COVID-19: A GLOBAL HEALTH EMERGENCY
(An Outbreak)

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ABSTRACT

COVID-19 is a global health emergency and this study includes almost everything which a person should know regarding the pandemic. In this paper different models of China, South Korea and also USA has been discussed as how these countries tried to combat this disease. The speculated mortality is 0.7% due to undiagnosed cases and various co-morbidities play a vital role in the mortality due to novel Corona Virus-19. Some of the medicine regimens are being in trials for the treatment purpose and vaccines are also under trials while public health measures and symptomatic treatment is being the most effective route to fight this invisible enemy yet. In this I have tried to explain about novel Corona Virus Disease with complete A to Z understanding and various public health measures and myths are also explained.

Introduction:

The name "coronavirus" is derived from Latin corona, meaning "crown" or "wreath", itself a borrowing from Greek κορώνη korṓnē, "garland, wreath". The name was first used in 1968 by an informal group of virologists in the journal Nature to designate the new family of viruses. The name refers to the characteristic appearance of virions (the infective form of the virus) by electron microscopy, which have a fringe of large, bulbous surface projections creating an image reminiscent of a crown or of a solar corona. This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus.

Corona Viruses are a large family of viruses which are common in people and many different species of animals including cats and bats. Commonly Human Corona Virus (HCoV) causes Upper Respiratory Tract Infections like the common cold. Most people get infected with one or more of these viruses at some point in their lives. Human CoV generally resolves on its own with basic rest and fluids intake. Rarely the CoVs which infect the animals can involve humans and become new HCoV which then infects and spreads between humans.

EVOLUTION:

The most recent common ancestor (MRCA) of all coronaviruses is estimated to have existed as recently as 8000 BCE, although some models place the common ancestor as far back as 55 million years or more, implying long term coevolution with bat and avian species. The most recent common ancestor of the alpha coronavirus line has been placed at about 2400 BCE, the betacoronavirus line at 3300 BCE, the gamma coronavirus line at 2800 BCE, and the delta coronavirus line at about 3000 BCE. Bats and birds, as warm-blooded flying vertebrates, are an ideal natural reservoir for the coronavirus gene pool (bats the reservoir for alpha coronavirus and beta coronavirus – and birds the reservoir for gamma coronavirus and delta coronavirus). The large number of host bat and avian species, and their global range, has enabled extensive evolution and dissemination of coronaviruses.
Discovery:

Coronaviruses were first discovered in the 1930s when an acute respiratory infection of domesticated chickens was shown to be caused by infectious bronchitis virus (IBV). In the 1940s, two more animal coronaviruses, mouse hepatitis virus (MHV) and transmissible gastroenteritis virus (TGEV), were isolated. Human coronaviruses were discovered in the 1960s. The earliest ones studied were from human patients with the common cold, which were later named human coronavirus 229E and human coronavirus OC43. Other human coronaviruses have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2004, HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 in 2019. Most of these have involved serious respiratory tract infections.

Genome:

Coronaviruses contain a positive-sense, single-stranded RNA genome. The genome size for coronaviruses ranges from 26.4 to 31.7 kilobases. The genome size is one of the largest among RNA viruses. The genome has a 5’ methylated cap and a 3’ polyadenylated tail. The genome organization for a coronavirus is 5’-leader-UTR-replicase/transcriptase-spike (S)-envelope (E)-membrane (M)-nucleocapsid (N)-3’UTR-poly (A) tail. The open reading frames 1a and 1b, which occupy the first two-thirds of the genome, encode the replicase/transcriptase polyprotein. The replicase/transcriptase polyprotein self cleaves to form nonstructural proteins.
Structure:

Coronaviruses are large pleomorphic spherical particles with bulbous surface projections. The average diameter of the virus particles is around 120 nm (.12 μm). The diameter of the envelope is ~80 nm (.08 μm) and the spikes are ~20 nm (.02 μm) long. The envelope of the virus in electron micrographs appears as a distinct pair of electron dense shells.

The viral envelope consists of a lipid bilayer where the membrane (M), envelope (E) and spike (S) structural proteins are anchored. A subset of coronaviruses (specifically the members of beta coronavirus subgroup A) also have a shorter spike-like surface protein called hemagglutinin esterase (HE).

Inside the envelope, there is the nucleocapsid, which is formed from multiple copies of the nucleocapsid (N) protein, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation. The lipid bilayer envelope, membrane proteins, and nucleo-capsid protect the virus when it is outside the host cell.

The spike protein of the novel coronavirus shares 98% sequence identity with the spike protein of the bat coronavirus, the researchers say.

Four families of Corona Viruses:

1. Alpha family
2. Beta family
3. Gamma family
4. Delta family

Most important types of CoV:

1. SARS (2003)- Severe Acute Respiratory Syndrome
2. MERS (2012)- Middle East Respiratory Syndrome
3. novel CoV-19- SARS CoV2/COVID-19

All of the above mentioned types belong to beta family.

History of COVID-19:

In December 2019 in Wuhan, Hubei province of China noted unusual cases of Pneumonia in the hospitals. These patients were most notably presented with the symptoms like:

- dry cough
- dyspnea
- fever
- B/L lung infiltrates in imaging
On 31st Dec 2019: cases of COVID-19 were reported to WHO Office in China. Most of the cases were searched as originated from Sea Food Market/ Vet Market of Wuhan city. In this market there were a large no. of varieties of vertebrates and invertebrates.

On 1st Jan 2020: Sea Food Market Wuhan was identified as origin and was closed.

On 7th Jan 2020: Chinese scientists identified the pathogen as novel CoV.

On 11th Jan 2020: China recorded its first death due to COVID-19.

On 12th Jan 2020: China shared the genetic sequence of virus with the world.

On 13th Jan 2020: first case was detected outside China, in Thailand.

On 20th Jan 2020: first USA case was reported.

On 24th Jan 2020: first 3 cases in Europe were reported.

By the end of January 2020: it was thought to be originated from bats and similar to SARS (2003) hence was named as SARS CoV2.

On 30th Jan 2020: WHO declares SARS CoV2 as a global public health emergency.

On 2nd Feb 2020: first death was reported in Philippines.

On 11th Feb 2020: WHO names the disease caused by SARS CoV2 as COVID-19.

On 15th Feb 2020: first death was reported in Europe in France.

On 19th Feb 2020: outbreak occurred in Iran.

On 11th Mar 2020: COVID-19 was declared as global pandemic.

On 20th Mar 2020: Italy surpasses the China with highest death toll.

On 24th Mar 2020: Japan’s PM postponed Japan Olympics to 2021.

On 26th Mar 2020: total no. of cases exceeded >500000 globally.

On 29th Mar 2020: US has the highest no. of cases followed by Italy and Spain.

On 2nd Apr 2020: cases surpasses > 10,00,000 globally.

On 6th Apr 2020: cases > 13,00,000 and deaths > 70,000 globally.

INCUBATION PERIOD : 2-14 days

PATHOPHYSIOLOGY : Virus targets and infects the Respiratory system and is transmitted by:

- Contact
- Droplets
- Fomites
of an infected person whether symptomatic or asymptomatic.

During the incubation period virus slowly triggers the air response within the lungs. The lungs contain sacs of alveoli where gases exchange takes place Oxygen in and Carbon dioxide out. Alveoli made up of alveolar cells.

Alveolar cells produce surfactant which coats the inner lining of alveoli which helps keep the alveoli open allowing O2 –CO2 exchange. SARS-CoV2 mainly invades alveolar epithelial cells resulting in respiratory symptoms. Virus targets and binds on ACE 2 – a receptor as well as an enzyme on the surface of type -2 alveolar cells. ACE 2 is needed by the virus to gain entry into the cell.

CoV enter via endocytosis or direct fusion with the host membrane, once inside the cell virus particle is uncoated and its genome enters the cell cytoplasm.

CoVs have + ss RNA genome. They can directly produce their protein and new genome in the cytoplasm by attaching to the host’s ribosomes. The host’s ribosome will translate the viral RNA to make proteins that will make RNA polymerase which will read +ss RNA again to make a – ss RNA strand. This – ve strand will be used by RNA polymerase again to produce a +ss RNA strand as well as other small +ve RNA strands. These small RNA strands will be again read by the host’s ribosomes in the Endoplasmic Reticulum to help make structural components of the virus. ER will transfer these exessory and structural components in the Golgi Apparatus where it will be nicely packaged up with the +ve RNA strands formed, to form an essential new virus. These progeny viruses are then released from the host’s cells by exocytosis through secretory vesicles. While the viruses are self-replicating in the alveolar cells they also damage alveolar cells. This will initiate the inflammatory response. Injured alveolar cells release the:-

- Interferons - protection against viruses
- Cytokines
- DAMPs

Alveolar macrophages detect cell injury via Damage Associated Molecular Pathogens (DAMPs) from the alveolar cells. They also respond to the cytokines released in the injured alveolar cells. This initiates the alveolar macrophages themselves to secrete the cytokines:-

- TNF-alpha
- IL 1
- IL8
- IL6
- CHEMOKINES

The inflammatory process occurring with the lung parenchyma stimulates nerve endings responsible for initiating the dry cough reflex so people often present the dry cough early on.

TNF-a and IL1-b are pro-inflammatory cytokines, they increase vascular permeability and increase in expression of adhesion molecule. This allows recruitment of more immune cells for ex. Neutrophils, Monocytes in circulation. They will bind to adhesion molecule and enter the site of injury. IL8 will recruit neutrophils. Chemokines will attract monocytes. Increased vascular permeability will lead to leak of fluids in interstitium causing interstitial edema and then into the alveoli causing pulmonary edema which will cause:-
- Dyspnea
- Impaired oxygenation (hypoxemia), low oxygen levels in blood.

Increase in circulating macrophages and neutrophils means increased WBC in serum.

Neutrophils engulf the virus and releases toxic byproduct. Toxins and cytokines damages alveolar cells all over and thus less surfactant being produced resulting in alveolar collapse which causes impaired oxygenation leading to hypoxemia.

WBC can damage endothelial cells to release other inflammatory mediators like Arachidonic acid metabolites including leukotrienes and prostaglandins.

Leukotrienes cause bronchoconstriction impairing ventilation leading to hypoxemia. Prostaglandins, TNFa, IL1, IL6 cause fever which is a prominent feature in COVID-19.

Decreased O2 levels in blood will stimulate chemoreceptors in aortic arch as well as in brain. Stimulated chemoreceptors will then stimulate cardio pulmonary synthase in the brain to tell the lungs to breathe more in order to increase the O2 levels in blood and also tells the heart to pump faster to deliver oxygen to the body so patients with hypoxemia have:-

- Tachypnoea
- Tachycardia

In viral infections including covid-19 there is Lymphopenia which is due to release of interferons which are released due to the response of viral infections.

IL6 is potent inflammatory Cytokine:-

It stimulates hepatocytes to produce acute phase reactants including:-

- CRP a marker of inflammation measured in blood.
- Fibrinogen
- Hepcidin

SUMMARY:

- Injured Lung
- Ventilation perfusion mismatch
- Accumulation of fluid
- Hypoxemia

all of the above are not related to Heart functions and is referred to as Acute Respiratory Distress Syndrome(ARDS) – a leading cause of mortality.
Varrying Degrees of Severity of COVID-19:

Critical Disease can be called as life-threatening which can lead to:

- Respiratory Failure
- Shock
- MODS (i.e. deranged LFTs, leakage of Troponin)
- Cytokine Release Syndrome
WHAT IS REPRODUCTIVE NO.? (R0)?

R0 is the no. which one infected person will infect to other person/persons on average.

Higher the Reproductive no. (R0) more contagious the disease is.

- R0 for COVID-19 = 2.2
- R0 for Influenza = 3
- R0 for Small Pox = 6
- R0 for Measles = 9-18

Impact of R0 on No. of Infected cases:

When R0 < 1 then infection will come down.

When R0 = 1 then infection will be steady.

When R0 > 1 then infection will spread.
MORTALITY RATE (%) of COVID-19:

Mortality Rate = (number of deaths / number of cases) = probability of dying if infected by the virus (%). (by 15 April 2020)

Mortality rate of COVID-19 varies between countries:

- Globally = 6.42%
- USA = 4.42%
- Italy = 13.10%
- Spain = 10.45%
- France = 11.61%
- Germany = 2.69%
- India = 3.28%
Mortality rate of different Viruses:

1. SARS (2003) - 9.5% (>8000 cases)
2. MERS (2012) - 35% (>2500 cases)
3. Influenza Virus - <0.2% (millions of cases)
4. nCoV-19 - 6.42% (>1.9 million cases)

Actual Mortality rate speculated is 0.7% due to the undiagnosed cases.
## Total Deaths of Novel Coronavirus (2019-nCoV):

<table>
<thead>
<tr>
<th>Date</th>
<th>Total Deaths</th>
<th>Change in Total</th>
<th>Change in Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apr. 14</td>
<td>126,601</td>
<td>6,983</td>
<td>6%</td>
</tr>
<tr>
<td>Apr. 13</td>
<td>119,618</td>
<td>5,421</td>
<td>5%</td>
</tr>
<tr>
<td>Apr. 12</td>
<td>114,197</td>
<td>5,417</td>
<td>5%</td>
</tr>
<tr>
<td>Apr. 11</td>
<td>108,780</td>
<td>6,092</td>
<td>6%</td>
</tr>
<tr>
<td>Apr. 10</td>
<td>102,688</td>
<td>6,974</td>
<td>7%</td>
</tr>
<tr>
<td>Apr. 9</td>
<td>95,714</td>
<td>7,234</td>
<td>8%</td>
</tr>
<tr>
<td>Apr. 8</td>
<td>88,480</td>
<td>6,417</td>
<td>8%</td>
</tr>
<tr>
<td>Apr. 7</td>
<td>82,063</td>
<td>7,385</td>
<td>10%</td>
</tr>
<tr>
<td>Apr. 6</td>
<td>74,678</td>
<td>5,231</td>
<td>8%</td>
</tr>
<tr>
<td>Apr. 5</td>
<td>69,447</td>
<td>4,739</td>
<td>7%</td>
</tr>
<tr>
<td>Apr. 4</td>
<td>64,708</td>
<td>5,799</td>
<td>10%</td>
</tr>
<tr>
<td>Apr. 3</td>
<td>58,909</td>
<td>5,720</td>
<td>11%</td>
</tr>
<tr>
<td>Apr. 2</td>
<td>53,189</td>
<td>5,979</td>
<td>13%</td>
</tr>
<tr>
<td>Apr. 1</td>
<td>47,210</td>
<td>4,890</td>
<td>12%</td>
</tr>
</tbody>
</table>
Correlation between Susceptibility/Fatality rate and risk factors i.e. Age/Sex/Comorbid conditions/Healthy Pregnant females/Blood Groups (ABO)/BCG Vaccination in COVID-19:

**COVID-19 Fatality Rate by AGE:**

<table>
<thead>
<tr>
<th>AGE</th>
<th>DEATH RATE confirmed cases</th>
<th>DEATH RATE all cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>80+ years old</td>
<td>21.9%</td>
<td>14.8%</td>
</tr>
<tr>
<td>70-79 years old</td>
<td></td>
<td>8.0%</td>
</tr>
<tr>
<td>60-69 years old</td>
<td></td>
<td>3.6%</td>
</tr>
<tr>
<td>50-59 years old</td>
<td></td>
<td>1.3%</td>
</tr>
<tr>
<td>40-49 years old</td>
<td></td>
<td>0.4%</td>
</tr>
<tr>
<td>30-39 years old</td>
<td></td>
<td>0.2%</td>
</tr>
<tr>
<td>20-29 years old</td>
<td></td>
<td>0.2%</td>
</tr>
<tr>
<td>10-19 years old</td>
<td></td>
<td>0.2%</td>
</tr>
<tr>
<td>0-9 years old</td>
<td></td>
<td>no fatalities</td>
</tr>
</tbody>
</table>

Pregnant females are not at high risk.
No intrauterine transmission of COVID-19 reported yet.
Virus not detected in breast milk.
COVID-19 Fatality Rate by SEX:

<table>
<thead>
<tr>
<th>SEX</th>
<th>DEATH RATE confirmed cases</th>
<th>DEATH RATE all cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4.7%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Female</td>
<td>2.8%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

COVID-19 Fatality Rate by COMORBIDITY:

<table>
<thead>
<tr>
<th>PRE-EXISTING CONDITION (COMORBIDITY)</th>
<th>DEATH RATE confirmed cases</th>
<th>DEATH RATE all cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>13.2%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9.2%</td>
<td>7.3%</td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
<td>8.0%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8.4%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Cancer</td>
<td>7.6%</td>
<td>5.6%</td>
</tr>
<tr>
<td>no pre-existing conditions</td>
<td>0.9%</td>
<td></td>
</tr>
</tbody>
</table>
ODDS RATIO of risk factors as per Chinese and South Korean cohort study:

Risk factors associated with mortality in subjects infected with Community Acquired Pneumonia (CAP) and COVID-19:

<table>
<thead>
<tr>
<th>Factor</th>
<th>CAP</th>
<th>COVID-19 Chinese Cohort</th>
<th>COVID-19 S Korea CDC Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥60†</td>
<td>5.2 (3.9 - 6.8)</td>
<td>9.9 (8.5 - 11.7)</td>
<td>30.7 (14.7 - 64)</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.7 (1.3 - 2.2)</td>
<td>1.7 (1.5 - 1.9)</td>
<td>2.0 (1.2 - 3.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-</td>
<td>3.3 (2.8 - 4.0)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.6 (1.9 - 3.5)</td>
<td>5.9 (4.6 - 7.5)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.1 (1.4 - 3.1)</td>
<td>3.5 (2.8 - 4.6)</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>1.5 (1.1 - 2.0)</td>
<td>2.8 (1.9 - 4.1)</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>3.2 (2.3 - 4.4)</td>
<td>2.4 (1.1 - 5.6)</td>
<td></td>
</tr>
</tbody>
</table>

In South Korea CDC Dataset, the odds ratio for death in age group ≥60 is 30.7 (95% CI, 14.7 – 64) and the odds ratio for death in male gender is 1.95 (95% CI, 1.23 – 3.07).
Role of Blood Groups in COVID-19:

A study reveals that people having A Blood Group are more susceptible to COVID-19 and people with Blood Group O are less susceptible to COVID-19.

Bacille Calmette-Guérin (BCG) vaccination and COVID-19:

BCG vaccination prevents severe forms of tuberculosis in children and diversion of local supplies may result in neonates not being vaccinated, resulting in an increase of disease and deaths from tuberculosis. There is experimental evidence from both animal and human studies that the BCG vaccine has non-specific effects on the immune system. These effects have not been well characterized and their clinical relevance is unknown. In the absence of evidence, WHO does not recommend BCG vaccination for the prevention of COVID-19. WHO continues to recommend neonatal BCG vaccination in countries or settings with a high incidence of tuberculosis.

There is no evidence that the Bacille Calmette-Guérin vaccine (BCG) protects people against infection with COVID-19 virus. Two clinical trials addressing this question are underway, and WHO will evaluate the evidence when it is available.

Country wise data of COVID-19 by 15th April 2020:

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Deaths</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>623,694</td>
<td>27,605</td>
<td>North America</td>
</tr>
<tr>
<td>Spain</td>
<td>177,633</td>
<td>18,579</td>
<td>Europe</td>
</tr>
<tr>
<td>Italy</td>
<td>165,155</td>
<td>21,645</td>
<td>Europe</td>
</tr>
<tr>
<td>France</td>
<td>147,863</td>
<td>17,167</td>
<td>Europe</td>
</tr>
<tr>
<td>Germany</td>
<td>133,209</td>
<td>3,592</td>
<td>Europe</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>98,476</td>
<td>12,868</td>
<td>Europe</td>
</tr>
<tr>
<td>China</td>
<td>82,295</td>
<td>3,342</td>
<td>Asia</td>
</tr>
<tr>
<td>Iran</td>
<td>76,389</td>
<td>4,777</td>
<td>Asia</td>
</tr>
<tr>
<td>Turkey</td>
<td>69,392</td>
<td>1,518</td>
<td>Asia</td>
</tr>
<tr>
<td>Belgium</td>
<td>33,573</td>
<td>4,440</td>
<td>Europe</td>
</tr>
<tr>
<td>Canada</td>
<td>28,205</td>
<td>1,006</td>
<td>North America</td>
</tr>
<tr>
<td>Netherlands</td>
<td>28,153</td>
<td>3,134</td>
<td>Europe</td>
</tr>
<tr>
<td>Country</td>
<td>Cases</td>
<td>Deaths</td>
<td>Region</td>
</tr>
<tr>
<td>--------------</td>
<td>---------</td>
<td>--------</td>
<td>----------</td>
</tr>
<tr>
<td>Switzerland</td>
<td>26,336</td>
<td>1,239</td>
<td>Europe</td>
</tr>
<tr>
<td>Brazil</td>
<td>26,113</td>
<td>1,590</td>
<td>South America</td>
</tr>
<tr>
<td>Portugal</td>
<td>18,091</td>
<td>599</td>
<td>Europe</td>
</tr>
<tr>
<td>Austria</td>
<td>14,335</td>
<td>393</td>
<td>Europe</td>
</tr>
<tr>
<td>Ireland</td>
<td>12,547</td>
<td>444</td>
<td>Europe</td>
</tr>
<tr>
<td>Israel</td>
<td>12,501</td>
<td>130</td>
<td>Asia</td>
</tr>
<tr>
<td>India</td>
<td>12,322</td>
<td>405</td>
<td>Asia</td>
</tr>
<tr>
<td>Sweden</td>
<td>11,927</td>
<td>1,203</td>
<td>Europe</td>
</tr>
<tr>
<td>South Korea</td>
<td>10,591</td>
<td>225</td>
<td>Asia</td>
</tr>
</tbody>
</table>

**SURVIVAL PERIOD (on surfaces):**

1. Aluminum and Latex   : upto 8 hours
2. Cardboard            : upto 24 hours
3. Plastics and Steel   : upto 72 hours
4. Wood and Glass       : upto 120 hours
5. Air Droplets         : upto 3 hours
CLINICAL FEATURES:

MEDIAN AGE GROUP: 49-56 years

SYMPTOMS:

- Fever
- Fatigue
- Dry cough
- Myalgia
- Dyspnea
- Anorexia
- Sputum production
- Loss of smell and taste

These symptoms may progress and people may develop Pneumonia leading to ARDS (ACUTE RESPIRATORY DISTRESS SYNDROME).

INVESTIGATION FINDINGS:

I. Lymphopenia
II. Leukocytosis
III. Deranged LFTs.
IV. Increased LDH levels
V. Increased CRP levels

CHEST X-RAYS are always important in suspected pneumonia which will show unilateral or bilateral infiltrates in lungs.

CT CHEST in patients most commonly demonstrates Ground glass opacification with or without consolidations.

Laboratory Values associated with mortality:

<table>
<thead>
<tr>
<th>Laboratory Value</th>
<th>Odds ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocyte count &lt;0.8 (x 10^9 / L)</td>
<td>8.8 (4.3 - 18.4)</td>
</tr>
<tr>
<td>Bilateral consolidations on imaging</td>
<td>1.98 (0.89 - 4.5)</td>
</tr>
<tr>
<td>Ground Glass Opacities on imaging</td>
<td>2.1 (0.99 - 4.7)</td>
</tr>
<tr>
<td>D-Dimer &gt; 1ug/L</td>
<td>14 (6.3 - 31)</td>
</tr>
<tr>
<td>Elevated C-Reactive Protein</td>
<td>10.5 (1.2 - 34.7)</td>
</tr>
<tr>
<td>LDH &gt; 245 u/L</td>
<td>45.4 (6.0 - 338)</td>
</tr>
</tbody>
</table>
DIAGNOSIS:

1. **RT-PCR:**
   Using real-time reverse transcription polymerase chain reaction (rRT-PCR) the test can be done on respiratory samples obtained by various methods, including a nasopharyngeal swab or sputum sample. Results are generally available within a few hours to 2 days. The RT-PCR test performed with throat swabs is only reliable in the first week of the disease. Later on the virus can disappear in the throat while it continues to multiply in the lungs. For infected people tested in the second week, alternatively sample material can then be taken from the deep airways by suction catheter or coughed up material (sputum) can be used.

2. **Isothermal amplification assays:**
   On 27 March 2020, the FDA approved an "automated assay" from Abbott Diagnostics that uses an isothermal nucleic acid amplification method. It detects viral RNA.

3. **Serology:**
   Most serology tests are in the research stage of development. As of 15 April, three tests had been approved for diagnosis in the United States, all under FDA Emergency Use Authorization (EUA). The tests are by Chembio Diagnostic System, Ortho Clinical Diagnostics and Cellex. All three tests must be performed in a laboratory. The tests by Cellex and Chembio are rapid diagnostic tests (RTD) that take 10–30 minutes to give results. The test by Ortho is a modified enzyme linked immunosorbent assay (ELISA) that takes 1–5 hours to give results. In China, the Cellex test had a specificity of 95.6% and a sensitivity of 93.8%.

4. **Medical imaging:**
   Chest CT scans may be helpful to diagnose COVID-19 in individuals with a high clinical suspicion of infection based on risk factors and symptoms but is not recommended for routine screening. Typical features on CT initially include bilateral multilobar ground-glass opacities with a peripheral, asymmetric and posterior distribution. Sub-pleural dominance, crazy paving, and consolidation may develop as the disease evolves.

5. **Look for other causes of symptoms:**
   - Flu Test
   - Respiratory Viral Panel

**COVID-19 Testing Trouble:**

- False Negative results
- 50-70% sensitivity
- can detect previous infections

**In case of Mild Infection (Home Care):**

- isolate at home.
- take rest.
- administer good amount of fluids.
In case of Severe Infections (Hospital Care):

- Oxygen
- IV fluids
- Ventilatory support
- Medications
- Supportive care

TREATMENT:

Based on evidence from laboratory, animal and clinical studies, the following medicational treatment options were selected:

- Remdesivir;
- Lopinavir/Ritonavir;
- Lopinavir/Ritonavir with Interferon beta-1a; and
- Chloroquine or Hydroxychloroquine
- HCQ + Azithromycin

Remdesivir was previously tested as an Ebola treatment. It has generated promising results in animal studies for Middle East Respiratory Syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS), which are also caused by coronaviruses, suggesting it may have some effect in patients with COVID-19.

Lopinavir/Ritonavir is a licensed treatment for HIV. Evidence for COVID-19, MERS and SARS is yet to show it can improve clinical outcomes or prevent infection. The trial aims to identify and confirm any benefit for COVID-19 patients. While there are indications from laboratory experiments that this combination may be effective against COVID-19, studies done so far in COVID-19 patients have been inconclusive.

Interferon beta-1a is used to treat multiple sclerosis.

Chloroquine and hydroxychloroquine are very closely related and used to treat malaria and rheumatology conditions respectively. In China and France, small studies provided some indications of possible benefit of chloroquine phosphate against pneumonia caused by COVID-19 but need confirmation through randomized trials.

All of the medications are being studied in fully randomized controlled clinical trials to see if they are safe and reliable treatment which can be used. On 22nd Mar 2020 WHO launched a megatrial globally to test these promising medications.

VACCINE:

are being developed across the globe and speculated to be available in 2021.

5 Vaccines are under Trials:

There are 115 vaccine candidates and 5 vaccines in Phase-I or II trials mentioned below:

1. MODERNA (Phase-I): Viral mRNA within a lipid nanoparticle enters cell.
2. CANSINO (Phase-II): AdenoVirus type-5 vector with viral DNA infects cells.
3. INOVIO (Phase-I): Viral DNA enters cell with Electrophoration.
4. SCHENZEN (Phase I and II): Immune cells extracted, Lenti Virus used to introduce viral genes, cells re-introduced.
5. SCHENZEN (Phase-I): Artificial immune cells with viral genes introduced.

Beating Coronavirus: Flattening the Curve, Raising the Line:

- Increasing the HEALTHCARE CAPACITY.
- Decreasing the total sick patients.
- Slowing the rate of new people getting sick.
CHINA STRATEGY (MODEL) TO COMBAT COVID-19:

1. **LOCKDOWN:**
   - 15 cities and 57 million people were affected.
   - People forced to live at home.

2. Everyone screened for symptoms.

3. Built multiple COVID Hospitals: to raise the line. An excellent example is the newly built Huoshenshan and Leishenshan Hospitals, which offer 2,600 beds in total. Containing the virus spread required additional facilities to handle the patient load and construction workers took just 10 days and 12 days respectively to build and equip both.

4. Flew in Doctors and Paramedical Staff from less affected areas and protected them from well-designed PPE from head to toe.

5. Used technology: Following the outbreak, Tencent, Alibaba and vertical online healthcare platforms like DXY began offering the public remote medical services. People consulted with online doctors, conducted self-assessments and decided whether to go to a hospital for further medical checks or remain at home. These simple screening tools reduced non-essential hospital visits and caregiver workloads while mitigating the risks of cross-infection.

Remote technology has enabled hospitals to share their best resources over great distances. Thanks to China’s 5G networks, many Wuhan hospitals, have been able to connect with counterparts in Beijing, allowing experts in the capital to provide real-time consultation based on ultra-high-definition images.

The industrial internet has empowered communities and people in the war against COVID-19. Through digital platforms, volunteer teams of residents within communities assist in disinfection and deliver supplies aided by digital community management and communication tools.

The advent of the “Health QR Code” lets users submit information regarding travel to major epidemic outbreak regions and details close contact with infected people and other relevant information. A three-color scale indicates the person’s recent virus-related health history, enabling them to cooperatively comply with virus-related prevention and control policies.

The involvement of Tencent, a Chinese internet technology company, in promoting the power of digital, is testament to the rise of the industrial internet in the fight against the virus. While the consumer internet provides services such as social networking and e-commerce to consumers who are self-isolating, its industrial counterpart, focusing primarily on business and industry, has worked to safeguard society’s normal operation, making a profound contribution which we will call the “ACE effect”.

By March:

- Economy began to return to normal.
- More cases of COVID-19 were from travellers.

SOUTH KOREAN MODEL TO COMBAT COVID-19:

1. Mass Testing: to flatten the curve. They offered:
   - Drive Through Testing Stations for testing while sitting in a car.
   - Phone Booth Testing Stations: person walks in, gets tested and walks out.
   - 15000 tests/day.
By March 20\textsuperscript{th} 2020: 317000 out of 51000000 people tested, (1/162 people).

2. Those who were tested positive were sent to Quarantine facility if mild symptoms and to hospitals in severe cases.

3. At the same time contact tracing was done by the Health Staff.

4. Lock Down: in South Korea lockdown was different from China:
   - South Korea did lockdown of sick individuals.
   - China did lockdown at Societal Level.

UNITED STATES MODEL OF COMBATTING COVID-19:

1. Testing(by 20\textsuperscript{th} Mar 2020):
   - 135000 people tested.
   - 1 out of 2424 people tested.
   - 15 times < than South Korea.

2. Partial Lock Down:
   - Only some states were lockdown with minimal enforcement.
   - Voluntary social distancing.
   - Business was running.

3. Raising the line(Health Care Measures):
   - Inadequate Personal Protection Equipments (PPEs).
   - Hundreds of Doctors and Nurses ill or quarantined.
   - ICU Beds started to run out.
   - Ventilators in short supply.
   - Runs on medications eg. Hydroxychloroquine.

4. Complete Enforced LockDown:
   After the exponential growth in no. of cases then USA implemented Complete Enforced Lock Down.

Voluntary Social Distancing is only as effective as the no. of people practicing it which was very minimal in USA so the cases sky rocketed in quick time.

Till date most cases are in USA in the entire world and rising day by day.

Public Health and Social Measures for the COVID-19 Pandemic:

Public health and social measures are measures or actions by individuals, institutions, communities, local and national governments and international bodies to slow or stop the spread of COVID-19.

These measures to reduce transmission of COVID-19 include:

1. Individual and environmental measures,
2. Early detecting and isolating cases,
3. Contact tracing and quarantine,
4. Social and physical distancing measures including for mass gatherings, international travel measures, and
5. Vaccines and treatments.
While vaccines and specific medications are not yet available for COVID-19, other public health and social measures play an essential role in reducing the number of infections and saving lives.

Wash your hands frequently

Regularly and thoroughly clean your hands with an alcohol-based hand rub or wash them with soap and water.

Why?

Washing your hands with soap and water or using alcohol-based hand rub kills viruses that may be on your hands.

Maintain social distancing

Maintain at least 1 meter (3 feet) distance between yourself and anyone who is coughing or sneezing.

Why?

When someone coughs or sneezes they spray small liquid droplets from their nose or mouth which may contain virus. If you are too close, you can breathe in the droplets, including the COVID-19 virus if the person coughing has the disease.

Avoid touching eyes, nose and mouth(T-zone)

Why?

Hands touch many surfaces and can pick up viruses. Once contaminated, hands can transfer the virus to your eyes, nose or mouth. From there, the virus can enter your body and can make you sick.

Clean and sterilize frequently touched surfaces:

- phones
- laptops
- door handles
- toilet seats

Practice respiratory hygiene

Make sure you, and the people around you, follow good respiratory hygiene. This means covering your mouth and nose with your bent elbow or tissue when you cough or sneeze. Then dispose of the used tissue immediately.

Why?

Droplets spread virus. By following good respiratory hygiene you protect the people around you from viruses such as cold, flu and COVID-19.

If you have fever, cough and difficulty breathing, seek medical care early.
Stay home if you feel unwell. If you have a fever, cough and difficulty breathing, seek medical attention and call in advance. Follow the directions of your local health authority.

Why?

National and local authorities will have the most up to date information on the situation in your area. Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also protect you and help prevent spread of viruses and other infections.

Stay informed and follow advice given by your healthcare provider.

Stay informed on the latest developments about COVID-19. Follow advice given by your healthcare provider, your national and local public health authority or your employer on how to protect yourself and others from COVID-19.

Why?

National and local authorities will have the most up to date information on whether COVID-19 is spreading in your area. They are best placed to advise on what people in your area should be doing to protect themselves.

WHO has described four levels of COVID-19 transmission. These are countries or local areas with:

1. No cases reported.
2. Sporadic cases.
3. Clusters of cases (grouped in place and time), or

Countries are putting in place a range of public health and social measures in different combinations and at varying times in the local evolution of the COVID-19 pandemic.

Myths around COVID-19:

1. There have been several myths around the disease, like consuming more garlic, curry leaves or cow’s urine would treat or protect one from the disease. The World Health Organization has busted such misleading claims. On garlic, WHO said it is a healthy food that may have some antimicrobial properties but there is no evidence that it has prevented people from contracting the 2019 nCoV.
2. COVID-19 virus cannot be transmitted in areas with hot and humid climates. From the evidence so far, the COVID-19 virus can be transmitted in ALL AREAS, including areas with hot and humid weather.
3. The new coronavirus can be transmitted through mosquito bites. To date there has been neither information nor evidence to suggest that the new coronavirus could be transmitted by mosquitoes.

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