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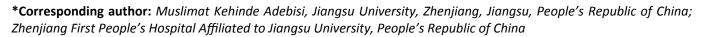
REVIEW ARTICLE

Past, Present and Future of Pandemics (COVID-19)

Mzee Said Abdulrahman Salim^{1,2} and Muslimat Kehinde Adebisi^{2,3*}

¹Affiliated Hospital of Jiangsu University, Zhenjiang, Jiangsu, People's Republic of China ²Jiangsu University, Zhenjiang, Jiangsu, People's Republic of China

³Zhenjiang First People's Hospital Affiliated to Jiangsu University, People's Republic of China





Background

From herpes and legionnaires' disease in the 1970s to AIDS, Ebola, the severe acute and respiratory syndrome (SARS), contagious diseases continue to threaten and disrupt human societies [1]. The end of last year (2019) doctors in Hubei province encountered patients with flu-like symptoms that are similar in characteristics to SARs having consistent aetiologies unfamiliar to them but with a possible link to their prior knowledge. A virus outbreak which has a genomic sequence similar to that of β viruses detected in bats 88% sequence identity [2]. These first cluster cases of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), previously called 2019 novel Coronavirus (2019-nCoV) is believed to be associated with Wuhan Hubei province Seafood Market, a 'wet' market at which a broad range of live or freshly slaughtered animals was sold including poultry, bats, and snakes. Previously the Chinese government ordered it to be shut down since the outbreak of SARS was recorded 17 years ago [3]. H-CoVs can be dated back to the 1960s, it belonged in the Corona viridae class CoVs well known by their characteristic feature crown-like spikes on the viral surface thereby named after the crown feature. Currently, the known types included Alpha, Beta, Delta and Gamma coronavirus [4]. This deadly virus acts on the respiratory system with stronger efficiency on the immunocompromised patients. Previous occurrence genre included SARs-co arises from Mammals namely Hcov-NL63, HCoV-229E, HCoV-OC43, HCoV-HKU1 these causes respiratory infections in CoV,SARS-CoV2 and the current COVID-19 [2,5,6]. Its pathways begin with contaminated droplets to host species through the mucous membrane, Larynx and Nasal mucosa and then migrate to the lungs through the respiratory tract, passes in the bloodstream via the lungs where it may damage vital organs such as the heart, kidneys, liver and the Gastrointestinal tract [7]. COVID-19 has been reported to affect more than 123 countries worldwide [8]. Up till 28-03-2020, there have been over 520000 confirmed cases, 24000 (4.6%) death and 59500 (11.4%) recovered except for china. Europe alone has one of the highest confirmed cases of (COVID-19) worldwide [9,10]. China reported over 82000 confirmed cases, 3300 deaths (4.02%), 75100 (91.6%) recovered where the majority of the incidences and prevalence's were reported in Hubei province PRC in which the incidence to recovered ratio has been outstanding and mainly associated to the governments respond methodologies. The pandemic results of this outbreak can be attributed to the initial lack of awareness accompanied by lack of preparation that led to its severity, cases of such have been recorded due to insufficient strategic open-mindedness to emergent threats at a time when borders of many kinds are going up across the globe [11]. Diamond princess cruise ship and religious gatherings that ignored the warnings of holding congregation at that time. Majority of people in these settings were older adults, as age has been understood to be a potential risk factor, people of old age represents the population with the risk of highest infection rate [7], children diagnosed with COVID-19 had better prognosis compared to the Old age [12]. Furthermore, studies have indicated that individuals with comorbidities such as pulmonary disease, cancer, diabetes, Parkinson's, hypertension, car-



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dio and cerebra-vascular [5,13,14]. Countries with low income, those at civil wars, refugee camps and severely devastating health care systems are at a much higher risk of being infected, due to overcrowding, poor hygiene, lack of enough testing kits, gloves, sanitizers, and patient management tools such as mechanical ventilators and so on [15].

Diagnosis

WHO recommended the rapid collection and nucleic acid amplification testing of appropriate respiratory samples for suspected cases [16]. The diagnosis currently used are two, First antibody detection against COVID-19 in samples, Second is a molecular-based assay [8]. History of travel to an epidemic area within two weeks or in close contact with an infected person within the past two weeks. Patients that present with fever, chills, dry cough, respiratory symptoms. The gold standard of diagnosis is a positive result of nucleic acid of SARS-CoV-2. Around half of the admitted patients develops dyspnoea a week after admission and worse cases lead to RDS (respiratory distress syndrome).

A report showed that the total number of targeting NKG2A might prevent the functional exhaustion of cytotoxic lymphocytes and consequently contribute to virus elimination in the early stage of SRAS-CoV-2 infection [17]. SARS-CoV-2 RNA, by real-time RT-PCR or gene sequencing, from the sputum, throat swab, lower [18]. Infection with COVID-19 is associated with significant morbidity, especially in patients with chronic medical conditions. At least one- fifth of cases require supportive care in medical intensive care units, which is especially limited in most developing countries. Despite the implementation of optimal supportive interventions, the case fatality rate among hospitalized patients is more than 10%. Similar to other viral respiratory pathogens, COVID-19 presents in the majority of cases with a rapidly progressive course of fever, cough and dyspnoea. At present, the golden clinical diagnosis method of COVID-19 is nucleic acid detection in the nasal and generation sequencing [19]. Important distinguishing factors are Leukopenia and the rapid progression to ARDS. Eliciting a history of recent travel to areas with ongoing outbreaks of this emerging pathogen or contact with a confirmed case of COVID-19 should prompt clinicians to initiate isolation precautions and obtain laboratory confirmation. Additional research is needed to elucidate viral and host factors in the pathogenesis of severe and fatal infections [20].

Signs and Symptoms

Clinical symptoms and imaging findings are inconsistent in early-stage of 2019-nCoV-infected pneumonia [21].

- Fever
- Respiratory symptoms

- Myalgia
- Fatigue
- Headaches
- GI symptoms

Investigation

A cohort study with 41 patients reported that 25% of the patients had Leukopenia and Lymphopenia with an increase in aminotransferase. Thirty seven percent, including seven of non-intensive treatment unit (ITU) patients, Patients in the intensive treatment unit (ITU) had Increased Prothrombin and D-dimer levels when admitted compared to those not in the ITU. There was a rise in troponin (hypersensitive troponin I (hs-cTnI)) seen in five of the patients which suggest virus-associated myocardial disease, another study also discussed the use of RT-PCR in diagnosing patients with 2019-nCoV the period and type of specimen collected for RT-PCR plays an essential role in the diagnosis of 2019-nCoV, Laboratory diagnosis can be performed by (a) Detecting the genetic material of the virus, (b) Detecting the antibodies that neutralize the viral particles of interest, (c) Detecting the viral epitopes of interest with antibodies (serological testing), or (d) Culture and isolation of viable virus particles [3,22]. Studies also show that elevated plasmin (ogen) and its enzymatic can be an essential biomarker in distinguishing severity of COVID-19 [23].

CT findings included ground-glass opacity, consolidation, air bronchogram and nodular opacities, this may be a useful tool to evaluate the extent of the disease in severe cases, providing prognostic information and guiding future treatment options. Imaging studies found that two old aged patients with comorbidities reported pleural effusion, lymphadenopathy enlargement of pulmonary vessels in areas where new lung infiltrates develop in the follow-up CT scan [24-26]. It is advised for patients to take CT and RT-PCR test for SARS-CoV-2, to exclude the diagnosis of COVID-19 before further investigations with radiopharmaceutical imaging [27].

Differential Diagnosis

- SARs-CoV, MERS-CoV, SARS-CoV2,
- Bronchitis
- Emphysema
- Empyema
- Asthma
- ARDS
- Influenza
- Allergies

Comorbidities and Risk Factors

A retrospective study showed that older age, chronic hypertension, cardiovascular disease were frequent in

diseased patients compared to those that recovered. Additionally, hypoxemia was also reported in diseased patients [28]. Several studies have linked comorbidities with poor prognosis. A nationwide study of 1590 COVID-19 investigated patients with either hypertension (HR = 1.58), diabetes (HR = 1.59), COPD (HR = 2.68), and malignancy (HR = 3.50). This study showed that patients with two or more comorbidities had significantly escalated risks of death compared to those without the risk factors with a (p-value of < 0.005) [29]. Further studies showed that the average fatality rate of COVID-19 is 2.3%, but fatality rate up to 8.2% increase was seen in patients with cardiovascular disease [30]. Asymptomatic, ARD, pneumonia, nosocomial infection are also high-risk factors to be considered [31]. The incidence in male with Cardiovascular, digestive and endocrine system diseases was commonly reported as an increased rate of infection [32]. Another study highlighted the increased risks of patients with cancer and COVID-19, 18% out of 1590 patients with COVID 19 had cancer [13].

Preventive Measures

Doctors, lab technicians, medical scientists and every sane human, in general, have fully deployed medical armamentarium at reach to face the conundrum of life and death. The awareness and ongoing efforts provided by health organisations, governments and medical practitioners at the front line are plausible. Governments have taken a preventive measure of conscious to its citizens including physical distancing, self-isolation, avoiding crowded areas, home isolation to travellers from areas with a high number of cases, establishing time-controlled curfews, providing antiviral tools such as alcohol and masks. Albeit the effort, intense education should be provided to further hygiene awareness. Moreover, testing tools, antivirals and ventilators should be accessible to all hospitals. As the more patients are treated more will have hospital access, and fewer patients affected will be mixed with a healthy population.

COVID-19 took less than a month to spread from Wuhan to the rest of China, and a few more days it expanded to the world at large. This growth rate of patients worldwide could be attributed to lack of extreme preventive measure, as discussed previously. Several studies reported a full-length spike containing receptor-binding domain (S) or S1/S2 could bring a breakthrough therapeutic and preventive pathway [33,34]. As to date, neither effective vaccines nor anti-viral therapeutic agents have been licenced to treat COVID-19 or any other human CoV infection [35].

It is difficult to understand all sources of viral contamination as it can happen on a wide aspect. A study performed by Gebhardt, et al. showed that cross-contamination during feeding manufacture is possible as they indicated dust collected after manufacturing feed ingredients contains a large quantity of viral RNA and has the potential to serve as a vector for a different type

viral transmission [36]. Hospital contamination should be taken seriously as studies show hospital-related transmission of the virus is still a substantial threat [37]. Several studies indicated the importance of disposable medical gowns, cap, mask and hand hygiene. For the medical staffs' safety goggles or face shield, isolation gown, thermal inactivation, disposable latex gloves, and shoe covers are needed for strict infection control measures at hospitals to contain contact and droplet contamination [27,38-40]. The world should be prepared for recurrence of the virus as premature and sudden lifting of interventions could lead to an earlier secondary peak, which could be flattened by relaxing the interventions gradually [41].

Rapid access to the emerging literature and the bioinformatics studies on the design of vaccine and a preventative tools available on the Internet, guided by human researchers, will for some time yet remain important weapons in the preventive battle against viruses [34].

Pharmacology Treatment

The use of antiviral drugs after the symptoms starts can help to reduce spread to other contact persons [42] a study from a minimum of hundred patients showed how superior chloroquine phosphate (an antimalaria, lupus erythematous and Rheumatoid arthritis medicine) is, in the treatment to inhibit the exacerbation of pneumonia, in addition to this none of these patients, showed any adverse reaction to the medication [43,44]. Antiviral drugs such as ledipasvir/sofosbuvir when combined are effective because they inhibit the action of viral enzymes [45]. Early initiation of Low molecular weight heparin and IVIg therapy is effective to improve the outcome of severe and critically ill patients [7]. Symptomatic treatment is recommended in cases of fever [46], Remdesivir a viral polymerase inhibitor has been said to be effective in combination with chloroquine to inhibit the replication of COVID-19 [47]. Lopinavir an anti-coronavirus in vitro drug when used reduces the risk of ARDs/death in patients. Oral oseltamivir was widely used in China as an empirical treatment and shown to be effective in reducing the symptoms [48]. Despite the fact that drugs announced to have a beneficial effect on COVID-19 should be easily accessible to the society, restrictions on them should be taken into consideration as well as evidence suggests; several countries reported on chloroquine poisoning when it is antiviral effects were made public.

Future Direction

A concurrent illness that makes an individual at risk, such as pregnancy, diabetes, respiratory disease, hypertension should be considered when preparing drugs/vaccine for relapse [14]. Survival rate can be improved if the provision is made for easily accessible medical

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care [49]. Provisions should be made for high-risk older adults like homes, centres where they have access to people around and still stay safe because it is not advisable to ask older people to social distance, this could affect their mental wellbeing [50]. Public awareness of the need for isolation by people who are travelling from the endemic region and the need to report symptoms promptly cannot be overemphasized [51].

Conclusion

An open line of communication and in time access to the database between countries and WHO to ensure understanding the severity of an outbreak and proper measures taken to prevent a pandemic, travel ban of an epidemic country no matter the intensity of an outbreak will help prevent pandemic in the future. Training programs should be made available to the populace on what to do in epidemic situations; basic safety needs should be readily available in countries to prevent hoarding and shortages when needed, low-income countries should have an accessible communicating database designed for the entire population. Every country should have a standby hospital for outbreaks purpose to avoid inpatient hospital contamination and avoid delayed patients isolation.

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