

An Update of COVID-19: Epidemiology, Pathogenesis and Laboratory Diagnosis

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Abstract

At the time of submitting this article, the number of new cases of COVID-19 is still increasing globally. High daily mortality rates continue to be reported in the USA and the UK. The immunocompromised elderly, and individuals with underlying medical conditions continue to predominate the cases. The commonest clinical presentation is fever. Cepheid Xpert Xpress SARS-CoV-2 (California, USA) was the first rapid, point of care molecular test for the Coronavirus.

Keywords: COVID-19; Wuhan; Global Burden; ACE2 Receptor; Xpert Xpress SARS-CoV2

Abbreviations

COVID-19: Coronavirus Disease 2019; RNA: Ribonucleic Acid; rRT-PCR: Real Time Reverse Transcription Polymerase Chain Reaction

Epidemiology

Genesis

The first case of the novel coronavirus disease (COVID-19) was reported on December 31, 2019, in Wuhan, China (WHO, 2020). The primary case emerged in the Huanan Seafood Market, where livestock animals are also traded, in Wuhan State of Hubei Province in China and as a pneumonia of unknown cause. A virus that showed 70% genotypic characteristics similar to Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) was isolated. It is notable that the rapid increase of cases from the primary case coincided with the Chinese spring festival of which Wuhan plays an important role as a transportation centre. This enormous scale traffic of celebrants from all over the world expedited the spread of the virus to other nations [1].

Global burden

The spread of COVID-19 over the globe has been fast and by 12/03/2020, the World Health Organisation (WHO) had declared the outbreak as a global pandemic. Towards the end of April, 2020 there were confirmed 2,544,792 cases globally of which 73,657 had been confirmed in 24 hours from the previous publication and a total of 175 694 deaths of which 0.04% occurred with 24 hours between the publishing of the situational reports (Figure 1).

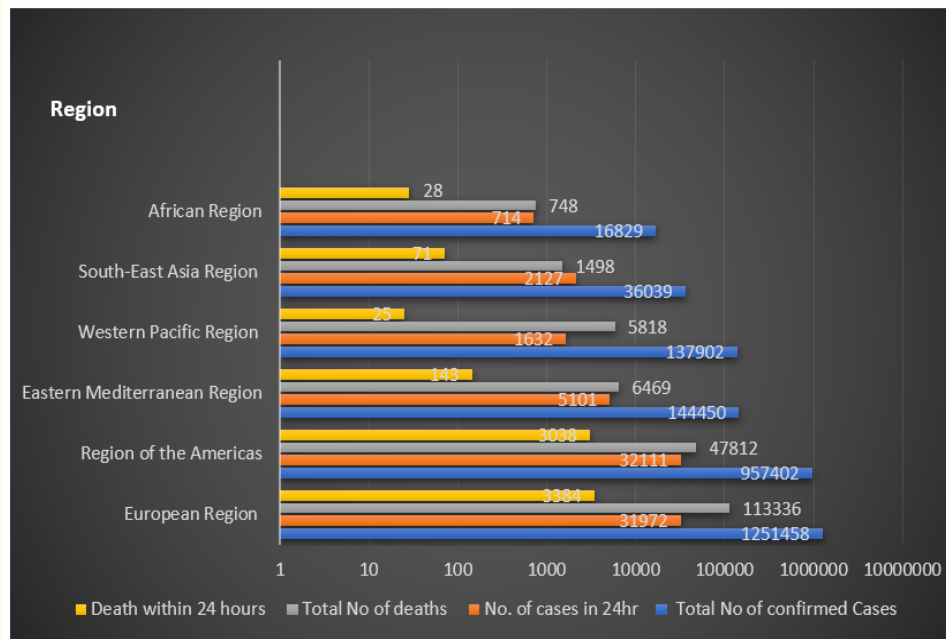


Figure 1: COVID-19 current situation.

The global burden of COVID-19 is ~ 4M cases. Most cases are in Europe while Africa is the least affected.

Data obtained from WHO situational report-94.

https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf?sfvrsn=b8304bf0_4 (Accessed on 24/4/2020 at 12 PM EAT).

Africa is the least affected with 0.007% of the global confirmed cases and the most affected is the European region having almost half; 49.2% of global confirmed cases. Incidence and mortality resulting from respiratory infections, for example, resulting from seasonal influenza increases in the cold seasons, coupled with a novel infection in which the community has no immunity could explain the exacerbated deaths in Europe and Western Pacific regions. The low number in Africa is possibly due to the viricidal effect of ultra-violet rays resulting from the hot, sunny tropical weather and/or under detection of cases resulting from shortage of testing facilities.

At risk groups

Although most upper respiratory infections appear to be more common in children than adults, children do not appear to be at a higher risk than adults [2]. The risk of severe disease associated with COVID-19 infection is considered moderate for the general population and high for older adults. The risk gradually increases from the age of 40 years [3]. This is one of the explanations on the high mortality rates among the 65 years and older population. Additional risk factors include male gender, blood group A and chronic underlying conditions for example, hypertension, cardiovascular diseases, chronic respiratory illness, diabetes and cancer [4]. It has been suggested that the increased risk is possibly associated with the higher expression of angiotensin converting enzyme II (ACE2) (the receptor for entry of the virus into the host cell) in the vulnerable groups compared to the healthy controls. The expression of ACE2 in the lung epithelia increases with age, hypertensive and tobacco use [5].

The incubation period ranges from 2 - 14 days; this is one of the shortcomings of screening using signs and symptoms as asymptomatic parties who may be infected are missed and transmission of the virus may continue. The case fatality rate has been estimated at 0.25 - 3% taking into account the lag time and based on data from Linton [6].

The average reproduction ratio ranges from 2.44 to 4.2; this depends on the method used for determination stochastic, mathematical methods or exponential growth [7]. The fact that the virus is very contagious and the escalated global spread it is certain that the R_0 is above 1.

The virus

CoVID-19 is a respiratory illness caused by severe acute respiratory syndrome-coronaviruses 2 (SARS-CoV2) [8]; a new strain of Coronavirus (CoV) that was described in Wuhan, China in December 2019 [8,9]. The CoV belongs to the family Coronaviridae, order Nidovirales. There are three genera (groups) (I to III) of five Coronaviruses (CoV) that are known to infect humans [8]. In group I, there are 229E and NL63 while group II has OC43 CoV [10,11]. Group III is composed of HKU1 and severe acute respiratory syndrome-associated (SARS-CoV) [10,11].

Coronavirus is descriptive of the crown-like morphology [12] of the virus particles. The CoV are spherical to pleomorphic, enveloped, single-stranded positive sense RNA viruses. The size of CoV ranges from 0.06 - 0.14 μm . They have the largest genome among RNA viruses of ~ 27 - 32 kb pairs [13]. The 5' and 3' ends of the RNA are capped and poly-adenylated, respectively, and codes for genes of both structural and non-structural proteins. The structural proteins include the spikes which are composed of two proteins; spike glycoprotein trimmer (S) and the haemagglutinin esterase (HE), envelope (E) [14], membrane (M) and nucleocapsids (N) [15]. The non-structural enzymatic proteins are proteases, replicase, helicase, and haemagglutinin-esterase [16]. The Coronaviridae have extremely high mutation rates that have led to various properties, host ranges, and disease manifestations [17].

Different viral origins have been suggested for the SARS-Cov2 virus. Genetic sequencing has shown a relation to the bat Coronavirus suggesting bats as a source, however there is also implication of another intermediate animal as it was originally isolated in a seafood market [18]. The origins of the virus are inconclusive since other SARS-Cov- 2 strains had been isolated prior to confirmation of COVID-19.

Physicochemical properties

The SARS-CoV-2 can be inactivated by ultraviolet rays or heated at 56°C 30 minutes and also sensitive to most disinfectants such as diethyl ether, 75% ethanol, chlorine, peracetic acid and chloroform but not inactivated by chlorohexidine [19].

Pathogenesis

It is believed that COVID-19 is a zoonotic infection as the initial infections were associated with the seafood and wild game in the wet animal market of Wuhan, China [20]. Person to person transmission is supported by reports of infection among family members who had not visited the wet animal market and the subsequent surge in the number of cases to the current pandemic level (WHO, 2020). Transmission of infection occurs through inhalation of aerosols from asymptomatic and symptomatic individuals and fomites [21]. The first step in the infection process seems to involve the binding of the virus particle to the host-derived ACE2 receptor [22], followed by fusion with the cell membrane. The epithelial cells of the lungs are the primary sites of infection. There is a quiescent incubation period of 1 - 14 days after which disease may manifest. Damage of the cells trigger production of inflammatory mediators to cause an increase in the respiratory secretions [23]. The spectrum of disease manifestation ranges from mild to severe dependent on the host risk factors as previously discussed. The most common symptoms and signs include fever, unproductive cough, easy fatiguability, expectoration of sputum, dyspnoea, sore throat, headache and myalgia. Infrequent symptoms are vomiting and diarrhoea. Significantly, about 80% of the reported cases were mild (both non-pneumonia and pneumonia cases) [24,25].

Diagnostic virology

Specimen collection and transport

There are a number of specimens that can be used for diagnosing of coronavirus ranging from nasopharyngeal and/or oropharyngeal swabs, saline wash for the upper airway samples as well as bronchoalveolar lavage, tracheal aspirates and/or sputum for the lower respiratory tract. For nasopharyngeal and oropharyngeal specimen, synthetic fibre swabs with flexible (plastic or wire) shafts are recommended. The swab should be immediately placed in a sterile container with a viral transport medium or normal saline. A sterile screw capped container should be used to collect at least 2 mL of the lower respiratory tract specimen. The collection must follow recommended procedures for collecting respiratory samples ensuring infection control including eye protection and a gown. However, induction of sputum is not recommended. Non-respiratory samples such as stool and blood could be used for detection of the virus although they have lower diagnostic yield.

The specimens should be stored between 2 - 8°C for immediate transportation or at least -70°C if shipment is to be delayed. The samples should be accompanied with request forms detailing the patient information such as patient identifiers, the sample type among other details.

Laboratory detection of the virus should be at facilities with BSL-2 or equivalent capacity by personnel that have been adequately trained on how to handle such infectious agents.

In addition to tests to directly identify the causative agent, other laboratory tests that are done include blood tests for complete blood count, C-reactive protein, liver function tests among other tests. These tests may facilitate patient management.

Laboratory testing

Current recommendations for testing prioritize symptomatic patients as well as individuals deemed to have a high risk of exposure such as those with close contact with individuals who have tested positive for SARS-CoV-2 and healthcare workers.

Laboratory diagnosis of the COVID-19 virus depends on detection of the viral nucleic acid amplification by rRT-PCR and confirmation by sequencing the nucleic acid. The rRT-PCR is done targeting a number of COVID-19 virus genes among which are ORF1ab, N, RdRP, E, etc. with different laboratories and countries having various combinations of the target genes (for in-house assays) as summarized in the table 1 below.

| Country | Institute | Gene targets |
|---------------|---|---|
| China | China CDC | ORF1ab and N |
| Germany | Charité | RdRP, E, N |
| Hong Kong SAR | HKU | ORF1b-nsp14, N |
| Japan | National Institute of Infectious Diseases, Department of Virology III | Pancorona and multiple targets, Spike protein |
| Thailand | National Institute of Health | N |
| US | US CDC | Three targets in N gene |
| France | Institut Pasteur, Paris | Two targets in RdRP |

Table 1: Target genes for molecular detection of COVID-19 virus.

Table 1 shows molecular tests for COVID-19.

Different countries have developed molecular tests for COVID-19 which target different genes.

There have been several attempts to make molecular testing faster and more automated and several innovations have been made including adoption of existing diagnostic tests such as the GeneXpert system. The Food and Drug Administration approved Cepheid Xpert Xpress SARS-CoV-2 (California, USA) as the first rapid, point of care molecular test for the coronavirus. The test principle operates on the company's automated GeneXpert Systems which are available globally. The Xpert Xpress SARS-CoV-2 is expected to revolutionise the testing as it eliminates the need for taking specimens to the central laboratory and waiting for days (cepheid.com/coronavirus) as it returns results within 45 minutes.

Rapid diagnostic tests have been developed that are based on either detection of viral antigens or detection of host's antibodies against the viral particles. The WHO recommends these tests to be validated for specific populations and settings for which they are to be adopted. However serological (antibody) tests may face a challenge of cross-reactivity with other coronaviruses. Viral cultures are not recommended for routine diagnosis and should be carried in a biosafety cabinet level-3 facility.

Conclusion

The global burden of COVID-19 rapidly increased from early March 2020, when the WHO declared the pandemic. The pathogenesis of the disease remains elusive as efforts to develop diagnostic methods continue.

Author Contributions

All authors contributed equally to the generation of this review.

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Conflict of Interest

All authors declare no conflict of interest.

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