Jaslok Hospital & Research Centre, Mumbai

Research eBulletin

Vol 5. Special Edition on 2019-nCoV. February 2020

Department of Medical Research
Jaslok Hospital & Research Centre, 15 Dr. G Deshmukh Marg, Mumbai 400026

Index

Web link: https://www.jaslokhospital.net/education-and-research/research-paper

Email: sac@jaslokhospital.net

Editorial

The Corona Virus Edition

The human toll of 2019-nCov has exceeded that of its predecessor which caused the Severe Acute Respratory Syndrome (SARS). We have collated a special issue with abstracts of some recent publications and have provided links to the original articles.

The influenza pandemic which occured a hundred years ago affected approximately 500 million people out of the then world population of 1.8 billion. Of these, between 50-100 million people died. The survivors had a considerabley higher risk of many illnesses such as Parkinson's Disease and Obssessive Compulsive Disorder. My interest in Neuropsychiatry stemmed from my exposure as a medical student in the late 70's to a patient who had treatment refractory Obssessive Compulsive Disorder with a history of childhood exposure to that pandemic.

The current pandemic is caused by the virus that shares its genetic structure with the ones that caused SARS and the Middle Eastern Respiratory Syndrome (MERS), wheras the virus that caused the influenza epidemic was H1N1. There is considerable uncertainty as to whether the spread of the current pandemic will be closer to that of SARS or that of the influenza pandemic. While we may be better prepared than we were a hundred years ago, much depends on the virulence of 2019-nCoV, its potential mutations and our ability to contain the spread. Besides the movement of humans across the world is much faster than it was earlier. Meanwhile, the secrecy of the Chinese government which witheld all information for three weeks during the onset and continues to be reticent is of concern.

Rajesh M. Parikh, M.D., D.P.M., D.N.B

Director, Medical Research

Abstracts

Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study

Joseph T Wu, Kathy Leung, Gabriel M Leung

The Lancet, January 31, 2020

https://www.thelancet.com/lancet/article/nowcasting-and-forecasting

BACKGROUND: Since Dec 31, 2019, the Chinese city of Wuhan has reported an outbreak of atypical pneumonia caused by the 2019 novel coronavirus (2019-nCoV). Cases have been exported to other Chinese cities, as well as internationally, threatening to trigger a global outbreak. Here, we provide an estimate of the size of the epidemic in Wuhan on the basis of the number of cases exported from Wuhan to cities outside mainland China and forecast the extent of the domestic and global public health risks of epidemics, accounting for social and non-pharmaceutical prevention interventions. **METHODS**: We used data from Dec 31, 2019, to Jan 28, 2020, on the number of cases exported from Wuhan internationally (known days of symptom onset from Dec 25, 2019, to Jan 19, 2020) to infer the number of infections in Wuhan from Dec 1, 2019, to Jan 25, 2020. Cases exported domestically were then estimated. We forecasted the national and global spread of 2019-nCoV, accounting for the effect of the metropolitan-wide quarantine of Wuhan and surrounding cities, which began Jan 23–24, 2020. We used data on monthly flight bookings from the Official Aviation Guide and data on human mobility across more than 300 prefecture-level cities in mainland China from the Tencent database. Data on confirmed cases were obtained from the reports published by the Chinese Center for Disease Control and Prevention. Serial interval estimates were based on previous studies of severe acute respiratory syndrome coronavirus (SARS-CoV). A susceptible-exposed-infectious-recovered metapopulation model was used to simulate the epidemics across all major cities in China. The basic reproductive number was estimated using Markov Chain Monte Carlo methods and presented using the resulting posterior mean and 95% credible interval. **FINDINGS**: In our baseline scenario, we estimated that the basic reproductive number for 2019-nCoV was 2·68 (95% CrI 2·47–2·86) and that 75 815 individuals (95% CrI 37 304–130 330) have been infected in Wuhan as of Jan 25, 2020. The epidemic doubling time was 6·4 days (95% CrI 5·8–7·1). We estimated that in the baseline scenario, Chongqing, Beijing, Shanghai, Guangzhou, and Shenzhen had imported 461 (95% CrI 227–805), 113 (57–193), 98 (49–168), 111 (56–191), and 80 (40–139) infections from Wuhan, respectively. If the transmissibility of 2019-nCoV were similar everywhere domestically and over time, we inferred that epidemics are already growing exponentially in multiple major cities of China with a lag time behind the Wuhan outbreak of about 1–2 weeks. **INTERPRETATION:** Given that 2019-nCoV is no longer contained within Wuhan, other major Chinese cities are probably sustaining localised outbreaks. Large cities overseas with close transport links to China could also become outbreak epicentres, unless substantial public health interventions at both the population and personal levels are implemented immediately. Independent self-sustaining outbreaks in major cities globally could become inevitable because of substantial exportation of pre-symptomatic cases and in the absence of large-scale public health interventions.

Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event

D. Paraskevis, E.G. Kostaki, G. Magiorkinis, G. Panayiotakopoulos, G. Sourvinos

Infection, Genetics and Evolution : Journal of molecular epidemiology and evolutionary genetics in infectious diseases 2020 Jan 29;79:104212.
https://www.ncbi.nlm.nih.gov/pubmed/32004758

BACKGROUND: A novel coronavirus (2019-nCoV) associated with human to human transmission and severe human infection has been recently reported from the city of Wuhan in China. Our objectives were to characterize the genetic relationships of the 2019-nCoV and to search for putative recombination within the subgenus of sarbecovirus.
METHODS: Putative recombination was investigated by RDP4 and Simplot v3.5.1 and discordant phylogenetic clustering in individual genomic fragments was confirmed by phylogenetic analysis using maximum likelihood and Bayesian methods.
RESULT: Our analysis suggests that the 2019-nCoV although closely related to BatCoV RaTG13 sequence throughout the genome (sequence similarity 96.3%), shows discordant clustering with the Bat_SARS-like coronavirus sequences. Specifically, in the 5′-part spanning the first 11,498 nucleotides and the last 3′-part spanning 24,341–30,696 positions, 2019-nCoV and RaTG13 formed a single cluster with Bat_SARS-like coronavirus sequences, whereas in the middle region spanning the 3′-end of ORF1a, the ORF1b and almost half of the spike regions, 2019-nCoV and RaTG13 grouped in a separate distant lineage within the sarbecovirus branch.
CONCLUSIONS: The levels of genetic similarity between the 2019-nCoV and RaTG13 suggest that the latter does not provide the exact variant that caused the outbreak in humans, but the hypothesis that 2019-nCoV has originated from bats is very likely. We show evidence that the novel coronavirus (2019-nCov) is not mosaic consisting in almost half of its genome of a distinct lineage within the betacoronavirus. These genomic features and their association with virus characteristics and virulence in humans need further attention.

The Novel Coronavirus Originating in Wuhan, China: Challenges for Global Health Governance

Alexandra L. Phelan, SJD, LLM, Rebecca Katz, PhD, MPH, Lawrence O. Gostin, JD

JAMA. Published online January 30, 2020.
https://jamanetwork.com/journals/jama/fullarticle/2760500

On December 31, 2019, China reported to the World Health Organization (WHO) cases of pneumonia in Wuhan, Hubei Province, China, caused by a novel coronavirus, currently designated 2019-nCoV. Mounting cases and deaths pose major public health and governance challenges. China's imposition of an unprecedented cordon sanitaire (a guarded area preventing anyone from leaving) in Hubei Province has also sparked controversy concerning its implementation and effectiveness. Cases have now spread to at least 4 continents. As of January 28, there are more than 4500 confirmed cases (98% in China) and more than 100 deaths.

Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

Chaolin Huang, Yeming Wang, Xingwang Li, Lili Ren, Jianping Zhao, Yi Hu, Li Zhang, Guohui Fan, Jiuyang Xu, Xiaoying Gu, Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, Jungang Xie,

The Lancet, January 24, 2020

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext

BACKGROUND:

A recent cluster of pneumonia cases in Wuhan, China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV). We report the epidemiological, clinical, laboratory, and radiological characteristics and treatment and clinical outcomes of these patients.

METHODS:

All patients with suspected 2019-nCoV were admitted to a designated hospital in Wuhan. We prospectively collected and analysed data on patients with laboratory-confirmed 2019-nCoV infection by real-time RT-PCR and next-generation sequencing. Data were obtained with standardised data collection forms shared by WHO and the International Severe Acute Respiratory and Emerging Infection Consortium from electronic medical records. Researchers also directly communicated with patients or their families to ascertain epidemiological and symptom data. Outcomes were also compared between patients who had been admitted to the intensive care unit (ICU) and those who had not.

FINDINGS:

By Jan 2, 2020, 41 admitted hospital patients had been identified as having laboratory-confirmed 2019-nCoV infection. Most of the infected patients were men (30 [73%] of 41); less than half had underlying diseases (13 [32%]), including diabetes (eight [20%]), hypertension (six [15%]), and cardiovascular disease (six [15%]). Median age was 49·0 years (IQR 41·0–58·0). 27 (66%) of 41 patients had been exposed to Huanan seafood market. One family cluster was found. Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median time from illness onset to dyspnoea 8·0 days [IQR 5·0–13·0]). 26 (63%) of 41 patients had lymphopenia. All 41 patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (12 [29%]), RNAaemia (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients were admitted to an ICU and six (15%) died. Compared with non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα.

INTERPRETATION:

The 2019-nCoV infection caused clusters of severe respiratory illness similar to severe acute respiratory syndrome coronavirus and was associated with ICU admission and high mortality.

Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding

Roujian Lu, Xiang Zhao, Juan Li, Peihua Niu, Bo Yang, Honglong Wu, Wenling Wang, Hao Song, Baoying Huang, Na Zhu, Yuhai Bi,*

The Lancet, January 29, 2020
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30251-8/fulltext

BACKGROUND: In late December, 2019, patients presenting with viral pneumonia due to an unidentified microbial agent were reported in Wuhan, China. A novel coronavirus was subsequently identified as the causative pathogen, provisionally named 2019 novel coronavirus (2019-nCoV). As of Jan 26, 2020, more than 2000 cases of 2019-nCoV infection have been confirmed, most of which involved people living in or visiting Wuhan, and human-to-human transmission has been confirmed.

METHODS: We did next-generation sequencing of samples from bronchoalveolar lavage fluid and cultured isolates from nine inpatients, eight of whom had visited the Huanan seafood market in Wuhan. Complete and partial 2019-nCoVgenome sequences were obtained from these individuals. Viral contigs were connected using Sanger sequencing to obtain the full-length genomes, with the terminal regions determined by rapid amplification of cDNA ends. Phylogenetic analysis of these 2019-nCoV genomes and those of other coronaviruses was used to determine the evolutionary history of the virus and help infer its likely origin. Homology modelling was done to explore the likely receptor-binding properties of the virus.

FINDINGS: The ten genome sequences of 2019-nCoV obtained from the nine patients were extremely similar, exhibiting more than 99·98% sequence identity. Notably, 2019-nCoV was closely related (with 88% identity) to two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, collected in 2018 in Zhoushan, eastern China, but were more distant from SARS-CoV (about 79%) and MERS-CoV (about 50%).Phylogenetic analysis revealed that 2019-nCoV fell within the subgenus Sarbecovirus of the genus Betacoronavirus, with a relatively long branch length to its closest relatives bat-SL-CoVZC45 and bat-SLCoVZXC21, and was genetically distinct from SARS-CoV. Notably, homology modelling revealed that 2019-nCoV had a similar receptor-binding domain structure to that of SARS-CoV, despite amino acid variation at some key residues.

INTERPRETATION: 2019-nCoV is sufficiently divergent from SARS-CoV to be considered a new human-infecting betacoronavirus. Although our phylogenetic analysis suggests that bats might be the original host of this virus, an animal sold at the seafood market in Wuhan might represent an intermediate host facilitating the emergence of the virus in humans. Importantly, structural analysis suggests that 2019-nCoV might be able to bind to the angiotensin converting enzyme 2 receptor in humans. The future evolution, adaptation, and spread of this virus warrant urgent investigation.

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.

Wang, Ying Liu, Yuan Wei, Jia'an Xia, Ting Yu, Xinxin Zhang, Li Zhang

The Lancet, January 30, 2020

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30211-7/fulltext

BACKGROUND:

In December, 2019, a pneumonia associated with the 2019 novel coronavirus (2019-nCoV) emerged in Wuhan, China. We aimed to further clarify the epidemiological and clinical characteristics of 2019-nCoV pneumonia.

METHODS:

In this retrospective, single-centre study, we included all confirmed cases of 2019-nCoV in Wuhan Jinyintan Hospital from Jan 1 to Jan 20, 2020. Cases were confirmed by real-time RT-PCR and were analysed for epidemiological, demographic, clinical, and radiological features and laboratory data. Outcomes were followed up until

FINDINGS:

Of the 99 patients with 2019-nCoV pneumonia, 49 (49%) had a history of exposure to the Huanan seafood market. The average age of the patients was 55·5 years (SD 13·1), including 67 men and 32 women. 2019-nCoV was detected in all patients by real-time RT-PCR. 50 (51%) patients had chronic diseases. Patients had clinical manifestations of fever (82 [83%] patients), cough (81 [82%] patients), shortness of breath (31 [31%] patients), muscle ache (11 [11%] patients), confusion (nine [9%] patients), headache (eight [8%] patients), sore throat (five [5%] patients), rhinorrhoea (four [4%] patients), chest pain (two [2%] patients), diarrhoea (two [2%] patients), and nausea and vomiting (one [1%] patient). According to imaging examination, 74 (75%) patients showed bilateral pneumonia, 14 (14%) patients showed multiple mottling and ground-glass opacity, and one (1%) patient had pneumothorax. 17 (17%) patients developed acute respiratory distress syndrome and, among them, 11 (11%) patients worsened in a short period of time and died of multiple organ failure.

INTERPRETATION:

The 2019-nCoV infection was of clustering onset, is more likely to affect older males with comorbidities, and can result in severe and even fatal respiratory diseases such as acute respiratory distress syndrome. In general, characteristics of patients who died were in line with the MuLBSTA score, an early warning model for predicting mortality in viral pneumonia. Further investigation is needed to explore the applicability of the MuLBSTA score in predicting the risk of mortality in 2019-nCoV infection.