and Prevention Control (IPC) undertaken by WHO has been proven to be effective to reduce transmission and death due to COVID-19 [2].

4. Conclusions

The socio-Economic impacts and public health impacts “Tetra Threats” of COVID-19, H5N8,EVD, and black fungi in Asia and Africa are concerning, while and their management is still difficult at this initial stage. So, proper studies and epidemiological surveillance are required not to deteriote the situation more. Some parts of Africa and Asia are currently fighting against the reported disasters simultaneously. Notably, Africa has faced the parallel effect of the two large-scale crises (COVID-19 pandemic, EVD) whereas some parts of Africa and Europe are fighting against the COVID-19 pandemic, H5N8 but unfortunately only India is facing parallel effects of three big crisis now (COVID-19 pandemic, Black Fungus, and H5N8). But such an outbreak is not limited only to a certain border rather spread throughout the world within a quick time causing devastating effects in both social, economic, and public health. The trio combination of the COVID-19 pandemic and the H5N8, black fungus in India is challenging considering their capacity to respond to these emergencies and address pre-existing crises and vulnerabilities. Although world-leading originations along with individual country authorities taking various controlling measurements to control the spreading, such as movement restrictions, border closures, social distancing, and vaccination efforts which might be helping in the destruction of the country's economy also. So, researchers should be encouraged to evaluate and monitor the concomitant use of COVID-19 vaccines along with seasonal influenza vaccines, black fungus, and Ebola vaccines in the priority groups.

Table 1: Possible consequence of Trio (COVID-19, H5N8, and Black Fungus) Outbreak in India

Outbreak	1 <sup>st</sup> line effects	2 <sup>nd</sup> line effects	Adverse effect
Social	Destruction of Social execution	Community imbalance	Vulnerable groups victimized
	Vulnerable groups become helpless	Imbalance of all social activities	Insectary in community
	Loss of lives	Unethical activity by vulnerable groups	Political Crisis
	Education system collapse	Insecurity on future generation educations	Destruction of total education systems



<b>Economic</b>	Scarcity of basics materials including Oxygens, medicine etc.  Rise of the products price  Country GDP decrease  Trading with neighboring country will disturb  Loss of Job  Unemployment problems increase	Loss of livelihoods  Destructions of local supply capacity  Country economy fall	Increase poverty  Higher scarcity of foods  Breakdown of all financial chain
<b>Public Health</b>	Health service insecurity  Impairment of basis needs of lives  Children and pregnant women health destruction  Development of prejudice  Loses of vision ability	Crisis in health sectors  Development of abnormal children  Environmental crisis  Disruption of working ability	Loses of valuable lives  Increasing of abnormal mental health  Malnutrition  Loses of total working ability

### Author's contributions

A.K., N.T.E., and O.S. carried out the studies (Data collection and data analysis). A.K., N.T.E., N.N.R., and O.S. drafted the manuscript. O.S. and M.M.R. developed the hypothesis, supervised the whole work and M.M.R., N.N.R. and O.S. critically reviewed the drafted manuscript. All authors read and approved the final manuscript.

### Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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### Ethical Statement

The authors confirm that the ethical policy of the journal, as mentioned on the journal authors guideline page, has been followed and no ethical approval was required as this did not collect any sample or questionnaires from animals and humans.

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