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Viewpoint on COVID-19 Pandemic

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ABSTRACT

Infections with COVID-19 are now global, reaching 213 countries, and as of May 29, 2020, more than 5M+ confirmed cases, with over 355.000+ deaths, although the number is still rising by the day. This short review aims to briefly highlight what is known about the epidemiology, aetiology, testing techniques and clinical features of COVID-19. The inter-human transmission of coronaviruses mainly occurs through saliva droplets, aerosols and direct/indirect contact through surfaces. Successful containment preceding any future effective vaccine includes social distancing, contact tracing, tracking of infected people, mass screening and providing healthcare professionals and social care workers with adequate personal protective equipment.

Keywords: COVID-19 pandemic, clinical pathology, coronavirus, pathogen transmission, microbiology

INTRODUCTION

COVID-19 pandemic poses a significant threat to global health. World Health Organisation (WHO) declared it a public health emergency on January 31, 2020. Within the first three months of the outbreak, the epidemic has spread rapidly to every corner or nook and cranny of the globe. As of April 26, 2020, a total of more than 3M cases in over 185 countries and mortality of higher than 200.000 were reported worldwide with continuous daily increase.[1] These numbers are staggering if we consider the short period when the outbreak happened locally in Wuhan and was spreading to the rest of the world.[2]

The speed and mode of transmission for COVID-19 are unprecedented and have taken the world by storm and raise many questions which the latter has currently little or no time to respond to. The major challenge facing most nations is how to both contain and reduce the number of new cases, re-infections and associated deaths accruing from it.[3]

While the world was the whole time busy to build all sorts of weaponry, e.g., conventional, biological, cyber and nuclear ones to mention but a few, who would have thought that a tiny virus of this nature will subject the entire world population to total lockdown, untold economic catastrophe, scrambling and no strategic coherence in dealing with COVID-19. The dignity of the human race has been eroded as a result of this pandemic since people cannot visit their loved ones in isolation, hospitalised and even buried without the attendance of closer relatives. Many lost lives have been in mass graves, such as in the USA, where the mighty of this world has fallen with COVID-19.[4]

It is also surprising to note that reports from the United Kingdom (UK) and America indicated that people of colour had suffered greater mortality than, for example, Caucasians.[5, 6] Could this be attributed to underlying health conditions, socio-economic impact, genetic makeup or that these individuals are prone to COVID-19 via their professional exposure to viral load and

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subsequent cytokine storm? Further research studies are needed to identify the underlying factors behind this high degree of mortality among people of colour.[7]

Aetiology

COVID-19 is believed to come from a "wet market" in Wuhan, which was selling both dead and live animals, including fish and birds. Such markets are breeding grounds for viruses and other forms of infection to jump from animals to humans because hygiene standards are difficult to maintain if live ones are being kept and butchered on site. Typically, they are densely packed allowing pathogenic diseases to be transmitted from species to another. The animal source of COVID-19 has not been confirmed yet, but it could be pangolins as the primary host is thought to be bats.[8, 9] The latter is hosting a wide range of zoonotic viruses, such as Ebola, HIV and rabies.

Based on various reports, a series of errors were made when this outbreak came about and these had culminated in possible transmissions and in the fight to contain it across the world. While other viral outbreaks, such as Ebola, SARS and MERS were in localities/countries where they emanated from, the COVID-19 is beyond control and has caused mayhem and devastation globally. Routine questions come into mind. Did the Chinese react quickly when they noticed the outbreak? If they did, how soon did they work in collaboration with WHO to determine the source, modes of transmission, including humans? Did the Chinese give accurate reports of death and others that are associated with the latter? How was Wuhan's lockdown different from others? Assuming the one in Wuhan was credible and effective, why did the virus not spread to other big cities of China, such as Beijing and Shanghai, before finding its way to Europe and other parts of the world? Up till January 14, 2020, the world did not know whether it could be transmitted to humans or not. This left all worldwide into limbo concerning its weird modes, other than this public announcement that Wuhan Municipal Health Commission.[10, 11]

While the world is in a battle field from all fronts with COVID-19, there are so many unanswered questions and lessons to be learnt by the way this pandemic has been handled, which had resulted in over thousands of deaths and countless challenges. There are many uncertainties about the origin of the virus, the extent and duration of transmission in humans, the ability to infect other animal hosts and its pathogenesis.[12]

Insights with Testing Techniques

There are various kinds of tests being used to identify COVID-19. These can be categorised into two, namely molecular diagnosis/polymerase chain reaction (PCR) - and serological-based testing. PCR-based technique remains the major method in a clinical setting for identifying SARS-CoV-2. Due to lack of reference standards for the diagnosis of COVID-19, the sensitivity and specificity of diagnostic testing are still unknown. Additionally, an inadequate amount of sample collected, especially with a swab, could reduce the sensitivity of the result. Is PCR always positive or can give once a while false-negative testing?[13]

The lower respiratory tract samples, for instance, those from mini bronchoalveolar lavage, are likely to be more sensitive than nasopharyngeal swabs. Therefore, it is crucial to emphasise that, depending on the clinical presentation, a negative real-time polymerase chain reaction (RT-PCR) result does not exclude COVID-19. Various stages of multiple serological tests are in the process of being developed. The availability of large-scale serological testing could help to determine whether patients have a false-negative result or not by PCR.[13]

Thermal inactivation at 56 °C has been recommended to inactivate SARS-CoV-2, and this procedure could theoretically disrupt nucleic acid integrity of this single-stranded RNA virus, resulting in false negatives in RT-PCR tests.[14] Longer storage or preservation at room temperature could cause this type of result in a portion of weak positive samples as observed by.[14] Improper materials or nonstandard operations in sampling, imperfect preservation or prolonged turn around time in transportation, expired kits or incompatible reagents and apparatus used for detection could determine test outcome results, as issued by the National Health Commission of China.[15]

Serological Methods

Serological assays are limited for routine application in the diagnosis of HCoV infections due to lack of commercial reagents, let alone the latter require vetting by clinical trials and the regulatory review process.[16, 17] On the other hand, serological tests are vital for understanding the epidemiology and burden of emerging HCoVs and the role played by asymptomatic infections.[18] When rapid antigen detection test and/or molecular assay are neither available nor stable, the serology technique can be used as a supplementary diagnostic tool.[14]

Early studies suggest that many of the patients seroconvert between 7 and 11 days post-exposure to the virus; however, some may develop antibodies sooner.[19] Owing to this natural delay, antibody testing is not useful in the setting of an acute illness.[20] It is not yet known whether individuals infected with COVID-19 who subsequently recovered will

be protected, either fully or partially from future infection with the same causative agent or how long any immunity may last; hence, further studies are required to throw more light on this.

The detection of specific IgM and IgG to COVID-19 can also be used for diagnosis, as China National Health Commission has indicated.[21] COVID-19 infection could be determined with one of the following criteria: positive result for specific IgM, the transformation from negative to positive for specific IgG, a 4-fold increase in IgG titers during the recovery period compared with the acute-phase outcome. Although antibody detection was considered simple, rapid, and inexpensive, it is still limited due to false negativity resulting from window period, non-comparable sensitivity and specificity with RT-PCR, absence of exclusion criteria, making it a diagnostic tool only. Table 1 features some laboratory test results.[22-24]

Microbiology of Coronaviruses

Coronaviruses (CoVs) are RNA viruses that belong to the subfamily Coronavirinae, in the family Coronaviridae, order Nidovirales.[25] Coronavirus has the appearance of a crown under electron microscopy. They have viral envelopes with a single-stranded positive-sense RNA, which is the largest known genome for an RNA virus (27 kb to 32 kb). The viral envelope is derived from the host cell and has glycoprotein spikes. The genome is protected within the nucleocapsid. The latter is helical in shape when relaxed and spherical when inside the virus. The coronavirus replicates its RNA only in the cytoplasm of the host cell.[26]

All CoVs have common similarities in organisation and genomic expression with 16 non-structural proteins and at least four to five structural ones: a spike, a membrane, an envelope, a nucleocapsid, and a hemagglutinin-esterase.[26] There are four genera of CoVs, namely alphaCoV, betaCoV, gammaCoV and deltaCoV.[12] Different hosts can be infected by CoVs and have distinct tissue tropism. Generally, alphaCoVs and betaCoVs infect mammals, whereas gammaCoVs and deltaCoVs cause infections in other animals, such as birds, fishes and only a few mammals (Table 2).[27, 28]

Table 1. Typical laboratories abnormalities in blood from patients with COVID-19

Increased	Decreased
Neutrophils	Lymphocytes
D-dimer	Platelets
C-reactive protein	Albumin
Lactate dehydrogenase	
Alanine aminotransferase	
Aspartate aminotransferase	
Creatinine	
Creatinine kinase	
IgGs and IgMs	

Clinical Features of COVID-19

The most common symptoms in patients with mild to moderate disease are fever (over 38.5 °C), fatigue and dry cough, followed by others, including headache, nasal congestion, sore throat, myalgia and arthralgia.[29-31] A minority could experience gastrointestinal symptoms, such as nausea, vomiting and diarrhoea, particularly in children. COVID-19 has an incubation period of 1–14 days, mostly ranging from 3 to 7 days, see and Table 3.[21, 26] Taste or olfactory disorders were noted in up to 53% of the cases in a small group from Italy, and new anosmia is proposed as a criterion for testing. Some patients with COVID-19 do not have a fever or radiological abnormalities on the initial presentation, which has complicated the diagnosis.[21, 32]

CONCLUSION

The emergence of COVID-19 represents a worldwide health emergency involving healthcare professionals from

Table 2. List of animals associated with pathogenic coronaviruses

Host	Genus	Virus
Human	Alpha	Human CoV-229E
		Human CoV-NL63
	Beta	Human CoV-HKU1
		Human CoV-OC43
		SARS-CoV
		MERS-CoV
Pig	Alpha	PRCV/ISU-1
		TGEV/PUR46-MAD
		PEDV/ZJU-G1-2013
		SeACoV-CH/GD-01
Dog	Alpha	Canine CoV/TU336/F/2008
Camel	Alpha	Camel alpha coronavirus isolate camel/Riyadh
Cat	Alpha	Feline infectious peritonitis virus
Cow	Beta	Bovine CoV/ENT
Horse	Beta	Equine CoV/Obihiro12-1
Mice	Beta	MHV-A59
Chicken	Gamma	IBV
Whale	Gamma	Beluga whale CoV/SW1
Bulbul	Delta	Bulbul coronavirus HKU11

Table 3. Characteristics of patients with COVID-19

Epidemiology	**COVID-19**
Outbreak onset date	December 31, 2019
Location of the first case	Wuhan, China
Confirmed cases	> 5M (worldwide)
Mortality	Over 355000 + (Hospitals + Care homes)
Time to infect first 1000 people (days)	48
Incubation period (days)	7–14
Transmission	Touching or eating an infected, yet unidentified animal. Human-to-human transmission occurs through close contact.
Clinical presentation	
Age (years)	All across the age spectrum
Male to female ratio	1.39:1
Fever	88.7%
Fatigue	29.4%
Non-productive cough	67.7%
Myalgia	14.8%
Dyspnoea	45.6%
Expectoration	13.3%
Sore throat	13.9%
Diarrhoea	6.1%
Nausea and/or vomiting	5.0%
Dizziness	3.7%
Headache	8.0%

all countries, especially since the pandemic was confirmed by WHO. The spread of the virus is on-going, increasing by the day, and the devastating impact of the infection is still growing despite all preventive measures, including lock-down taken to overcome and contain it. Evidently, the impact is not only from a clinical but also from an economic point of view.

The astronomical cost relative to infected/dead healthcare workers, who unfortunately are on the frontline, and as such, are particularly exposed in most cases without adequate personal protective equipment, should not be underestimated. The international effort to fight it is huge and it poses a tremendous challenge to world scientists and experts in finding an urgent/long-lasting vaccine to tackle it. At the same time, the world deserves the right to know the real circumstances from Wuhan surrounding the outbreak as to mitigate future occurrences. There is no known weapon of mass destruction to harm humans in the 21st century than COVID-19, as evidenced in its speed of transmission and corresponding mortality.

Interestingly, South Korea's strategic approach to fighting COVID-19 by reducing new infections to single digits through social distancing, contact tracing, tracking of infected individuals and mass screening could be helpful hints to other countries.

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