**Chapter (1)**

**What is COVID 19**

Since December 2019, an outbreak of novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had started from Wuhan city, Hubei province, China ***(Yu et al., 2020*** and ***Carlos et al., 2020).***

Coronaviruses are a large group of viruses that are rather common throughout the community. Historically, evidence has shown that the virus is transmitted through birds and mammals, with humans being particularly vulnerable to infection and transmission of the virus ***(Schoeman and Fielding, 2019).***

There were two previous outbreaks of coronaviruses; SARS and Middle East respiratory syndrome-corona virus (MERS or MERS-CoV) in 2002 and 2012, which resemble the novel coronavirus ***(Wahed et al., 2020*** and ***Huynh et al., 2020).***

This disease was named as corona virus disease 19 (COVID-19) by the World Health Organization (WHO) ***(Morgul et al., 2020*** and ***Verma and Prakash, 2020),*** and the causative virus was named as SARS-CoV-2 by the International Committee on Taxonomy of Viruses ***(Sohrabi et al., 2020*** and ***Kasemy et al., 2020).***

SARS-CoV-2 is a non-segmented positive-sense RNA virus ***(Guan et al., 2020),*** that belongs to the β-coronavirus genus, coronaviridae family, and Nidovirales order. Many RNA viruses, such as the flu virus, are prone to mutations due to the lack of proofreading in their genetic evolutions. Viral mutations are driven by a variety of factors, including the replication mechanism, polymerase fidelity, access to proofreading or post-replicative repair, sequence context, cellular environment, and host immune responses or gene editing ***(Wang et al., 2020 a).***

The SARS-CoV-2 viral particles are spherical and have mushroom shaped protein called spikes protruding from their surface, giving the particle a crown like appearance. The spikes bind to the human cells and allowing virus to gain entry. The spike protein of novel corona virus shares 98% sequence identity with the spike protein of bat coronavirus. The researchers found that spike protein of SARS-CoV-2 binds to the cellular receptor called angiotensin converting enzyme 2, which is entry point into human cells. It has 10 to 20-fold higher binding affinity than SARS. The higher binding affinity causes higher human to human transmission ***(Ankita and Sangeeta, 2020*** and ***Verma and Prakash, 2020).***

COVID-19 is a zoonotic disease with intermediate host. Although the intermediate source of origin and transfer to humans is not clearly known. Intermediate host for SARS-CoV is palm civet and camel while the possible intermediate host for SARS-CoV-2 is pangolin or snakes. The reserve host for all the three (MERS-CoV, SARS-CoV and SARS-CoV 2) is bat. Bat carries so many viruses and around 200 corona viruses without getting sick. So, the primary mode of transmission is from bats to intermediate host to humans ***(Verma and Prakash, 2020).***

On 31 Dec 2019, Wuhan Municipal Health Commission, China, reported [a cluster of cases of pneumonia](https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/) in Wuhan, Hubei Province. A novel coronavirus was eventually identified*.* **On 4 January 2020,** WHO [reported on social media](https://twitter.com/WHO/status/1213523866703814656?s=20) that there was a cluster of pneumonia cases – with no deaths – in Wuhan, Hubei province ***(WHO, 2020 a).***

The first reported infections had a direct relation to the Huanan seafood wholesale market in Wuhan, China; it was assumed that bats act as a reservoir, and Malayan pangolins might act as an intermediate to facilitate transfer to humans ***(Lam et al., 2020).***

The Chinese Center for Disease Control and Prevention offi­cially announced a novel coronavirus as the causative pathogen of COVID-19 four days later ***(Zhu et al., 2020).***

**After another 4 days (12th of Jan 2020),** China publicly [shared](https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/) the genetic sequence of COVID-19 ***(WHO, 2020 a).***

**Then one day later, the Ministry of Public Health, Thailand reported the first imported case of** lab-confirmed novel coronavirus (2019-nCoV) from Wuhan, Hubei Province, China ***(WHO, 2020 b).***

**On 22 January 2020,** WHO mission to China issued a [statement](https://www.who.int/china/news/detail/22-01-2020-field-visit-wuhan-china-jan-2020) saying that there was evidence of human-to-human transmission in Wuhan but more investigation was needed to understand the full extent of transmission ***(WHO, 2020 a).***

On the 30th of January 2020, WHO declared that COVID-19 is a public Health Emergency ***(WHO, 2020 a).***

Sustained local transmission of the disease all over the world led the WHO to declare COVID-19 as a pan­demic on 11 March 2020 **(Kasemy et al*., 2020***; ***Kronbichler et al., 2020*** and ***Wahed et al., 2020).***

It has rapidly spread around the world, posing enormous health, economic, environmental and social challenges to the entire human population. The coronavirus pandemic is severely disrupting the global economy (***Verma and Prakash, 2020).***

The novel corona virus has no border, no religion and spread beyond cast and creed. It is highly contagious in nature and easily unpredictable. World was never prepared for this kind of pandemic ***(Kumari and Shukla 2020).***

**Chapter (2):**

**Epidemiological features of COVID 19**

**Incubation period**

The time between catching the virus and beginning of symptoms of the disease is known as incubation period ***(Verma and Prakash, 2020).***

The Incubation Period of COVID-19 is about 2–14 days ***(CDC, 2020)***, but most commonly around five days ***(Verma and Prakash, 2020),*** and the period from the onset of symptoms to death was estimated to range from 6 to 41 days ***(Kasemy et al., 2020).***

**Mode of transmission**

Although the overall mortality rate of COVID-19 is low, the disease can be transmitted rapidly ***(Chen et al., 2020)***, and people are generally susceptible to its infection ***(Del Rio and Malani, 2020).***

The transmission of COVID-19 can be direct in the form of droplets produced during sneezing, coughing, speaking and accidently inhaling the droplets in a closed proximity of an infected person. Droplets are water holding entities of diameter more than 5μm and these can be caught by a healthy person within a certain range of 1 m approximately ***(Van Doremalen et al., 2020).***

The indirect transmission is through touching contaminated surface ***(Kumari and Shukla 2020).***

As the SARS-CoV-2 was found in stool of patients from China and the United States (U.S), there is a risk of fecal-oral trans­mission ***(Holshue et al., 2020).***

Faecal shedding seems to occur in COVID-19 patients with or without gastrointestinal symptoms which could enable asymptomatic individuals with no respiratory symptoms to be a potential source of faecal transmission ***(Vardoulakis et al., 2022).***

Studies showed that virus takes entry to the respiratory mucosa by angiotensin receptor 2 (ACE**2**) present in lower respiratory tract in abundance mainly in type-2 alveolar cells ***(Singhal, 2020)***. The same receptor is used by SARS-CoV ***(Zhou et al., 2020).***

The sources of infection are patients with symptomatic COVID-19 and asymptomatic patients and patients in IP who are carriers of SARS-CoV-2 ***(Kasemy et al., 2020).***

The novel coronavirus has four stages of transmission *namely* stage-1 (imported cases), stage-2 (local transmission), stage-3 (community transmission) and stage-4 (transmission out of control) ***(Verma and Prakash, 2020).***

**Clinical features**

In terms of symptoms, the WHO reported that more than 80% of COVID-19 patients showed mild symptoms and recovered without any medical intervention, approximately 20% of infected cases had a severe illness such as shortness of breath, septic shock and multi-organ failure, and it has been reported that an estimated 2% of cases can be fatal ***(Huynh et al., 2020).*** Recovery in mild cases occurred after 1 week, while in severe cases, death may be the fate ***(Kasemy et al., 2020).***

The presentation of COVID-19 and its disease course are unpredictable and range from asymptomatic to mild respiratory infections to pneumonia and even to acute respiratory distress syndrome (ARDS) ***(Guan et al., 2020).***

According to WHO, the most common symptoms of COVID-19 are fever, dry cough and fatigue, while other symptoms that are less common and may affect some patients include loss of taste or smell, nasal congestion, conjunctivitis (also known as red eyes), sore throat, headache, muscle or joint pain, different types of skin rash, nausea or vomiting, diarrhea and chills or dizziness ***(WHO, 2020 c).***

Symptoms of severe COVID‐19 disease include sshortness of breath, loss of appetite, confusion, persistent pain or pressure in the chest, high temperature (above 38 °C) ***(Wang et al., 2020 a*** and ***Wang et al., 2020 b).*** While other less common symptoms are irritability, confusion, reduced consciousness (sometimes associated with seizures), anxiety, depression, sleep disorders and more severe and rare neurological complications such as strokes, brain inflammation, delirium and nerve damage ***(WHO, 2020 c).***

Unlike SARS-CoV that mainly infects the lower respiratory tract, SARS-CoV-2 is observed with a high level of shedding in the upper respiratory tract. ***(Wölfel et al., 2020).***

Older patients and those with comorbidities, such as cardiovascular disease, diabetes mellitus, obesity, and cancer patients have an increased risk of severe disease and mortality ***(Kasemy et al., 2020***; ***Huynh et al.,*** and ***Zavascki and Falci, 2020).***

In severe cases, the virus causes fatal pneumonia similar to that caused by SARS-CoV, and MERS-CoV, which have emerged in the past 20 years in sporadic countries all over the world ***(Li et al., 2020 a).***

It was observed globally that males suffered greater COVID-19 severity and mortality. Researchers proposed delayed viral RNA clearance in males, sex-related immune response differences and hormonal milieus differences contributed to this male preponderance ***(Omar et al., 2021).***

**Asymptomatic patients**

The epidemiological and virological characteristics of COVID-19 asymptomatic pathogenicity remain a mystery ***(Wang et al., 2020 a).***

Asymptomatic and presymptomatic cases can play an important role in transmitting coronavirus ***(Furukawa et al., 2020)*** because viable viruses have also been isolated from many asymptomatic cases ***(Oran and Topol 2020).***

The rapid spread of the disease, in part fuelled by asymptomatic carriers and a delayed onset of symptoms, created many challenges for healthcare systems ***(Hall, 2020).***

Some reports suggested that 10-30% of patients infected with SARS-CoV-2 are asymptomatic. Thus, considering that the asymptomatic carriers are infectious, it’s essential to identify them in order to effectively contain the spread of the virus ***(Yu et al., 2020).***

Younger people seem to have mild or even asymptomatic presentations and thus might be crucial in further spreading of the disease ***(Guan et al., 2020).***

They are a majority of the workforce and are more likely to be socially active. Hence, younger, infected people may spread the disease unknowingly to a more substantial proportion of contacts. Given the lack of symptoms, they may not be screened and diagnosed with the infection (***Kronbichler et al., 2020).***

As a result of that, Elusive asymptomatic transmission is regarded as the Achilles’ heel of current strategies for controlling COVID-19 ***(Wang et al., 2020 a).***

**Diagnosis of COVID 19**

Early identification of severity and prognosis of COVID-19 is very important to enable intervention for the reduction of mortality risk ***(Ghweil et al., 2020).***

Highly sensitive and specific tests are crucial to identify and manage COVID-19 patients and implement control measures to limit the outbreak ***(Scohy et al., 2020).***

Detecting viral particles using real-time reverse-transcription polymerase chain reaction (RT-PCR) is the gold standard of diagnosis and monitoring ***(Araujo-Filho et al., 2020).*** It usesnasopharyngeal specimens to detect viral RNA (***Fenollar et al., 2020).***

 The main disadvantage of RT-PCR is that it requires special equipment and skilled laboratory personnel familiar with molecular techniques. Moreover, it is costly and often time consuming ***(Scohy et al., 2020).***

An important issue with the real-time RT-PCR test is the risk of eliciting false-negative and false-positive results. It is reported that many ‘suspected’ cases with typical clinical characteristics of COVID-19 and identical specific computed tomography (CT) images were not diagnosed. Thus, a negative result does not exclude the possibility of COVID- 19 infection and should not be used as the only criterion for treatment or patient management decisions ***(Tahamtan & Ardebili, 2020).***

 There is another test that is used for diagnosis of COVID-19, It is called rapid antigen tests (sometimes known as a rapid diagnostic test – RDT) detect viral proteins (known as antigens). Samples are collected from the nose and/or throat with a swab (nasopharyngeal secretions) ***(WHO 2020 c*** and ***Scohy et al., 2020).***

Rapid antigen detection (RAD) test, has many advantages as follow: The test is very rapid (15 – 30 minutes) ***(Fenollar et al., 2020*** and ***Scohy et al., 2020),*** also it is less laborious and require short training ***(Scohy et al., 2020),*** cheaper than PCR ***(WHO, 2020 c).*** However, in terms of sensitivity, RAD tests are inferior to PCR, and test results are highly dependent on the swabbing method ***(Wölfl-Duchek et al., 2022).***

These tests perform best when there are more viruses circulating in the community and when sampled from an individual during the time they are most infectious ***(WHO, 2020 c).***

Other laboratory tests, such as whole white blood cells (WBCs) count, neutrophil ratio, lymphocyte count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), hemoglobin, platelets, myoglobin, D-dimer, lactate dehydrogenase (LDH) and numerous other laboratory parameters have been described to change with COVID-19 infection ***(El Kassas et al., 2020).***

Laboratory findings in patients diagnosed with COVID-19 are not remarkably different from those diagnosed with the other coronavirus infections, with lymphopenia as the most common finding together with low platelet count, decreased albumin levels and increased aminotransferases, lactic dehydrogenase, creatine kinase and C-reactive protein levels ***(Petrosillo et al., 2020).***

Radiological presentation of COVID-19 is not much different from the other two coronavirus associated pneumonia, even though the proportion of cases with bilateral findings seems to be higher in COVID-19 cases. The most common CT findings in COVID-19 is bilateral pulmonary parenchymal ground-glass, consolidative or “crazy paving” pulmonary lesions, often with a rounded shape and a peripheral distribution ***(Chung et al., 2020).***

Also, serological or antibody tests can detect whether someone has had an infection in the past, even if they have not had symptoms. It is usually done on a blood sample, these tests detect antibodies produced in response to an infection. In most people, antibodies start to develop after days to weeks and can indicate if a person has had past infection. Antibody tests cannot be used to diagnose COVID-19 in the early stages of infection or disease but can indicate whether or not someone has had the disease in the past ***(WHO, 2020 c).***

**Difference between COVID 19, SARS and MERS**

SARS-CoV-2 is a recently discovered virus in the coronavirus family. SARS-CoV-2 is more closely related to the other two coronaviruses that led to two recent outbreaks, SARS-CoV-1 that caused the SARS outbreak in 2002 and MERS-CoV that caused the MERS outbreak in 2012 ***(Lu, et al., 2020 a).***

Although SARS-CoV-2 belongs to the same betacoronavirusgenus of the coronaviruses responsible for the SARS and MERS (i.e SARS-CoV and MERS-CoV, respectively), this novel virus (COVID 19) seems to be related to milder infections. Moreover, SARS and MERS were mainly associated with nosocomial spread, whereas SARS-CoV-2 is much widely transmitted in the community ***(Munster et al., 2020*** and ***Petrosillo et al., 2020).***

Interestingly, despite the high virological similarity between the SARS-CoV-2 and SARS-CoV, gastrointestinal (GI) symptoms and diarrhea seem to be much more common in SARS ***(Petrosillo et al., 2020).***

In patients affected by COVID-19, viral load progressively decreases within days, following a different pattern than SARS, in which the highest shedding is recorded after 10 days from the symptoms’ onset ***(Zou et al., 2020).***

The reproductive number (R0) of the novel infection is estimated by WHO to range between 2 and 2.5, which is higher than SARS (1.7-1.9) and MERS (<1), suggesting that SARS-CoV-2 has a higher pandemic potential ***(Wu et al., 2020 a).***

MERS-CoV has a higher mortality but a lower transmissibility probably because it causes a more severe clinical picture than COVID-19 and SARS, requiring hospitalization more frequently, thus reducing the community spreading of the infection and increasing the nosocomial transmission ***(Chen, 2020).***

The fatality rate of novel coronavirus infection is estimated to be 2.3, lower than SARS (9.5%) and much lower than MERS (34.4%) ***(Petrosillo et al., 2020).***

**Table (І): Difference in clinical features between COVID-19, SARS and MERS *(Pustake et al., 2022).***

|  |  |  |  |
| --- | --- | --- | --- |
| **Feature** | **SARS** | **MERS** | **COVID-19** |
| **Incubation Period** | 2‑10 Days | 2‑12 days | 2‑14 days |
| **Fever** | ~100% | 81‑98% | 34‑80% |
| **Cough (Nonproductive)** | 75‑80% | 57‑83% | 19‑57% |
| **Chills or Rigor** | 15‑90% | 87% | 25% |
| **Myalgia** | 45‑50% | 43% | 6.5‑34% |
| **Headache** | 20‑70% | 20.4% | 2.5‑38% |
| **Dyspnea** | 35‑60% | 22‑72% | 6‑36% |
| **Tachypnea** | 40‑75% | - | 30‑35% |
| **Tachycardia** | 40‑75% | - | 20‑27% |
| **Hypoxemia** | 40‑75% | - | 40‑50% |
| **Cachexia** | - | - | 37% |
| **Malaise** | 40‑75% | 38% | 56% |
| **Nausea/Vomiting** | 35% | 14‑21% | 2‑13% |
| **Diarrhea** | 6‑25% | 19.4‑26% | 5‑21% |
| **Sore throat** | 25% | 9.1‑14% | 2.5‑10% |
| **Rhinorrhea** | 15% | 1.6% | 5‑10% |
| **Hemoptysis** | ‑ | 4.3% | 22.4% |
| **Asymptomatic** | ‑ | ‑ | 6.5% |

**Table (Π): Epidemiologic characteristics of COVID-19, SARS and MERS *(Petrosillo et al., 2020).***

|  |  |  |  |
| --- | --- | --- | --- |
|  | **SARS** | **MERS** | **COVID-19** |
| **Year of appearance** | 2002 | 2012 | 2019 |
| **Animal reservoir** | Bats | Bats | Bats |
| **Intermediate host** | Palm civets | Camels | Unknown |
| **Receptor** | Angiotensin-converting enzyme 2 (ACE2) | Dipeptidyl peptidase 4 (DPP4) | Angiotensin-converting enzyme 2 (ACE2) |
| **Case fatality rate** | 9.5% | 34.4% | 2.3% |
| **R0** | 1.7–1.9 | 0.7 | 2–2.5 |

**Difference between COVID 19 and Seasonal Influenza**

Early studies with 235 cases of influenza virus infection indicate that the duration of influenza viral shedding was shorter and decayed faster than COVID 19 and quantitative viral loads were lower in asymptomatic than in symptomatic cases ***(Ip et al., 2017).***

 Significant differences exist between patients with COVID-19 and seasonal influenza requiring hospitalisation. SARS-CoV-2 appears to have a higher potential for respiratory pathogenicity, leading to more respiratory complications and to higher mortality ***(Piroth et al., 2020).***

Also, case-fatality rate in COVID-19 appears to be higher than in seasonal influenza, even though both diseases mainly affect older adults (>65 years) with fatality. The higher case-fatality of COVID-19 could be due to differences in underlying comorbidities of patients, the pathogenicity of the virus, population immunity, and host responses to infection ***(Piroth et al., 2020).***