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Review Article

CLINICAL FEATURES, DIAGNOSIS AND TREATMENT OF COVID-19

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Abstract: *The COVID-19 has affected worldwide population at every level from advance to under developed countries and also majorly affected clinical microbiology labs. This critique covers current issues furthermore, challenges for the research facility determination of diseases brought about by extreme intense respiratory disorder coronavirus 2 (SARS-CoV-2). In the pre analytical stage, gathering the best possible respiratory diseases information at the time from the privilege has become fundamental for a brief and exact basic finding of COVID-19. Appropriate measures are required to protect lab staffs, performing the test outcomes for COVID-19. In the investigative stage, constant converse translation PCR (RT-PCR) tests remain the basic trial of decision for the etiologic determination of SARS-CoV-2 contamination while counteracting agent-based procedures are being presented as supplemental tests. In the post-analytical stage, testing results ought to be cautiously deciphered utilizing both basic and serological findings. At long last, arbitrary access, testing kits accessible for the purpose of care with versatile limits are encouraging the fast and exact finding and observing of SARS-CoV-2 contaminations and extraordinarily aid the control of this episode.*

Keywords: COVID-19, diagnosis, epidemiology, treatment, real time PCR

Introduction

The illness of the coronavirus is found in humans and animals alone. A total of six animal classes have been reported to cause human infections. They are considered to be damaging agents for immune system caused by the physiological, viral, enteric and hepatic processes. Over the intervening decades, there were sporadic flare-ups including Middle East coronavirus respiratory syndrome (MERS-COV) and extremely severe coronavirus disease (SARS-COV). Nevertheless, we now see a further outbreak due to another virus, the infection SARS-CoV-2 (Dhama et al., 2020; Diao et al., 2020; Hassan et al., 2020). The major symptoms of this infection are include nausea, vomiting, fever, nonprocreative cough, diarrhea, myalgias, and dyspnea. Coronavirus disease first of all originated from Wuhan, the city of China on 31 December 2019. That's why it was named as COVID-19. The major source of spreading of this infection has been considered as bats. It has been spread near about 213 countries and affected 31.28 million people in the world and 0.934 million died by this infection. Due to its spreading ratio, WHO described this infection as a pandemic (Faiq et al., 2020; Wu and McGoogan, 2020). Recently a rare family of human corona RNA virus was found in Wuhan, China. Corona virus is an important family of positive RNA viruses (Wang et al., 2020b). Coronavirus is formally considered a severe acute respiratory syndrome-corona virus (SARS-COV-2) by the International Group of Viruses (Guan et al., 2020; Huarcaya-Victoria, 2020; Kandeel et al., 2020; Mannan and Mannan, 2020) used of SARS-COV-2 beta-corona virus. The 2019 Corona Genome Review showed that 87.99 per cent bat genes and 80 percent nucleotide similarity with the original severe acute respiratory syndrome outbreak virus were shared by this extraordinary virus (Aziz et al., 2020; Trilla, 2020). Prior information of this unique virus evaluated that SARS COV-2 illustrated the animal containing the virus which transmitted to human corona virus of the century (Chen et al., 2020b; Gralinski and Menachery, 2020; Zhang et al., 2020). Human infectious subtype of coronavirus occurred with mild symptoms (Shereen et al., 2020; Wang et al., 2020b). The 2019 severe acute corona viral syndrome disease outbreak was identical to other beta corona viruses in bats, but differs from the SARS corona virus and the corona virus in the Middle East (Corona et al., 2020; Guan et al., 2020). China has announced a group of idiopathic pneumonia cases in hospitals (Wang et al., 2020b). The whole sale market of Huanan seafood was reported as the source of infection, and the area was taken under complete lock down. Anyhow, during spring festival a large number of outsiders were there due to them virus extremely spread to other areas of China and entire

world countries. The origins of the later identified as the 2019 Corona Virus disease (COVID-19) was found among 2019 Special Coronavirus Researchers with Reverse Transcription Polymerase Chain Reaction (Li et al., 2020b; Zhu et al., 2020). The number of successful cases of RT-PCR has been increasingly growing. The mainland of china announced 77780 cases during February 2020. Other thirty three countries announced 2549 cases along with 34 mortalities. The 80239 cases around the world wide appeared with 2700 fatalities (Lu et al., 2020; Yang et al., 2020b). Repeated exposure and epidemic COV have shown that the health is facilities are being terrifying day by day. It suggests the likelihood of newly emerging COVs from animal to human and from human to human. Continuing environmental developments may make the detection of such pathogens more likely in future (Chen et al., 2020a; Pan et al., 2020).

Coronavirus is RNA enveloped virus which contains helical nucleocapsid. All Coronavirus contains 29 proteins, only four types of proteins make up the specific structural body of coronavirus. These are Spike glycoprotein, Integral membrane protein, Small membrane protein, Hemaglutinin esterase glycoprotein. (Heo and Feig, 2020) Membrane (M) protein and Envelope protein (E) are mainly used for virus assembly, while Spike protein helped the virus to enter the host body. D-dimer levels are also used for the diagnosing of SARS-COV-2. The level of D-dimer is higher inpatient which is infected by COVID-19. A higher level of D-dimer used as a prognostic indicator for mortality in hospitals (Fang et al., 2020; Zhang et al., 2020). In Wuhan, China the new viral outbreak was identified, in the family of coronaviridae eventually classified as coronavirus 2 (SARS-CoV-2) ERS (Cai, 2020; Lippi and Plebani, 2020). The virus has spread across the globe now and in 2009-2010, 10 years after the H1N1 swine flu outbreak, the World Health Organization (WHO) called this infectious disease the final pandemic. COVID-19 has already infected millions of people around the world, causing such high mortality that it could be responsible for more than 5.0 million deaths if national health authorities and policymakers do not take prompt and effective steps, such as regional lockdowns and social distancing (Deng et al., 2020; Yang et al., 2020a).

Like other coronaviruses, SARS-CoV-2 is an enveloped virus with a positive-sense, single-stranded RNA genome that includes four large structural proteins known as Spike (S), including the receptor-binding domain known as RBD, Envelope (E), Membrane (M), and Nucleocapside (N), along with additional genes such as ORF1 a/b, ORF3a, ORF6, ORF7 a/b, ORF8, and ORF10, which encode accessory proteins. This microorganism probably originated as a result of bats spillover, likely from another intermediate animal (pangolin, perhaps). Human transition was largely fostered by the emergence of S-protein mutations, which enhanced the affinity of this protein moiety (within a furin-cleavage site) to angiotensin-converting enzyme 2 (ACE2), its natural receptor on the surface of cells of a wide range of organs and tissues, particularly alveolar type 2 cells in the lung (AT2), but also lymphocytes and h-cells (Guo et al., 2020). SARS-CoV-2 binding to ACE2 is fostered by the priming of S proteins catalyzed by the serine protease 2 (TMPRSS2) transmembrane. The wide and widespread diffusion of ACE2 on the cell surface clearly explains the frequent involvement of the lung with interstitial pneumonia, which occasionally develops into an acute respiratory distress syndrome (ARDS), together with possible injury to many other organs and tissues, thus justifying the risk of multiple organ failure (MOF), which is then associated with an extremely high mortality rate, especially (Chan et al., 2020; Gupta et al., 2020). Histological analysis of the lung tissue often shows diffuse alveolar injury, distinguished by the existence of cellular fibromyxoid exudates, pneumocyte desquamation and ARDS-consistent hyaline membrane formation. While it has now been convincingly developed that COVID-19 has an almost favorable clinical path in as many as 80 percent of infected patients, who may be totally asymptomatic or may display only mild respiratory symptoms, the disease progresses into serious or even critical forms in 10-15 percent of SARS-CoV-2 positive patients, requiring mechanical ventilation, subintensive or even intensive care (Hussain et al., 2020; Ogen, 2020).

It is possibly based on certain demographic (advanced age, male sex) and clinical risk factors (hypertension, diabetes, cardiovascular disease, chronic respiratory disorders, cancer, obesity), but also on the existence of polymorphisms in the ACE2 gene sequence, which can affect SARS-CoV-2 virulence and pathogenicity by affecting receptor binding (Sheahan et al., 2020). Despite many biological aspects of this severe infectious disease remaining largely obscure, it has now been clearly recognized that early management is associated with far better outcome, with lower progression to systemic complications, including immunosuppression, development of a "cytokine storm" and severe inflammatory response syndrome (SIRS) (Driggin et al., 2020; Li et al., 2020a). Throughout this context, it is now almost unquestionable that in COVID-19, as in many other

human disorders, laboratory diagnostics plays an important, almost crucial, function as will be addressed further in the following sections of this article. COVID-19 is not a single virus but a huge population. Coronavirus are four types: alpha, beta, delta, and gamma based on their genetic and antigenic effects. SARS-CoV, SARS-CoV and SARS-CoV-2 are human most frequent diagnosed with Stirane Coronavirus. Of those, the four most common are 229E (Alpha), NL63 (Alpha) and OC43 (Beta) and HKU1 (Beta). SARS-CoV and SARS-CoV-2 are human most frequent viruses (Fang et al., 2020; Khailany et al., 2020; Lechien et al., 2020). The bat virus is believed to have contributed to SARS-CoV-2. It appears like a bat coronavirus with some altered nucleocapside and spicy protein (S protein) (Benvenuto et al., 2020; Tang et al., 2020). SARS-CoV, MERS-Co V and SARS-CoV-1 genomes have a base of roughly 29 900 copies, a base pair of 27 900, and a base pair of 30, 100 (Wu and McGoogan, 2020) respectively. The SARs-CoV-2 produces up to ten ORFs, creating an abnormality of 27 proteins. The arrangement of different sequences reveals that SARS-CoV-2 genome shows 80% similar and 50% similar to the genome MERSA-Co V (Cai, 2020; Islam et al., 2020). The path through the respiratory system is the latest delivery of coronavirus. It comprises three elements, SAR-CoV-2, such as membrane proteins (M) Spike glycoprotein (S) (E) and nuclear protein (N). SAR-CoV-2 includes four structural proteins (Chan et al., 2020; Wang et al., 2020a).

The genome sequencing of the new coronavirus was shared by the Chinese CDC on 12 January 2020. The institute uses this sequence to develop primers for SARS-CoV-2 and to detect the virus through the work of RT-PCR. RT-PCR was used for COVID-19 which is between 59 and 60% in frequency. This means that 43 per cent of patients with SAR-CoV-2 infection will become permanently infected following diagnosis (Benedetti et al., 2020; Campos et al., 2020; Chan et al., 2020; Yang et al., 2020b). This incoherent sensitivity can be due to patients who are tracked at an early stage of the disease when the virus load is below the detection level and the RT-PCR sample preparation is not correct. Additionally, COVID-19 is not excluded by a negative RT-PCR so a double RT-PCR must be performed. There are questions regarding the repeated RT-PCR period, the right duration between 24 and 72 hours of the adverse effects(Tu et al., 2020; Velavan and Meyer, 2020). The new coronavirus disease Corona Virus (COVID-19) was officially named by the World Health Organization in February 2020 (Zhu et al., 2020; Zu et al., 2020). Several prognostic indicators for this infection are proposed, and some are recognized by the scientist, for example, age. The layering shall be based on methodological considerations (independent or combination risk management models). Clinical findings were primarily linked to fatigue, exhaustion, non-reproductive cough and shortness of breath in patients with COVID-19. Laboratory studies revealed stable or reduced white blood cells, reducing lymphocyte levels, thrombocytopenia and increasing lactate dehydrogenase (LDH) transaminases in patients. The number of lymphocytes reduces with serious cases. Less critical are the predictions today (Remuzzi and Remuzzi, 2020; Sheahan et al., 2020).

Clinical characteristics of SARS-CoV-2 infection

- COVID-19 is a viral infection that severely infects humans, also known as the corona virus. Its incubation time is an average of 3.0 days. This duration is close to the incubation time of SRAS, which ranges from 2 to 10 days. The signs and features of COVID-19 are stronger and simpler in adults. The common symptoms of SARS-CoV-2 are as follows:
- Fever (87.9%)
- Fatigue (38.1%)
- Cough (67.7%)

On the other hand, the rare symptoms which were similar to other coronavirus are as following

- Vomiting (5.0%)
- Diarrhea (3.7%)

These patients may have a degree of dyspnea, and this is because only nine days were expected for the preliminary patients with COVID-19 infections from the beginning of the symptoms to the development of ARDS (Cai, 2020; Chen et al., 2020b). Furthermore, patients who suffer severely with COVOD-19 can be exposed to various complications such as acute respiratory distress syndrome, acute heart injury and secondary infection. There is enough evidence that proves that, apart from lungs, COVID-19 can damage other organs and tissues as well. A research conducted to study 214 patients of COVID-19 tells that there was neurological manifestation in 78 (36.4%) patients. Moreover, evidence also indicates that there was ocular surface infection in COVID-19 patients and their eye secretions also had SARD-CoV-2 RNA. There were other infections also present in COVID-19 patients such as arrhythmia, impaired renal function, acute heart damage, and abnormality in liver functioning (50.7%) at admission (Clerkin et al., 2020; Croda et al., 2020). A patient who suffered due to uncontrolled manifestation of pneumonia had moderate micro vesicular steatosis in the tissues of liver. Apart from that, duodenum, stomach tissues, and rectal mucosa had been also confirmed for SARS-CoV-2 RNA. Generally, the

features of corona virus observed radio graphically are same as to the features of pneumonia which is acquired at community level through other organisms. In order to diagnose this pneumonia, CT scan is an essential tool. However, there is a number of imaging features which happen to occur frequently and observed in pneumonia of COVID-19 (Grech, 2020; Hurst and Faulds, 2000; Mohammed et al., 2020). It also included the following features:

- Ground-glass opacity (65%)
- Smooth or unbalanced interlobular septal thickening (35%)
- Consolidations (50%)
- Bronchgram (47%)
- Thickening in adjacent pleura (32%)

The lower and peripheral lobes were also included. A report indicating 90% bilateral chest CT findings and chest CT response, 90% of the patients reported COVID-19 was 97%. If chest CT imaging features, laboratory test and clinical symptoms all combined together then COVID-19 pneumonia can be diagnosed early. Moreover, it was revealed by laboratory examination that there was lymphopenia in 82.1% patients and 36.2% patients had hrombocytopenia. It was observed that 33.7% patients have leukopenia whereas most of the patients did have normal leukocytes (Cao et al., 2020; Clerkin et al., 2020). Additionally, majority of patients showed high levels of C-reactive (CRP), creatinine kinase (CK), and lactate dehydrogenase (LDH). On the other hand, there were few patients who showed increased abnormal myocardial enzyme spectrum, transaminase or increased serum creatinine. Patients suffering from SARS-CoV-2 exhibited lower index of oxygenation as compared to those suffering from bacterial pneumonia. An important factor, cytokine release syndrome, intensifies the progression of disease. It was observed in patients of COVID-19 that there were increased levels of IL-6 and IL-10 and reduced levels of CD4+T and CD8+T which were also beside the intensity of disease (Diao et al., 2020; Guo et al., 2020).

Clinical Presentation and Features of SARS-CoV-2 Infection in Children

The common symptoms in confirmed 171 cases of COVID-19 were fever, cough and pharyngeal erythema whereas 16% of patients were asymptomatic. The epicenter of COVID-19 which is Wuhan, China was taken as a major example by researchers to classify the clinical symptoms and short-term results of SARS-CoV-2 infection in children. There were 1391 children, whose health was evaluated from 28 January to 26 February, 2020. Among those 1391 children, 171 children which make 12% of total were observed to have confirmed infection of SARS-CoV-2. Infected children constituted of 60% of boys and the average age was seven years and the range of age was from day 1 to fifteen years. The asymptomatic confirmed cases without pneumonia were 27 which make 16% of the total (Adhikari et al., 2020; Chakraborty and Das, 2020; D'Marco et al., 2020). Following were the clinical features which included:

- Fever (42%) and cough (49%) were the commonest features.
- There were 9% confirmed cases which had fever higher than 39ºC.
- Diarrhea, vomiting, fatigue, and nasal congestion were less-common.
- 111 children had pneumonia out of which 12 children were asymptomatic.
- There were 6 children who had lymphopenia and rest of the children had unremarkable blood tests.
- There was ground-glass opacity which has shown in 33% of cases through pneumonia's computed tomography appearance.
- Intensive care by mechanical ventilation was provided to 3 children and all of them had chronic essential health conditions.
- After four weeks of being hospitalized, a ten-month old child died.

The electronic medical record of 140 patients who were hospitalized due to COVID-19 and SARS-CoV-2 were extracted, evaluated and analyzed. The records included clinical manifestation, demographics, laboratory data, comorbidities as well as radiological materials. SARS-CoV-2 does not take asthma, allergic diseases and COPD as risk factor. Comorbidities in large number, old age, and other obvious abnormalities of laboratories were related to severe patients. Old age was linked with serious cases, the high number of comorbidities and the more common test anomalies (Smith and Regnery, 1950).

Epidemiology

On December 29th, 2019, four cases were unexplained in Wuhan city. The local seafood market was used by people in the Hubei province ('wet market') (Chan et al., 2020; Clerkin et al., 2020). Most cases were initially linked to the revolutionary market of seafood (Benvenuto et al., 2020). Secondary source of infection was founded by the direct contact with the infected people but despite of visiting Wuhan or no exposure to the wild life there was a spread of the infection among the medical professionals (Adhikari et al., 2020). This has been found that COVID-19 infection occurs by virus prone transmission, and both the immune-compromised and normal population will be at risk (Table 1). The age of infection with the virus was estimated at 25 to 89 y. Adult infections were recorded among children

and babies between 35 and 55 years of age (Gralinski and Menachery, 2020). The Dynamic Distribution Study found that patients had a mid-aged 59 years, with a majority (59 percent) of males between 15 and 89 years (Adhikari et al., 2020). This has been proposed that patients with autoimmune disease are vulnerable to infection and those with renal and hepatic impairment (Wang et al., 2020b; Yi et al., 2020). COVID-19 emerged from elevated rates of pandemic risk relative to SARS-COV, as COVID-19 (2.9) is estimated to have a capable reproductive number (R) higher than SARS (1.77) at this initial point. Earlier March 3,2020 WHO reported 87,317 cases worldwide while 2,977 (3.42%) patients buckled to the virus(4) 79,968 (92%) patients were confirmed in china. Moreover, the highest lethality 2,873 (96.5%) was also registered in china. There have been 7,169 incidents in 59 countries (Rajkumar, 2020; Zhang et al., 2020).

Table 1. Features of different strains of corona virus

Features	SARS-CoV-2	SARS-CoV-2	MERS-Cov
Estimated R0	2.68	2-5	>1
Host of Virus	Bats are natural hosts, pangolins are intermidiate hosts and humans are terminal hosts	Chinese horseshoe are natural hosts, masked palm civets are intermediate hosts and humans are terminal hosts	Bats are natural hosts, dromedary cameis are intermediate hosts and humans are terminal hosts
Transmission mode	Human to human through fomites, physical contact, aerosol droplets, nosocomial and zoonotic transmission	Human to human through aerosol droplets, opportunistic airbome, nosocomial, focal-oral and zoonotic transmission	Respiratory, zoonotic, nosocomial, limited human to human and aerosol transmission
Incubation period	6.4 days	4.6 days	5.2 days

Etiology

Corona virus are positive stranded crowned RNA virus (Coronam is the Latin word for the crown), which is targeted around spike glycoproteins in the container. In acute respiratory diseases, coronaviruses are responsible for 5-10 percent (Cai, 2020; Cao et al., 2020). 2 % of the population assumes that the healthy carriers of these viruses are. The popular human coronaviruses are small, HCoV-OC43, HCoV-HKU1, HCoV-229E and HCoV-NL63. For people with strong immunity, these Corona viruses have historically begun to be respiratory and coryza infections, while they will link trachea, bronchi and lungs for immunosuppressed individuals. SARS-COV, MERS corona virus and corona virus of 2019 begun with lungs and pulmonary vein, bronchial artery etc (Wichmann et al., 2020). The Corona virus 2019 is a COV beta type causing a genetic mutation in COVID-19. 89% of nucleotides have extreme, acute bat breathing dysfunction syndrome, such as CoVZXC21 (Hassan et al., 2020; Islam et al., 2020) doubled in bat. Only 82% identical to human severe acute respiratory syndrome virus is the new lineage called SARS-CoV-2 which ranges from 29,891 to 29,903 nucleotides with a genomic duration. Ultraviolet heat and light are known as a virus (Chen et al., 2020b; COVID and Team, 2020; Dhama et al., 2020). The SARS-Cov-2 is bound to the target lung cell, as Angiotensin Converting Enzyme (ACE2) is responsible.

Transmission

China's early appearance of patients at a seafood market in Wuhan was possibly related to direct susceptibility of infected animals. But the old days have indicated psychiatric cases of miscellaneousness of appearance. It also will demonstrate the transmitting of the virus from humans to humans is also possible. Hence the primary cause of communication is now thought to be human-to - human communication. Individuals that did not exhibit the signs could have transmit the virus (Boettler et al., 2020; Diao et al., 2020; Driggin et al., 2020). Though the most prevalent route of infection is symptomatic people (Figure 1). Transmission is caused by coughing or sneezing breathable droplets. Facts also suggest that close interaction with people may also result in transmission. Due to high aerosol concentration these likely items clearly spread in congested areas. It means a patient may spread the infection to two (Lake, 2020; West et al., 2020). Such results are focused on prime cases. Thus further experiments are required to communicate successful transmission and growth cycles.

Clinical Features

In the case of asymptomatic, pauci symptomatic and severe organ failure pneumonia, SARS-COV-2 patients with infection differs in clinical spectrum. Fever (77.4-98.6%), tingling (59.4-81.8%) fatigue (38.1-69.6%), dyspnea (3.2-55.0%), myalgia (11.1-34.8%), sputum (28.2-56.5%) and pain (6.5%-33.9%) were the most frequent signs with SAS-COV-2. Rather seldom, sore throat, hemorrhage and chest pain, hemoptysis, conjunctive irritations and diarrhea, and vomiting have occurred (Table 2). However, 39.9% of 140 trial patients who accepted COVID-19 recorded 39.9% gastrointestinal symptoms with

10.1% initially gastrointestinal disturbance in a Wang sample (Huang et al., 2020; Tu et al., 2020). At the beginning of hospitalization, the patients suffering with this disease did not experience fever (Wu and McGoogan, 2020; Yang et al., 2020a). Yet patients did not even have fever in serious cases. Medical characteristics close to SARS-COV2, SARS-COV, MEERS-COV, nausea, cough, myalgia, and dyspnea. There is, in any case, a greater gastrointestinal impact in SARS and MERS patients (Around one third) than in COVID-19 patients. Renal failure have high occurrence in MERS which is a distinctive feature not often found in other human corona virus infections (Gralinski and Menachery, 2020; Guan et al., 2020).

Statement on the extent on scientific findings categorized by the Chinese Writer Center for Disease Control (CDC) into: Mild disease, Severe disease and Critical disease

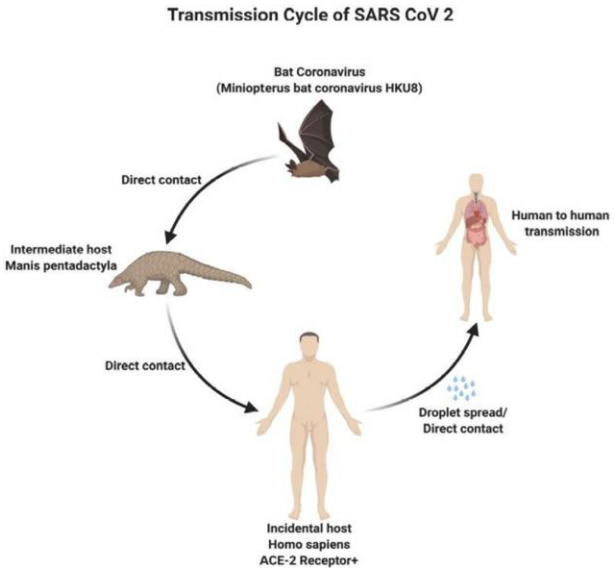

Figure 1. Transmission cycle of SARS CoV-2 (Chen et al., 2020a)

Tabl 2. Clinical Laborartory findings of patients with SARS-CoV-2 infection

Common Symptoms	**Probabilty**	**Laboratory findings**	**Probabilty**
Fever	77.4-98.6%	Lymphopenia	35.3-82.1%
Cough	59.4-81.8%	Thrombocytopenia	5.0-36.2%
Fatigue	38.1-69.6%	Leukopenia	9.1-33.7%
Dyspnea	3.2-55.0%	Increased CRP	60.7-86.3%
Myalgia	11.1-34.8%	Increased D-dinner	36.4-46.4%
Sputum production	28.2-55.6%	Increased LDH	27.4-75.8%
Headache	6.5-33.9%	Increased CK	8.0-32.5%
Underlying diseases	25.2-50.5%	Increased ALT	16.1-27.3%
Complications		Increased AST	22.2-36.7%
ARDS	3.4-29.3%	Increased interleulin-6	51.5%
Automatic renal injury	0.5-7.3%	Increased serum fenitin	62.6%
Secondary Ifections	9.8%	Increased ESR	84.8%
Shock	1.0-12.2%	Increased procalcitonin	5.5-11.3%

This occurred in 81% of cases with mild non-pneumonia disease and mild pneumonia. Blood oxygen saturation is lower or equivalent to 93% of the ratio of oxygen blood pressure (partial oxygen pressure) and the oxygen percentage supplied less than 300 minutes in extreme dyspnea, and lung infiltrates more than 50 percent within 24 to 48 minutes; in 14 percent of cases this occurred. This appeared in 5 percent of cases (McGonagle et al., 2020; Siddiqi and Mehra, 2020) in the case of serious respiratory failure, septic shock and multiple organ damages. COVID-19 can be mildly to seriously ill. In the case of severe pneumonia disease a comparison may be made to sepsis and septic shock based on respiratory insatisfaction and diagnosis (Castagnoli et al., 2020).

Mild Illness

Patient included for mild disease are usually with symptoms, including moderate fever, dry cough, sore throat nasal congression and vomiting, of severe upper respiratory tract infections. No symptoms such as dyspnea are evident with a severe illness.

Moderate Pneumonia

There are no signs of serious pneumonia in respiratory symptoms of cough and shortness of breath (or tachypnea in children).

Severe Inflammation

Fever is synonymous with severe dyspnea, breathlessness, tachypnea and hypoxia.

Acute Pain Respiratory Syndrome

Clinically and ventilatingly, understandings are required. This condition is suggestive of severe respiratory disease reoccurrence.

Sepsis

Sepsis and septic shock defined as “life threatening illness caused by your body response to an infection” (Troyer et al., 2020; Xu et al., 2020). Their sign symptom include respiratory problem such as dyspnea, hypoxemia, renal dysfunction, tachycardia,

mental illness and functional alteration of organs expressed the laboratory findings.

Laboratory and Radiologic Characteristics

On patient conformation, results such as 35.3-82.1%, 5-36.2%, and 9.1-33.7% respectively have lymphopenia, thrombocytopenia, and leukopenia as seen in Table 2. In chen study, CRP, ESR, and interleukin-6 (IL-6) showed elevated rates (Alhazzani et al., 2020; Poyiadji et al., 2020). Any patients had elevated levels of D-Dimer, Lactates (LDH), creatinekinesis (CK), severe prothrombin, ALT, and Aspartate Aminotransferase (AST). Rundary-glass light differences, bilateral patchies, and convergence sub-sectional regions with a rounded morphology and a peripheral lung distribution were seen in the imaging properties of chest computed tomography (CT) for particular coronary coronation virus pneumonia. Any condition modifications lead to better CT imaging, which suggests seriousness of the condition. Chest CT scan showed that about 10 days after the start of the initial symptoms the most severe pulmonary abnormalities occurred. The CT properties of the remarkable corona virus are thus contradictory and rapidly evolving. Therefore, a regular chest CT cannot be used to treat SARS-COV-2 infections (Mehta et al., 2020; Tu et al., 2020).

Pathological Findings

We also acquired bilateral diffuse alveolar damage with cellular Fibromyxoid exudates by collecting COVID-19 samples from patient autopia while conducting a lung biopsy examination. The pulmonary edema with the formation of hyaline membranes was obtained by bilateral lung tissue, a finding suggesting ARDS. The reductions in the CD4 and CD8 T-cell levels were demonstrated by cytometric peripheral blood research. The appearance of a white patchy lesion found in the lungs on autopsy also causes deep airway and alveolar injury. COVID-19 the result was, however, less serious but more frequently exuded pulmonary fibrosis and convergence (Schwartz et al., 2020; Shereen et al., 2020).

Diagnosis

COVID-19 cases from around the world have been diagnosed by WHO. China has updated the unique coronavirus pneumonia diagnosis and treatment. The positive high throughput sequencing, or the reverse transcriptase polymerase chain (RT-PCR), is a laboratory confirmed case for the SARS-COV-2 infection. Chest CT (Siddiqi and Mehra, 2020; Wu et al., 2020) is a COVID-19 screening tool. Chest CT experiences heavy COVID-19 radiation.

Treatment

There is no known and no antidote currently available as effective antiviral treatment for COVID-19. The greater role in severe infection was demonstrated by symptomatic symptoms and oxygen therapy. In respiratory failure cases, mechanical ventilation may be required rather than oxygen therapy. In patients with septic shock the hemodynamic support is critical, because it improves their tissue oxygenation. On 28 January 2020, the WHO released a paper on recommendations and care for previous HCOVs. This paper deals with patients with extreme acute respiratory disease, with their diagnosis and isolation, infection, surveillance and preventive methods, immediate care for assistance, and control of coronavirus as set out in this Report. Such recommendations include measures on respiratory collapse including controlled mechanical breathing, high-flow nasal oxygen and non-invasive breathing (Wang et al., 2020b; Yi et al., 2020).

Mechanical ventilation with intubation and protection

Precautions during intubation are important. Expert operator who uses the safety equipment such as gloves will carry out the operation. It can be used in extreme COVID-19 situations.

Ventilation not invasive

It should be used with extreme respiratory insufficiencies.

Other Therapies

For viral pneumonia and other ARDS conditions, other treatment strategies such as systemic corticosteroids are not advised. Inappropriate antibiotic application, no antiviral therapy yet also other methods such as:

Lopinavir / Retonavir (400/100 mg)

Chloroquine (500mg) and **Hydroxychloroquine** (200mg)

Interferon Alpha (5 million)

Remdesivi; it is an inhibitor against RNA polymerase having in vitro activity against many RNA viruses.

Ebola also affective for prophylaxis and therapy of HCOVs.

These drugs were positively tested for MERS-COV. When diseases are multiple organ dysfunction then for respiratory support is needed by extracorporeal membrane oxygenation (Wu and McGoogan, 2020; Yang et al., 2020b).

Diagnostic for Covid-19

Clinically, COVID-19 is diagnosed by many laboratory tests, like as X-ray, CT scan, PCR, Serological tests, antibody, NAAT (Nucleic Acid Amplification Test), D dimer, CRP level check, CBC tests are important. By laboratory examination results proved the disease, results include high C reactive protein level, high lactate Dehydrogenase (LDH) level, lymphopenia, liver enzyme, thrombocytopenia,

presence of the elevated amount of blood urea nitrogen, high amount of Creatinine (Kandeel et al., 2020; McGonagle et al., 2020).

CT scan

CT scan test identified the changes occurring in the lungs, and this finding is sometimes considered as a prognosis of patients. And also this test recognizes the high body temperature and low level of blood oxygen in the body (Klok et al., 2020; Terpos et al., 2020). NAAT test is also used to check that the SARS-CoV-2 virus is responsible for the COVID-19 disease. Real-time PCR used to distinguish the presence of "pathogenic specific genetic material" (Guo et al., 2020). To test the COVID-19 in the suspected patient through RT-PCR, fluids of pharyngeal, nasal or bronchial swab are taken. Results of this RT-PCR or high sequencing throughput are positive its means the patient is infected with SARS-COV-2 (Chan et al., 2020; Xu et al., 2020). Radiological organizations from all over the world CT scan for chest is not reliable as a tool for diagnostic for COVID-19 (Benvenuto et al., 2020). CT chest is not a criterion for COVID-19 diagnostic published by American and Singaporean radiologists (Saadat et al., 2020; Shams et al., 2020). But CT results are still used by some for diagnostics. It is discouraged because its sensitivity of 94% and specificity is 37% (Boettler et al., 2020; Croda et al., 2020). The Patient does not require a contrast CT scan. In adults, CT findings are bilateral, peripheral, and basal in lung distribution. Finding inpatients suffer from pneumonia is mediastinal lymphadenopathy, pleural effusion, multiple tiny pulmonary nodules, the tree in bud, pneumothorax, and cavitation (Jia et al., 2020b; Jouzdani, 2020). Changings in the lungs are in four stages: in the initial stage normal CT, in progressive stage ground glass appearance increased, in peak stage swelling and hardening of lung tissues (Huang et al., 2020).

C-reactive protein

C-reactive protein (CRP) level used to early-stage diagnose of pneumonia. The patient which is suffered from severe pneumonia had an elevated CRP level. CRP directly associated with lung lesion and severity of disease which pointed to clinical treatment. CT scan and X-rays results showed that with an increase of CRP levels, lung lesions size also increases (Wang, 2020). Antibody tests used to identify the patient or people who already infected with COVID-19. This test is a better way to identify the spread of coronavirus through the population. Many labs used another antibody test, which is known as Elisa (Enzyme-linked immunoassay) which is more reliable but this test is not commonly available (Borba et al., 2020; Menter et al., 2020). Antigen tests also used to identify the people who are now with coronavirus. This test is faster to identify the infection. Antigen's test results are expressed only when a virus that causes the infection is dynamically replicating; so that's why an antigen test is more appropriate to detect acute or early-stage infection (Cattaneo et al., 2020; Tang et al., 2020).

Isothermal Amplification Assay

Another test Isothermal amplification assay test also used for the identification of coronavirus. It amplifies the genome of the virus. This process of amplification is faster than PCR because this test is involved in repeated heating and cooling processes. Fluorescent tags are used to identify the test these tags are read out with a specific machine. CRISPR gene-editing technology, this is mainly used for identification. If the enzyme of CRISPR is attached to anyone sequence its color was paper mint. Examiners and Researchers expect that result should be simple, inexpensive, and easy to use in point of care situation (Pons et al., 2020; Rajkumar, 2020; Ray et al., 2020). Isothermal nucleic acid amplification amplifies the viral genome but it is faster than PCR. It used tags to detect the viral genome with the help of a special operating system. CRISPR techniques are used with modification (Montalvan et al., 2020; Nishiura et al., 2020; Rapkiewicz et al., 2020). It is expensive than PCR but researchers are working on the assays to make it cheap and easy to use (O'Dowd et al., 2020; Ogen, 2020). In one of the study show, this test has sensitivity about 85%. One study rejected it because in their study they found that it has low sensitivity.

CBC for COVID-19

CBC test is performed for the diagnosing of COVID-19, which helps to count the total number of blood cells. It gives the most important information about what types and how many in the number of cells are present in the blood. I.e. red blood cells, white blood cells, platelets, etc. CBC tests detect the CRP levels and WBCs differential which are important factors to recognize the COVID-19 (Singh et al., 2020; Sultan et al., 2020). Laboratory examination revealed that patient infected with coronavirus disease have less number of leukocytes, reduced lymphocytes count, the higher amount of transaminase, higher level of Lactate dehydrogenase (LDH), the higher level of creatine kinase (CK), the higher level of myoglobin and thrombocytopenia (La Vignera et al., 2020; Long et al., 2020).

RT-PCR

RT-PCR obtains DNA by using reverse transcription, PCR than amplified DNA. The sample is obtained by different methods some are throat swabs, nasal swab, or sputum. Sputum contains more viral content than

nasal or throat swabs (Nishiga et al., 2020; Wortham, 2020). The detection of the virus depends upon the methods of collection. The collection of saliva is as effective as nasal or throat swabs but sometimes maybe not (Paoli et al., 2020; Pei et al., 2020; Pons et al., 2020). It detects the nucleic acid of the virus. It is very accurate but required a special type of machine and results will take approximately 48 hours. The sensitivity of RT-PCR was 66% to 80% (Lechien et al., 2020; Montalvan et al., 2020). It has been found that RT-PCR is the most accurate diagnostic test.

Serological testing

Serological testing is conventionally classified as a diagnostic technique that is used to determine an immune response to an infectious agent. Inherent in this description is the basis of many misunderstandings and misunderstandings about the use of serological testing in COVID-19, by which this method of testing is not intended to replace the detection of viral RNA for COVID-19 etiological diagnosis, but rather to assess if individuals have been infected with the virus and/or developed an immune response. The CDC endorses a highly reasonable concept underlying serological testing in COVID-19, which is a strategy mostly used for purposes of epidemiology and surveillance (Abdelmaksoud et al., 2020; Harahap, 2020). To put this in the context of COVID-19, serology testing includes the identification (by qualitative testing) and/or measurement (using quantitative testing) of different classes of immunoglobulins (IgA, IgM, IgG) against SARS-CoV-2 to determine whether a person has been infected with SARS-CoV-2 and has developed antibodies that, if they have neutralizing effects, may prevent future re-occurrence. Even though the emergence of COVID-19 is still too recent to allow us to present definitive data about the individual response to this new coronavirus. The median period of antibodies occurring in COVID-19 patients' serum or plasma starts 3-6 days after the onset of IgM and IgA symptoms, while IgG is delayed to 10-18 days (Xu et al., 2020; Yang et al., 2020b). For the various classes of antibodies the positive rate is 85.4 percent for IgM, 92.7 percent for IgA and 77.9 percent for IgG, respectively. Padoan et al studied the kinetics of anti-COVID-19 antibodies in another recent review, finding that IgM and IgG appeared to appear 6-7 days after the onset of symptoms. Notably, although 100 percent of COVID-19 patients appear to develop anti-SARS-CoV-2 IgG antibodies twelve days after symptom onset, IgM could only be found in < 90 percent of this same patient group. These important results were confirmed in a subsequent study in which we showed that the anti-SARS-CoV-2 antibody positivity rate is as high as 100 per cent for both IgA and IgM up to two weeks after the onset of symptoms, while IgM could only be tested in 60 per cent of COVID-19 patients after the same time. Different data showing that 50% and 95% are positive for anti-SARS-CoV-2 IgM and IgG antibodies (Wang et al., 2020b; Zhang et al., 2020). Who indicated that in convalescent patients the levels of detectable anti-SARSCoV-2 IgM and IgG antibodies was 78% and 100 % respectively. Pan et al also found in a more recent study that the average incidence of positive for anti-SARS-CoV-2 IgM and IgG antibodies 15 days from symptom onset is around 74 percent and 97 percent, respectively. An interesting aspect that has recently been highlighted is that SARS-CoV-2 can trigger effective secretory IgA generation even in asymptomatic or mild infections, so that their assessment in both the blood and saliva may complement and may improve the diagnostic process. One of the main unanswered problems, almost entirely due to the recent advent of this novel coronavirus disease, is whether anti-SARSCoV-2 antibodies are to be regarded as neutralizing (i.e., effective in neutralizing virulence and/or pathogenicity), as well as their persistence in the blood (Terpos et al., 2020; Troyer et al., 2020).

Encouraging evidence on the former dimension emerged from a recent study, showing that human anti-SARS-CoV-2 antibodies tend to directly target nucleocapsid and spike proteins, and thus have a neutralizing effect on the viruses (Adhikari et al., 2020). In a separate investigation, (Contini et al., 2020; Recalcati et al., 2020)confirmed that SARS-CoV-2 infection can be neutralized by serum obtained from COVID-19 patients. With regard to the persistence of neutralizing antibodies in the circulation, some details can be translated from earlier findings on the former and fairly similar SARS coronavirus disease, whereby the titer of anti-SARS-CoV-1 neutralizing antibodies was found to be stably high for 16 months after infection, but decreased gradually after 4 years to 50-75% and ~1. The possible cross-reaction of current anti-SARS-CoV-2 immunoassays with previous coronaviruses such as SARS-CoV-1, MERS-CoV, HCoV-HKU1, HCoV-OC43, HCoVNL63, and HCoV-229E is a final issue that needs to be clarified.

Rapid serological testing

The first serological approach includes qualitative (or semi-quantitative) evaluation through the so-called "rapid tests," which are essentially portable instruments to be used individually with non-automated procedures to obtain rapid test results (i.e., approximately 5-20 minutes). Because the key advantages of these membrane-based immunoassays

include low sample volume (a decrease in blood will usually be enough), low operator training, low cost , easy efficiency, and fairly simple interpretation, their use is mainly reserved for bedside or near-patient rapid testing (Baj et al., 2020; Yi et al., 2020). Conventionally, these tests could involve two strategies, the former involving direct detection of SARS-CoV-2 antigens, the latter based on anti-SARSCoV-2 identification of antibodies instead. The European Center for Disease Control and Prevention (ECDC) has given a detailed overview of this technology, which is regularly updated. Recently, major concerns have been raised about the analytical and diagnostic performance of these tests , particularly after Spain and some other European countries have complained that many rapid test kits are inaccurate and do not allow for reliable COVID-19 diagnosis and surveillance. Additional focus was then put on the recent release of a study which stated that the sensitivity of one of these rapid tests was < 20 percent, potentially leading to under-diagnosis of COVID-19 in a wide subset of patients. This would persuade us to conclude that the general paradigm that "one-size-fits-all" does not (and will not) apply here, and that each device must be validated adequately before entering clinical routine use (Jia et al., 2020a; Mastrolonardo et al., 2020). The underlying issue is the fact that some of these experiments, without proper analytical and clinical testing, underwent rapid commercialization. Our clear recommendation, also supported by the ECDC, is that prior to its incorporation into routine diagnostics, clinical management and public health or epidemiological surveillance, scientific articles should be made available as a matter of urgency for clarifying efficiency and limitations of each single rapid diagnostic test (Guo et al., 2020; Hassan et al., 2020). It must also be clear that the most reasonable placement of these tests in the clinical decision-making process is to support decentralized testing capacity, but they should not be considered as a replacement for central laboratory diagnostics.

Centralized serological laboratory testing

The second serological option includes centralized testing in microbiological and clinical laboratories through the use of fully automated immune testing. Although this alternative approach is more costly, involves the processing by venipuncture of whole blood samples rather than capillary blood, and is largely dependent on the availability of different laboratory analyzers, it has some significant advantages. Which include increased accuracy and reliability, the possibility of producing quantitative data (essential for longitudinal titer monitoring), performance by trained laboratory staff (thus potentially reducing the likelihood of errors and subjective interpretation), permanent storage of test results inside the Laboratory Information System (LIS), and higher quality (Lake, 2020; Li et al., 2020a). Modern laboratory analyzer generation is characterized by excellent performance and very limited turnaround time (i.e., several hundred tests per hour can be performed). The use of centralized laboratory diagnostics is therefore to be considered a reliable and effective epidemiological surveillance technique. Importantly, the University Hospitals of Padova and Verona (Italy) have been precursors worldwide in the design and implementation of a project approved by the Scientific Committee of the Veneto Region and currently underway, involving comprehensive epidemiological screening through validated full-automated immunoassays of all healthcare workers working in the Veneto region (i.e., between 50,000-70,000 people). Phase 2 of this project concerns the prospect of applying this epidemiological study to the approximately 5 million inhabitants of the entire area of Veneto (Adhikari et al., 2020; Roca-Ginés et al., 2020).

ELISA

ELISA gives both qualitative and quantitative value. These types of tests usually required blood, plasma, or serum for testing. Use the plate which is coated with viral protein in the case of SARS-CoV-2 spike proteins mostly. Then these proteins are allowed to incubate than antibodies are allowed to attach with protein than it detected after washing (West et al., 2020).

Testing protocols

Drive-through testing

In this type of testing, all precautions are taken before taking the sample by the professional. This type of center is working perfectly in many countries like South Kore (Baj et al., 2020; Chan et al., 2020).

Home collection

In many countries, the sample is taken in a tube or container by the professional from the homes of the patients. Then the sample transferred to the lab and processed. The results are transferred online (Huarcaya-Victoria, 2020; Jia et al., 2020b).

Required volume

Approximately 1 to 2 ml of plasma is required for testing. 3ml of required for nasal and throat swab. It may be different for different kits and machines that are being used (West et al., 2020).

Therapeutics

Sadly, no drug or vaccination has yet been approved for coronavirus patients, as the most recent drug or vaccination takes a month or year. A variety of approaches have been developed, including vaccines, mAbs (monoclonal antibodies), oligonucleotides,

peptides, interferons and small molecular drugs, to control or avoid nCoV infections from 2019. In this report, we will analyze the present clinical status of COVID-19 and gather details, some of the knowledge obtained from news reports and government websites from various universities, hospitals and research centers (Kaya et al., 2020).

COVID-19 etiological treatment

It should be remembered that the WHO officially defines the "good event" of the COVID-19 as a patient receiving laboratory confirmation of infection by SARS-CoV-2 independently of the presence of clinical signs and symptoms, thus specifically challenging the current weapons armamentarium for etiological diagnosis (Guan et al., 2020; Kaya et al., 2020). This clear connotation almost naturally means that COVID-19 etiological diagnosis can only be made by recognizing the contents of SARS-CoV-2 nucleic acid (i.e., RNA) in biological samples. The materials for initial COVID 19 study are the upper respiratory samples (nasopharyngeal AND oropharyngeal swab, or outpatient wash) and/or lower respiratory specimens (sputum and/or endotracheal aspirate or broncho-alveolar lavage) according to the WHO and US Center for Disease Control and Prevention (CDC). Additional biological samples that can be examined include blood, vomit, urine , saliva, and throat washing, although the importance of virus detection remains undetermined in these matrices (Huang et al., 2020; Neri et al., 2020). Once properly and accurately collected, the biological specimens (especially nasopharyngeal and oropharyngeal swabs) shall be placed in separate sterile tubes containing 2-3 mL of viral transport media and refrigerated for less than 4 days at 2-4 ° C or frozen at -70 ° C (or below) until the test is performed. Processing specimens that do not meet such rigorous pre-analytical criteria that be correlated with the generation of outcomes of "false negative" tests, and thus should be avoided (La Vignera et al., 2020; Lechien et al., 2020).

Using molecular biology techniques on top and bottom respiratory products, the definitive diagnosis of SARS-CoV-2 infection, as supported by both the WHO and CDC, is then performed. The diagnostic strategy therefore involves the use of real-time reverse-transcription polymerase chain reaction (rRT-PCR) assays, which target one or more genes in the SARS-CoV-2 genome. A typical RT-PCR procedure for detecting this coronavirus includes, in sequence, RNA isolation, its purification, cDNA reverse transcription, RT-PCR instrumentation cDNA amplification, followed by (fluorescent) signal detection (Wichmann et al., 2020; Yang et al., 2020b). A validated diagnostic procedure, which has been endorsed by the WHO and is therefore now widely used in Europe, involves a first-line screening test with an amplification of the E gene, followed by a confirmatory test with an amplification of the RdRp (RNA-dependent RNA polymerase) gene, followed by an additional possible confirmatory test with an amplification of the N-gene. The CDC also developed a molecular biology assay, which was defined as the 2019-Novel Coronavirus (2019-nCoV) Real-Time Reverse Transcriptase (RT)-PCR Diagnostic Panel (Tu et al., 2020; Wang et al., 2020b). The primers and probes for detecting SARS-CoV-2 were identified from genetic regions belonging to the N gene, encompassing the use of two primers / probe sets according to the CDC. An additional collection of primers/samples can then be used in the control specimens to amplify the human RNase P gene (RP). Importantly, a recent study analyzing the comparative performance of several primer / probe sets showed that the protocols of WHO and CDC display exceptional sensitivity compared to other assays. Importantly, the detection of SARS-CoV-2 through molecular biology techniques in either upper or lower respiratory specimens allows for the diagnosis of active infection from this coronavirus, but does not rule out any co-infection with other micro-organisms (e.g., bacteria, fungi , viruses, etc.) (Velavan and Meyer, 2020; Wu et al., 2020).

RT-PCR's accuracy and reliability for the diagnosis of infection with SARS-CoV-2 depends on many biological and technological variables. The biological source is primarily informed by the effect of procedures used to collect, transport and store specimens, as well as the concomitant identification of antiviral therapy viruses. Wang et al recently stated that in patients with COVID-19 diagnosis, for example, the RT-PCR SARSCoV-2 concentration in bronchoalveolar wash fluid is as high as 93% but decreases to 72% in sputal and 63% in the nasal swabs, while the concentration is only 32% in pharyngeal swabs and 29% in stools. The positive RT-PCR level is also shown as 15-30% in the blood and 14-38% in rectal swabs, respectively. SARS-CoV-2 is stable (Gianotti et al., 2020; Magro et al., 2020). Several other published studies have confirmed the suboptimal diagnostic accuracy of the nasopharyngeal and oropharyngeal swabs. For example (Ghazal et al., 2020; Jia et al., 2020b), reported that the positive rate of RT-PCR for SARS-CoV-2 in these materials is only 70%, decreasing to approximately 60%. Wang *et al*., (2020) has also recently highlighted a significant influence of the analytical techniques used to detect viral RNA, which revealed that the detection limit (i.e., the lowest

detectable amount of virus) shown by six commercial RT-PCR kits is extremely heterogeneous, so that the use of any of these tests may theoretically yield false negative results due to inadequate analytical sensitivity.

This finding is important, suggesting that certain symptomatic patients who were not initially diagnosed with RT-PCR infection with SARSCoV-2 (or who were then diagnosed with re-infection after two consecutive negative RT-PCR tests) may have been misclassified due to the use of methods with insufficient analytical sensitivity. It is also important to note here that some of these initially false-negative test results can later become positive if swabs are retrieved a few days after the initial test (Nobari and Goodarzi, 2020; Seirafianpour et al., 2020). Significant data showing that 14.1% of patients who are eventually diagnosed with COVID-19 may initially have negative test results, but that rate will then decrease in tandem with the number of repeated follow-up tests, from 6.9% to 0.3% from 2 to 5 consecutive subsequent tests, respectively. The important thing that resulted from this research is that in patients with initially positive testing, the probability of progressing to more serious disease stages was almost double that of patients with initially negative tests (44.6% vs. 24.4%; p=0.015). Recent studies have also been published on the possibility of using rapid reverse transcription loop-mediated isothermal amplification (RT-LAMP) assays to detect SARS-CoV-2, but additional evidence is required to support their routine use in COVID-19 diagnostics at this point in time. Importantly, full-automated commercial RT-PCR has also recently been introduced in the diagnostic industry, which is characterized by high-throughput and quick turnaround time , enabling the bench time per sample to be reduced by almost 90 percent and allowing for the study of larger patient volumes in a shorter time frame (Behbahani et al., 2020; Ladha et al., 2020).

Drugs as Therapeutics

We focus on the use of previous anti-virus medicines, including severe acute respiratory syndrome (ASARS) (Askin et al., 2020), which can treat HIV, HBV, HCV and influenza without coronavira infection. Since of the non-curable outbreak of 2019, we rely mostly on licensing or cure for HIV, (HBV), (HCV) or influenza infection with previously approved anti-viral medicines. Therapeutic procedures that could be a choice in the Middle East for Coronavirus-related infections, i.e. serious acute air syndrome (SARS) (Goldman et al., 2020; Kaushik et al., 2020).

Antiviral drugs against COVID-19

Several pre-existing antiviral medicines have been thought to work against coronavirus, which has locked the entire planet with its fear and harms. This paper deals with each of those.

Favipiravir

The study found that favipiravir (T-705) is an antiviral and has been approved to be effective in the prevention of influenza. It has the ability to inhibit numerous viruses from the RNA-dependent catalytic retained RNA polymerase domain such as Ebola virus, influenza virus, yellow fever, norovirus, and chikungunya enterovirus Favipiravi is said to be a guanine analog and to have a potent effect on the catalytically retained RNA polymerase of RNA-dependent viruses (Pangti et al., 2020; Yazdanpanah et al., 2020). Recent research on the efficacy of favipiravir+interferon-α and favipiravir+ Baloxavir marboxil (the approved inhibitor of influenza targeting cap-independent endonucleases) has already been published in 2019 and patients with COVId-19 are being used to evaluate and enhance the lung condition of the patient (Dogan et al., 2020; Jafarzadeh et al., 2020).

Ribavirin

Ribavirin has a manufactured antiviral activity containing nucleoside, used a tiny drop of aerosol (virazole), and was used against respiratory syncytial virus as tested against lethal COVID-19 (Castelli et al., 2020; Mansourabadi et al., 2020). A study revealed the mechanism of action of ribavirin, was first absorbed through the cell membrane, and is enzymatically transformed together with the deribosylated base by host cell enzymes into 5'-phosphate derivatives (Rezaei, 2020). These metabolites impede the process of mRNA cover-up and stretching. It was also shown that ribavirin reduces the guanine nucleosides by inhibiting feedback. It is widely used against virus of smallpox, myxovirus and so on (Lebeau et al., 2020). However, this medication showed some side effects when monitoring patients with SARS and MERS, such as anemia, which can get severe at high doses (Liu et al., 2020). Whether it offers enough potential for COVID-19 isn't yet known.

Remdesivir

Remdesivir (GS-5734) is an adene-based phosphoramidite medication with a chemical structure often similar to the HIV RT inhibitor of tenofovir alafenamide. Remdesivi is an antiviral drug of the broad variety used in RNA viruses such as MERS and SARS in cell culture and animal models (Noval et al., 2020; Qiang et al., 2020) and is also targeted by Ebola in animals (Magro et al., 2020; Morokutti-Kurz et al., 2020). Coronavirus was shown to be effective and multiple experiments and clinical

trials to confirm the dosage are in progress. This drug has a positive impact. National Institutes of Health of the United States (NIH). USA They announced the first clinical trial for coronavirus treatments in the world, using the medicinal drug. After several studies and experiments in animal models, this medication has been shown to prevent and inhibit replication of many coronaviruses, but the way this is achieved is still unclear (Mansourabadi et al., 2020; Mehta et al., 2020). Researchers of the University of Alberta, USA. In Gilead, USA, the drug's effects on coronavirus have been critically observed and studied and confirmed that remdesivir blocks the enzyme that is essential for viral reproduction. Gotte's laboratory scientists provided information about the coronavirus remediesivir mechanism. By using MERS-CoV polymerase enzymes, the enzymes can absorb remdesivir, because it resembles an RNA building block. The cell shall stop replication immediately after an inhibitor is inserted (Neri et al., 2020; Nishiga et al., 2020). In 2019, a new study also found remdesivir that inhibited COVID-19 in infected Rhessus macaques (O'Dowd et al., 2020; Organization, 2020).

Galidesivir

Galidesivir is an adenosine that was initially developed in HCV clinical studies of the yellow fever and the Ebola Virus and is currently in early stage. Galidesivir is a related adenosine. When given, phosphorylate galidesivir is administered by cellular kinases in triphosphate which mimics ATP. The viral RNA polymerases bind the nucleotide of the drug to its RNA-strand, leading to premature strand termination. In vitro, MERS and SARS are considered involved (Recalcati et al., 2020; Rezaei, 2020). It can be delivered by mouth, intramuscularly and intraperitoneally (Morokutti-Kurz et al., 2020). In the course of the study the effect of galidesivir on COVID-19 patients has been studied by BioCryst. This research is funded by the United States National Institute for Allergy and Infectious Disease (NIAID) USA (Li et al., 2020b; Wortham, 2020).

Protease Inhibitor drugs against COVID-19

Disulfiram

Disulfiram is an essential drug product which has been approved for use in patients with alcohol addiction (Sheahan et al., 2020; Sultan et al., 2020). Papain, like MERS and SARS proteases that have been visualized in cell culture, tends to be halted. Nevertheless, in the case of alcohol-dependent patients it is worth remembering how it acts as a protease inhibitor. Disulfiram is given only as an oral and mild-acting tablet (for example, nausea, skin problems (sweat, heat and flushing)). Disulfiram can also be used against COVID-19, and scientists are using disulfiram in a new targeted oxidation technique in order to oxidize the cytosolic protein structure. Molecular coupling provides experimental evidence that two 2019 nCoV thiol proteases Mpro and PLpro can be oxidised by disulfiram. It is undergoing phase III anti-2019 nCoV therapy study (Paoli et al., 2020; Roca-Ginés et al., 2020).

Stimulation of Host immunity against COVID-19

Nitazoxanide

Nitazoxanide is an important antiparasite and antifungal drug with a wide scope. It is 3 1/2 hours for half-life. His coronaviral activity has been shown to be measured (Pei et al., 2020; Qiang et al., 2020). Such drugs are approved mainly for rotavirus, norovirus etc. It interacts with pathways regulated by host, which play a key role in viral replication. Nitazoxanide abolished influenza virus clinical trials in September 2019, although the effects remain uncertain (Mohammed et al., 2020; Ray et al., 2020). But phase 2 nitazoxanide did not reduce the hospitalization or symptoms when randomized SARS patients were monitored. Although in vitro SARS-CoV-2 monitoring is promising, additional data and correct dosing guidelines are required in order for it to play its role in overall coronaviral recovery (Pastor, 2020; Poyiadji et al., 2020).

Immunosuppressive drugs against COVID-19

Immunosuppressive drugs are being used for patients suffering from renal diseases to increase their immunity. Such types of drugs are more specific in action and less side effects and these drug are being used against COVID-19 (Recalcati et al., 2020; Saadat et al., 2020).

Tocilizumab

Tocilizumab is a monoclonal antibody which can block the interleukin 6 (IL-6) receptor that is soluble and membrane-bound. Macrophages and monocytes secrete the IL6 and is the principal regulator for immune response in cytokine syndrome (CRS) patients (D'Marco et al., 2020; Emanuel et al., 2020). The FDA approved the rheumatoid arthritis treatment drug in 2010 and progressed as a corticosteroid protecting agent in CAR T (Chimeric Antigen T Cell) (Dhama et al., 2020; Emanuel et al., 2020). The care alternative in China is COVID-19 patients who are pandemic. In most important coronaviral cases (Goldman et al., 2020; Gralinski and Menachery, 2020), high inflammatory and cytokine attacks, including high IL-6 were observed. In extreme cases of coronavirus, immunotherapy with tocilizumab is now a safe option. This medication should be given intravenously once at the dose of 4 to 8 mg kg-1 or 400 mg. In China, there are two more clinical studies on coronavirus tocilizumab safety and dosage (Søreide et al., 2020). The FDA has approved this

medicine in the hospitalized patient for the Phase III clinical trial against COVID-19 (Søreide et al., 2020; Yuan et al., 2020).

Corticosteroids

Corticosteroids are effective in reducing body inflammation, and also cause severe COVID-19 pneumonia. Patients suffering from corticosteroid disease are in intensive care due to a drastic disease. The right dose, protection and effectiveness when using corticosteroids is also very important because certain patients or people are responsive. There is a mixture of clinical evidence on the use of corticosteroids in SARS-CoV-1 infections. Corticosteroid use findings are not influenced by specific tests and trials. One study shows that mortality rates have fallen in critically ill patients, although patients have demonstrated that corticosteroid disease is severe, even for the longest period of time to clear the virus. The MERS-CoV virus delays in the patients undergoing corticosteroid therapy. A recent event showed that, with the use of corticosteroids and without any risk, patients with coronavirus had a reduced mortality rate in the very ill. "Gucocorticoid is considered equivalent to 1-2 mg/kg/day of methyl prednisolone given over duration of at least 3–5 days or less based on respiration discomfort and chest imaging; consider that increased glucocorticoid doses suppress the immune system and may also postpone the removal of glucocorti for at least 3-5 days. The National Commission on Health of the People's Republic of China states (Smith and Regnery, 1950; Troyer et al., 2020).

Bevacizumab

Bevacizumab is also human-like a monoclonal antibody. Bevacizumab is approved for use in anti-tumour therapies for its efficacy as a VEGF medication (vascular endothelial growth factor). Any of the mild side effects include hypertension, IGD, diarrhea and fatigue. The most serious side effects include bleeding and arterial thromboembolism (Yang et al., 2020a; Yuan et al., 2020). A clinical trial of bevacizumab was performed by the coronavirus on 15 February 2020. Blood gas checks are performed and laboratory tests are carried out after treatment, including CBC and chest imaging to verify and measure the effectiveness and safety of bevacizumab (Wu and McGoogan, 2020; Yazdanpanah et al., 2020).

Vaccines

Vaccines introduced to prepare the antibodies for disease in the body. The pathogen is recognized by the body defense system and the body is protected against them. Nearly 100 companies worldwide try to vaccinate against SARS-COV-2 virus using different techniques (Schwartz et al., 2020; Singh et al., 2020).

Messenger RNA based Vaccines

The world's leading vaccine companies are trying to use mRNA to develop vaccines because they have several advantages over conventional vaccines, such as lower cost of production and high performance (Pei et al., 2020; Qiang et al., 2020). Several groups are working to use mRNA technology to produce the SARS-COV-2 vaccine. Arcturus Therapeutics, an American company, has announced the use of the mRNA technique in testing COVID-19 vaccines (Pan et al., 2020). In March a BioNTech company developed in Germany the mRNA-based vaccine COVID-19, and phase 1/2 started in Germany in April (Pastor, 2020). A phase 1/2 is the first phase in Germany. In the preclinical stage of development Biotech company CureVac in Germany concentrates on mRNA-based prophylactic vaccines (Pons et al., 2020). Sequencing of mRNA-1273 (lipid-encapsulated mRNA-based vaccine (LNP)) and the experimental coronavirus vaccine was completed by the United States of America (NIH). Phase 2 studies began at NIH (Pangti et al., 2020).

DNA based Vaccines

These vaccines are known as 3rd generation vaccines. In contrast to protein-related vaccines, DNAs are more successful. DNA vaccines are also being used by clinicians for various disorders like cancer, asthma, and autoimmune diseases (Rajkumar, 2020). Also in research stages are DNA vaccines against COVID-19. The EpiVax associates in the production of COVID-19 DNA vaccines (Morokutti-Kurz et al., 2020; Pons et al., 2020) with pharmaceutical companies. The focus of INOVIO is also on other DNA vaccines for coronavirus. In January, ongoing trials of COVID-19 continued in April of clinical phase 1(Noval et al., 2020; Paoli et al., 2020).

Peptide-based Vaccines

A small volume of amino acids that enhance body immunity are used for the production of peptide vaccines (Neri et al., 2020). Phase II (Liu et al., 2020; Magro et al., 2020) is currently undergoing clinical trials of peptide-Based Cancer Vaccine (PBV). Protein fragments for the production of vaccines to enhance COVID-19 T cell activity have been identified by the Generex Biotechnology Company and Epivax (Menter et al., 2020; Morokutti-Kurz et al., 2020). IMV has been able to identify epitopes using the modern coronavirus genome, and others have been used to produce antibodies. In September 2020, IMV is hopeful that the clinical trial will take place (Huang et al., 2020; Nishiura et al., 2020). Novavax developed the COVID-19 vaccine that uses

peak protein to produce antigen. Phase 1 clinical trials are expected to commence in May or June (Jia et al., 2020a).

Virus-Like Particle Vaccines

Particles similar to viruses (VLPs) are virus-like, but do not contain nucleic acid. The vaccines based on VLP bind to host immune cells and activate cell and humoral responses. iBio used that technique to improve the immunity of the host to COVID-19. The composition of VLP is close to that of the virus in the preclinical phase (Kandeel et al., 2020). In order to set the production goal for vaccines, GeoVax used the VLP development tool (Kaya et al., 2020). Medicago has developed the COVID-19 VLPs scheduled to be evaluated in the summer of 2020. In collaboration with the National Research Council of Canada, IBV vaccines have developed pan-coronavirus vaccines using enveloped virus-like particles imitating the viral structure (Hurst and Faulds, 2000; Klok et al., 2020).

Laboratory monitoring and risk prediction

Since the current epidemiological figures contribute to raising many doubts that the pandemic will soon cease, it is imperative to identify accurate predictors of the severity of the epidemic, which may enable earlier clinical interventions and better use of healthcare resources within a care system whose responsiveness has been literally overwhelmed by this unprecedented and virtual (Lebeau et al., 2020; Li et al., 2020a). Therefore, an additional and almost necessary benefit offered by laboratory medicine is the possibility of defining a subset of subjects that would be more likely to progress towards severe / critical illness. This community of patients can be classified by the preferential use of laboratory services, with unfavorable clinical course correlated with lymphopenia, thombocytopenia, neutrophilia, increased concentration of cardiac injury biomarkers (i.e., cardiac troponins), C reactive protein and other inflammatory cytokines, liver and kidney function tests, as well as D-dimer and calcitonin pro (Siddiqi and Mehra, 2020; Tang et al., 2020).

Conclusion

Many other companies and organizations, such as Can-Sino Biologics at the Shenzhen Genoimmune Medical Institute Baharat Biotechnology University of Oxford and CSL Behring, are also focused on developing vaccines using different technologies and methods, such as recombinant nucleic acid and plasma therapy. Some teams are designing other virus vaccines that could be used against COVID-19. Doctors and researchers are exploring several other methods that may be effective in therapies such as plasma therapy and stem cell therapy. We all hope that scientists and doctors will find COVID-19 therapy as soon as possible so that we can save a decent amount of worth living.

Conflict of interest

The authors declared absence of any conflict of interest.

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