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Epidemiology of Covid–19: An epidemic into a pandemic

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Abstract

The 2019 novel coronavirus epidemic has transformed into a pandemic and has become an ongoing global health threat. The SARS-CoV-2 infection is still spreading, and this virus poses a serious threat to public health, though joint prevention and quarantine mechanisms have been confirmed to be enacted globally. There is limited support for many of its key epidemiologic features, including the incubation period, which has important implications for surveillance and control activities. Human to human transmission has been reported to occur primarily via direct or indirect contact through respiratory droplets or secretions. WHO reported a mean incubation period of 6.4 days and a case fatality rate of 6.3 %. Increased severity of cases is reported in males, the elderly, and in presence of co-morbidities. There are no reports of vertical transmission from mother to child. Health care workers as well as families of cases and health care workers are at increased risk. WHO in a recent report has stated that there is no evidence of immunity to secondary infection in COVID 19 patients. The viral load of SARS-CoV-2 might be a useful marker for assessing disease severity and prognosis. The importance of hand hygiene and social distancing play a vital role in halting the spread of this pandemic. Various bodies including the WHO and US Centers for Disease Control and Prevention (CDC) are issuing continued advice and education on preventing the further spread of COVID-19.

Keywords: COVID 19, epidemiology, challenges, prevention

Introduction

Background

Coronaviruses have been reported as causes of mild and moderate respiratory infections for over 50 years **[1]** These viruses can also cause enteric, hepatic, and neurologic diseases.**[2,3]** They are large, enveloped, positive-strand RNA viruses that can be divided into 4 genera, a, b, d, and g, of which a and b coronaviruses are known to infect humans, which are called Human Corona Viruses(HCoVs).**[3]** Four HCoVs (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10 % to 30 % of upper respiratory tract infections in adults. **[4]** Coronaviruses were found in 30 % of acute respiratory tract infections of children under 6 years of age **[5]**. Monto and Lim **[6]** also reported a 29 % infection rate with HCV OC43 in children below 5 years who had a 29 % infection rate with HCV OC43.

The epidemic of the 2019 novel coronavirus has expanded from Wuhan throughout China to a growing number of countries. The impact of an epidemic depends on the number of persons infected, the infection's transmissibility, and the spectrum of clinical severity.**[7]** On January 7, 2020, the World Health Organization (WHO) named it the 2019 novel Corona Virus (2019-nCoV). On February 11, 2020, the WHO named the illness associated with 2019-nCoV as the 2019 novel Corona Virus Disease (COVID-19). **[8]** On the same day, the International Committee on Taxonomy of Viruses (ICTV) named this novel coronavirus as Severe Acute Respiratory Syndrome Corona Virus -2 (SARS CoV-2). **[9]** Emergence of 2019-nCoV has attracted global attention, and the WHO has declared the COVID-19 a Public Health Emergency of International Concern (PHEIC).**[10]** COVID 19 outbreak was declared a pandemic by WHO on March 12, 2020.

The epidemic, now transformed into a pandemic has become an ongoing global health threat. The SARS-CoV-2 infection is still spreading, and this virus poses a serious threat to public health, though joint prevention and quarantine mechanisms have been confirmed to be enacted globally. Due to a lack of specific antiviral treatments and pressure of clinical treatment, thousands of severe cases are dying every day worldwide. **[11]** There is limited support for many of its key epidemiologic features, including the incubation period, which has important implications for surveillance and control activities.

Transmissibility of the infection

Understanding transmissibility remains crucial for predicting the course of the pandemic and the likelihood of sustained transmission.**[12]** It is highly likely that the human-to-human

transmissibility of 2019-nCoV is sufficient to support sustained human transmission unless effective control measures are implemented.**[13]** Initial thoughts were that patients were presumed to be infected in hospitals due to nosocomial infection and hence it was concluded that the COVID-19 is not a super spreader virus (spread by one patient too many others), but later it was reported that many patients were getting infected at various locations throughout the hospital through unknown mechanisms.**[14]**

Human to human transmission has been reported to occur primarily via direct or indirect contact through respiratory droplets or secretions spread by coughing or sneezing from an infected individual. **[11,15]** Strong evidence of human-to-human transmission in this emerging acute respiratory tract infection has also been reported in various studies in China by Dong et al,**[16]** Li et al **[17]** and Lee et al. **[18]**

Incubation period

The incubation period can facilitate several important public health activities for infectious diseases, including active monitoring, surveillance, control, and modeling. **[19]** Our current understanding of the incubation period for COVID-19 is limited. WHO did an early analysis **[20]** on confirmed cases in Chinese provinces outside Wuhan, and reported a mean incubation period of 6.4 days with a range of 2.1 to 11.1 days. Another analysis **[21]** based on 158 confirmed cases outside Wuhan estimated a median incubation period of 5.0 days with a range of 2 to 14 days. These estimates are generally consistent with estimates from confirmed cases in China **[17]** (mean incubation period, 5.2 days) and from clinical reports of a familial cluster of COVID-19 in which symptom onset occurred 3 to 6 days after assumed exposure in Wuhan.**[22]**

Jin et al **[23]** reported the incubation period from 1 to 14 days, mostly 3–7 days. However, the mean incubation period ranged from 5.2 days to 6.7 days. **[11,15,19]** The time from onset of symptoms to hospitalization (and isolation) ranged between 0 and 10 days with a mean of 3.7 days. The mean number of days to hospitalization was 2.5 days for cases imported from China, but 4.6 days for those infected in Europe.**[24]**

Case fatality rate

As interventions are gradually implemented and calibrated during the course of an outbreak, early estimates of the Case-Fatality Ratio (CFR) provide crucial information for policymakers to decide the intensity, timing, and duration of interventions. However, the assessment of epidemiologic characteristics, including the CFR, during the course of an outbreak tends to be affected by right censoring and ascertainment bias. **[25,26]**

CFR is multifactorial and is strongly influenced by a number of factors, including age, gender, comorbidities, availability of health care facilities, etc. It was found to be increased in the elderly, especially over 80 years, and ranged from 14.8 % to 27 %. **[11,27-29]** Research in China **[30]** reported increased CFR in males when compared to females. Patients with underlying comorbidities showed poor prognosis and increased CFR ranging from 5.6 % to 10.5 % **[11,27,31]** to as alarming as 50 % in critically ill patients. **[32,33]** The total CFR was 2.3 % of 44,672 confirmed cases in China.**[27]** The overall fatality rate of persons with confirmed COVID-19 in the Italian population, was reported as 7.2 %.**[34]** This rate is higher than that observed in other countries.**[8]** Thus, the overall older age distribution in Italy relative to that in China may explain, in part, the higher average CFR in Italy.**[35]**

As for healthcare workers, the CFR was approximately 0.17 % of 3019 cases.**[27]** A study by Mc Michael et al **[36]**, reported a CFR of 33.7 % for hospital residents and 6.2 % for hospital visitors.

Epidemiological triad

The epidemiological triad of COVID-19 is illustrated in **Figure 1**.

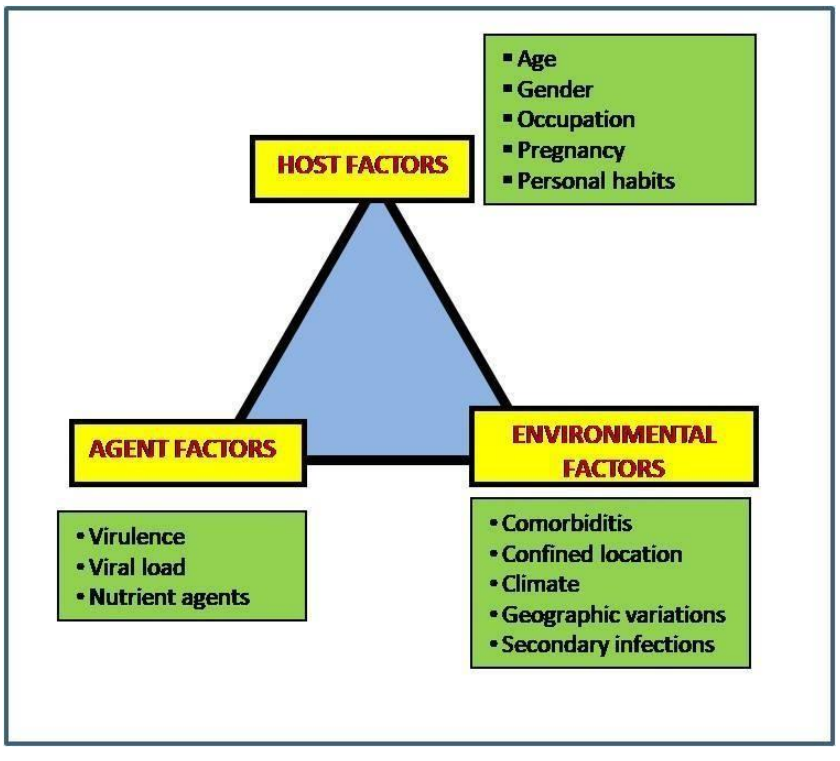

Figure 1: Epidemiological Triad of COVID 19

Host factors

Age

In a study reported by Fan et al **[37]**, in China, the youngest patient was 20 months of age; the oldest was 94 years of age. This suggests the wide age range of the infection. A general pattern has been reported from multiple countries that COVID-positive children have a milder form of the disease.**[16,38]** This could be attributed to the various reasons: children have well cared at home, composition and functional responses of the developing immune system,**[39]** the decreased prevalence of comorbidities in children, presence of other simultaneous viruses in the mucosa of the lungs and airways & levels of antibodies to the virus due to more frequent respiratory tract infections. These antibodies limit the growth of SARS-CoV2, by the direct virus to virus interactions and competition. Another thought suggests that it is probably due to the differences in the expression of the Angiotensin-Converting Enzyme (ACE) 2 receptor necessary for the virus binding and infection. Treatment with ACE inhibitors or angiotensin receptor blockers induces expression of ACE 2. Since the therapies are more common in adults, it has accounted for the milder form of the disease in children.**[38]**

In children up to 15 years of age, the median age was reported as 7 years, with an age range from 1 day to 18 years, suggesting that all ages of childhood are prone to COVID 19 infection.**[16]** However, increased vulnerability of infants to COVID 19 infection was reported by Dong et al **[16]** and in a report by Bialek et al - US Centers for Disease Control and Prevention (CDC) COVID 19 Response Team **[40]** in which infants accounted for the highest percentage (15 %–62 %) of hospitalization among pediatric patients with COVID-19. Similarly, the highest rate of cases among children and adolescents was reported in infants by the WHO-China Joint Commission **[41]** and by Wang et al. **[42]**

Various studies have reported varied median age ranges: ranging from 42 years to 72 years, **[17,19,24,33,36,43-47] (Table 1)**. China CDC data **[27]** showed that more than 85 % of patients were mainly concentrated at the age range of 30–79 years.**[11]** Similar results of higher severity in older age groups were reported in Wuhan **[28]** and United States. **[29,48]** Although the majority of reported COVID-19 cases in China were mild (81 %), approximately 80 % of deaths occurred among adults aged ≥ 60 years; with the highest percentage of severe outcomes among persons aged ≥ 85 years. Similar to reports from other countries **[8,33,43,49,50]**, this finding suggests that the risk for serious disease and death from COVID-19 is higher in older age groups. These results suggest that vigorous efforts should be made to protect and reduce transmission and symptom progression in vulnerable populations including both elderly people and young children.

Gender

Results of various studies **[2,16]** have reported that there are no major differences in the gender distribution. However, a male predilection was reported by Bailek et al - CDC COVID 19 Response Team **[40]** among children and adults and by Bhatraju et al **[51]** in Seattle in the US. Similar results were reported by Lauer et al **[19]** in Hubei Province, China, Wang et al, **[44]** Guan et al, **[33]** Li et al,**[17]** Chen et al **[52]**, and Zhou et al **[47]** in the Wuhan outbreak. **(Table 1)** Spiteri et al **[24]** reported that the proportion of male cases was higher in Europe (66 %) when compared with those acquired in China (57 %). Fan et al **[37]** reported that the distribution of illness by gender did not differ significantly, but female patients predominated slightly. Similar results were reported by Pan et al, **[45]** and Shi et al **[46]** in Wuhan, China. Mc Michael et al **[36]** in Washington and Spiteri et al **[24]** reported a predominant female predilection **(Table 1)**. Though females had a higher rate of confirmed cases compared with males, males were more likely to have a severe or critical illness. This is consistent with previous reports from China **[53,54]** suggesting a higher crude fatality rate among men compared with women and another study in critically ill patients demonstrating that more men were affected (67 %) than women (33 %).**[55]**

Table 1: Age and gender distribution of COVID 19 cases

AUTHOR/ YEAR	LOCATION OF STUDY	AGE DISTRIBUTION (years)		GENDER DISTRIBUTION (%)	
		Median	Range	Males	Females
Dong, et al [16]	China	7	1day -18yrs	No major gender differences	
Li et al, [17]	Wuhan, China	59	15 - 89	56	44
Lauer, et al [19]	Hubei Province, China	44.5	34 - 55.5	60	40
Spiteri, et al [24]	Europe	42	2 - 81	34	66
Guan, et al [33]	China	47	35 -58	58	42
Mc Michael, et al [36]	Washington, USA	72	21 -100	33	67
Bialek, et al [40]	USA	11	0 – 17 18 – 64	57 53	43 47

Wang, et al [44]	Wuhan, China	56		54	46
Pan, et al [45]	Wuhan, China	56.7	0 - 103	48	52
Shi, et al [46]	Wuhan, China	64	21 - 95	49	51
Zhou, et al [47]	Wuhan, China	56	18 - 87	Majority	
Bhatraju, et al [51]	Seattle, USA	64	23 -97	63	37
Chen, et al [52]	Wuhan, China	55.5	21 - 82	68	32

Table 2: Comparison of COVID 19, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS)

Characteristics		**Corona Virus Disease 2019 (COVID 19)**	**Severe Acute Respiratory Syndrome (SARS)**	**Middle East Respiratory Syndrome (MERS)**
Mean Generation time (days)		8.4	8.4	10.7
Incubation Period (days)	**Mean**	6.4	5	6
	Range	2.1-11.1	5 2 -14	2 - 14
Increased severity in presence of co morbidities		Present	Present	Present
Case to case variation		Greater	Greater	Greater
Risk in Pregnant women		Not reported	Increased	Increased
Case-fatality rate		6.9 %,	9.6 %	34 %,
Virulence		Less	More	More
Viremia		Less than 1 week	First week	Lesser duration
Peak respiratory viral shedding		2nd week	2nd week	Longer duration
Persistent stool viral shedding		longer	Beyond second week	Lesser
Increased severity with age		Present	Present	Present
Virus RNA in respiratory specimens		20 days	4 weeks	3 weeks

Occupation

Persons who are in close contact with patients or sub clinically symptomatic infected persons are part of the high-risk population, who are mostly healthcare workers and the family members of patients and health care workers.**[56]**

The rate of cases in Health Care Workers (HCWs) was substantially higher than in the general population initially, indicating a high risk of nosocomial infection. However, it quickly decreased in the later periods, after increasing awareness of and wider use of personal protective equipment, proper training, adequate hospital-level prevention and management, and support.**[57]**

A study **[58]** conducted among health care professionals reported that the high-risk department group had 2.13 times higher risk of developing COVID-19 compared with the general department group. HCWs working in the high-risk departments, with suboptimal hand hygiene, longer duty hours, and those in contact with patients had a higher risk of COVID-19.

Pregnancy

Research on pregnant COVID-19 patients in China,**[59]** indicates pregnant women are also susceptible to SARS-CoV-2. However, no evidence of vertical transmission was reported. Many other studies **[59-61]** globally have also not reported clinical or serologic evidence suggestive of vertical transmission of SARS-CoV-2. In a study **[15]** conducted on COVID 19 positive women in their third trimester, there was no evidence that there is a transmission from mother to child.

Personal habits

Smoking has been reported as a susceptible factor by Jia et al[62] and in a report by the National Health Commission.**[56]**

Agent factors

Virulence

Virulence is the proportion of clinical cases resulting in severe clinical manifestations and resulting sequelae. CFR is one way of measuring virulence. Overall CFR was 6.9 % according to the WHO situation report as of April 28, 2020.**[8]**

Viral load

The mean viral load of severe cases was around 60 times higher than that of mild cases, suggesting that higher viral loads might be associated with severe clinical outcomes. Patients with severe COVID-19 tend to have a high viral load and a long virus-shedding period. This suggests that the viral load of SARS-CoV-2 might be a useful marker for assessing disease severity and prognosis.**[63]**

Nutrient agents

Obesity, caused due to lack of intake of a balanced diet has been reported as a susceptible factor by Jia et al **[62]** and in a report by the National Health Commission.**[56]**

Environmental Factors

Comorbidity

Comorbidities were present in nearly 50 % of patients, with hypertension being the most common comorbidity **[36]**, followed by diabetes **[51]**, coronary heart disease. **[22,47]** and cerebrovascular disease.**[46]** A meta-analysis by Yang et al,**[64]** also reported that the most prevalent comorbidities were hypertension, diabetes mellitus, cardiovascular diseases, and respiratory diseases. Yang's study **[64]** also reported that these comorbidities were more likely detected in severe patients. Another meta-analysis by Emami et al,**[65]** showed that hypertension, cardiovascular diseases, diabetes mellitus, smoking, chronic obstructive pulmonary disease, malignancy, and chronic kidney disease were the most frequently detected underlying diseases among hospitalized patients. Data from China **[50]** have indicated that particularly those with serious underlying health conditions, are at higher risk for severe COVID-19–associated illness and death. Similar results were reported by Guan et al,**[33]** Guo et al,**[43]** Chen et al **[52]**, and Jia et al. **[62]** Similarly, in a recent report,**[44]** 25 % and 58.3 % of patients who were critically ill with COVID-19 had underlying heart diseases and hypertension, respectively.

Confined location

Evidence indicating that COVID-19 transmission is facilitated in confined settings was reported by Mizumoto et al **[66,67]** in a cruise ship in Japan where a large cluster of confirmed cases was reported. This finding indicates the high transmissibility of COVID-19 in enclosed spaces.

Climate

American studies **[5,6]** have reported that epidemics occur duringthe winter and early spring, with the peak period varying by several months. A study in the United Kingdom **[68]** reported that HCV infection in adults occurred throughout the year with major peaks of infection during the summer and winter. Similar results were reported in a study by Isaac et al. **[5]**

Scientists report that the new coronavirus is most likely to become a seasonal respiratory disease based on its current infectivity and lethality. It has been reported by McGraw, a professor of infectious diseases at Penn State University, that COVID-19 is more seasonal. It becomes more active in winter and spreads faster in cold and dry air. The virus has basically zero infectivity during summer as it cannot usually withstand high temperatures. Contrarily, disease expert Amesh Adalja disagrees with McGraw, arguing that the evidence suggests it is not seasonal.[39] Hence, there is a need for further research in this perspective.

Geographic variations

Studies have reported that in remote, mountainous, rural, or hard-to- reach areas, the spread of COVID -19 has been restricted or slowed down. Studies have also reported that the outbreaks occurred faster (hotspots) in developed populated cities at the high end of economic, medical, and cultural development.**[37]**

Secondary infections

Cyclic patterns of recurrence in 2 to 3 years were reported by American studies **[5,6]** in infections caused by HCV 229E and HCV OC43. Re-infections with HCVs were common. Furthermore, we found HCVs in secretions taken from consecutive acute infections more than 3 months apart. WHO in a recent report has stated that there is no evidence that coronavirus patients are immune to secondary infections. **[8]**

Challenges for control of COVID 19

COVID-19 outbreak poses challenges for curtailing global spread and maintaining global health. Implementation of collective infection control measures has been useful. However, these measures should be executed in a sagacious manner while considering their cost- efficiency. It is required to continue the collective infection control measures though there may be a prolongation of the epidemic period. Public health perspectives to control the pandemic

The first pillar for interventions is to preserve the healthcare system by protecting health care workers and preventing hospital outbreaks. There is a growing need for providing advice on the proper management of COVID-19 patients so that they receive the most appropriate treatment and avoid overtreatment. The trust

between people and institutions must be maintained by respecting temporary individual restrictive measures. Any antagonism between countries and their governments must be carefully avoided.**[31]**

Because the risk for death from COVID-19 is probably associated with hampering the healthcare system, especially with the lack of appropriate drug interventions or vaccines, enhanced public health interventions like social distancing measures, quarantine, effective infection control in healthcare settings, improved hygienic measures in the general population and an increase in healthcare system capacity, should be implemented to rapidly contain the pandemic.

Prevention

Prevention is better than cure! With the limited awareness of curative treatment, the best practice to reduce the impact of COVID-19 is prevention. Contact transmission is one of the main routes of the SARS-CoV-2. Hand hygiene through hand washing is considered the most important prevention measure for healthcare-associated infections, as it significantly reduces the residual viruses. Several types of research have highlighted the importance of hand hygiene after contacting or caring for COVID-19 patients. **[69,70]** While the majority of transmission has occurred in community settings, super- spreading events in healthcare settings have already been described.**[71]** Various bodies including the WHO and US CDC are issuing continued advice and education on preventing the further spread of COVID-19.

Conclusion

The pandemic potential of COVID 19 is still spreading. Hence regular updates on the disease pathogenicity, transmissibility, risk factors, and treatment modalities must be precisely monitored.

The rapidly evolving nature of the COVID-2019 pandemic, altering statistics, and constant results of new research findings represent a major limitation to the present review.

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