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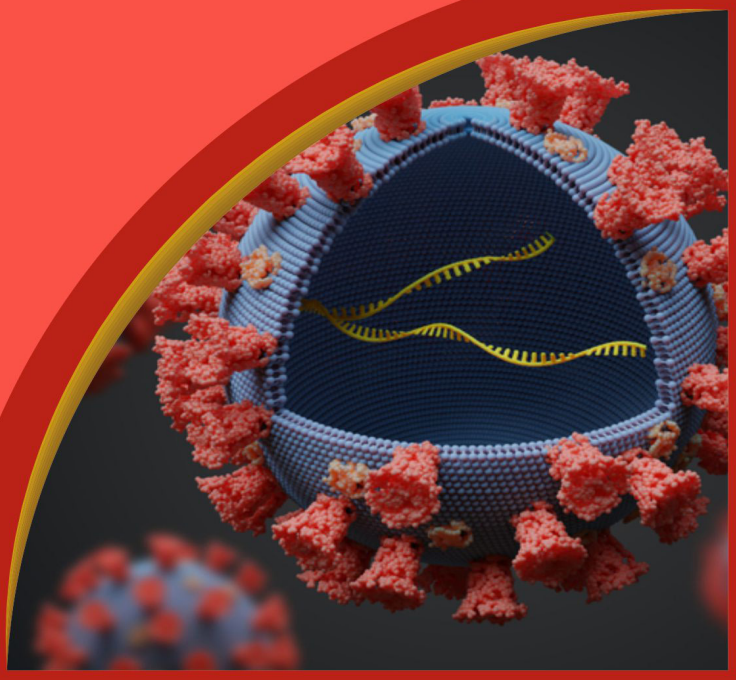

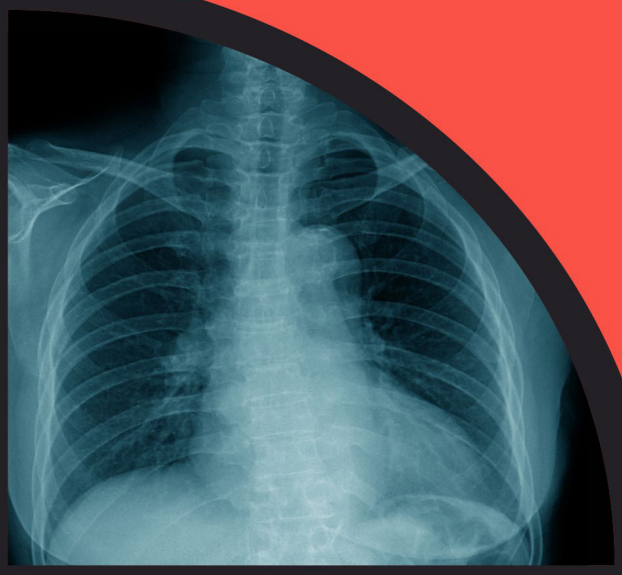

THE COVID-19 PANDEMIC: EPIDEMIOLOGY, GENETICS AND MANAGEMENT OF MEDICOLEGAL CASES

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The COVID-19 Pandemic: Epidemiology, Genetics, and Management of Medicolegal Cases

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Abbreviations

CoVs: Coronaviruses; α-COV: Alpha-Coronavirus; β-COV: Beta-Coronavirus; δ-COV: Gamma-Coronavirus; γ-COV: Delta-Coronavirus; SARS-CoV: Syndrome Coronavirus; MERS-CoV: Middle East Respiratory Syndrome Coronavirus; ACE: Angiotensin Converting Enzyme; G-CSF: Granulocyte-Colony Stimulating Factor; TNF: Tumor Necrosis Factor; NK: Natural Killer; DIC: Disseminated intravascular Coagulation; NMT: Nasal Mid Turbinate; CDC: Center for Diseases Control; NP: Nasopharyngeal; OP: Oropharyngea; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction; CT: Computed Tomography; PPE: Personal Protective Equipment

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Abstract

With the emergence of the new pandemic of sever acute respiratory distress syndrome coronavirus 2 (COVID-19) in late 2019, many concerns have been raised on the forensic practices that involve dealing with samples related to legal incidents in which suspected or confirmed COVID-19 case(s) are involved. This review work aims at providing information on COVID-19 epidemiology, diagnosis protocols and procedures for managing medicolegal cases in order to proceed safely with the process of criminal investigation. In this work, we reviewed the recent literature on the possible routes of transmission of the disease in the different circumstances with special focus on the disease pathogenesis. A detailed review of the guidelines and reports concerned about COVID-19 diagnosis is discussed including clinical, molecular, serological, and radiological diagnosis with special attention to the sampling and genetic profile of the disease. In addition, the review considered the increased risk of exposure among medicolegal examiners while performing the medicolegal examination. Therefore, the review covered the prerequisites, precautions, and regulations to be fulfilled by the medicolegal examination team to ensure a safe environment during autopsy. This enclosed the indications for autopsy, requirements within the autopsy room, personal protective equipment, and autopsy practices and findings in suspected COVID-19 cases. Finally, the review highlighted the current available treatment protocols in addition to the prospective treatment and vaccination trials.

Keywords: COVID-19; Forensics; Genetics; Diagnosis; Autopsy; Vaccine; Treatment

Introduction

Coronaviruses (CoVs) are a family of viruses that characterized by crown-like spikes on their surface (Latin: corona = crown) and comprise four genera, alpha-coronavirus (α-COV), beta-coronavirus (β-COV), gamma-coronavirus (δ-COV) and delta-coronavirus (γ-COV) [1]. In nature, α-coronavirus and β-coronavirus are mammals' viruses, in contrast, δ-coronavirus and γ-coronavirus are birds' viruses [2]. Human coronaviruses, including 229E, NL63, and OC43 are classified as α coronavirus, on the other hand, pandemic coronaviruses including Severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are allocated as β coronaviruses [3]. Coronaviruses are the largest type of positive-stranded enveloped RNA viruses, with 26-32 kb and 125 nm diameter [4]. As a single-stranded RNA virus, coronaviruses mutate rapidly, and they have a moderate-to-high recombination rate (approximately 10−4 substitutions per year per site). They share several features and characteristics including nosocomial transmission, viral immunopathology, and replication, and mainly they cause respiratory and gastrointestinal tract infections that are mainly transmitted through direct or indirect respiratory tract exposure (Table 1) [5]. In the following review the epidemiology, pathogenesis, genetics, and diagnosis of COVID-19 will be highlighted

Table 1 **Epidemiological and biological characteristics of coronaviruses outbreaks and pandemics[11,12,15,16]:**

Pandemic	SARS	MERS	COVID-19
Period	December 2003 to January 2004	June 2012 –	December 2019 –
Etiology	SARS-CoV	MERS-CoV	SARS-CoV2
The functional receptor	Angiotensin-converting enzyme 2 (ACE2)	Dipeptidyl peptidase 4 (DPP4 or CD26)	Angiotensin-converting enzyme 2 (ACE2)
Origin country	China	Arabian Peninsula	China
Possible Natural Origin	Bats		
Possible Intermediate Host (Vector)	Palm civet and raccoon dogs	Dromedary camels	Pangolins, Turtles, and Snakes
Active cases	8096	2494	More than 15.7 million
Total Mortality	774	858	More than 0.6 million
Mortality rate	More than 9.5%	More than 34%	More than 4.0 %
Incubation period	2–10 days	2–14 days	2–14 days
Transmission patterns	Animal to human and human to human		
Common Symptoms	Fever, myalgia, cough, shortness of breath		
Major complications	Pneumonia, severe acute respiratory distress syndrome, death		

Coronaviruses Pandemics

Severe acute respiratory syndrome (SARS) infection

Severe acute respiratory syndrome coronavirus (SARS CoV) is a coronavirus that caused an outbreak of SARS infection in humans from 2002 to 2004 [6,7]. The infection first appeared in late 2002 in Guangdong, Province in Southern China. SARS CoV has been isolated from two animal species (palm civets and raccoon dogs) as natural animal reservoirs of the virus [8]. Angiotensin-converting enzyme 2 (ACE2) was determined as the functional receptor utilized by SARS CoV to cause cell evasion and viral replication in the target cell and subsequently causing SARS infection [9]. The clinical manifestations of SARS are mainly flu-like symptoms including fever, chills, cough, malaise, or myalgia that may develop to pneumonia [10]. The mortality associated with the SARS illness in 2002 to 2004 was approximately 10%, infecting 8096 cases and causing 774 deaths, where approximately 20% of infected individuals were health care workers (Table 1) [11-14].

Middle east respiratory syndrome (MERS) infection

The etiology of Middle East Respiratory Syndrome (MERS) coronavirus was first isolated in a hospital in Jeddah, Saudi Arabia, from the sputum of a patient with severe pneumonia at the end of 2012 [10]. The patient died as a result of severe respiratory failure where the virus was described as MERS-CoV [17]. The natural origin of MERS-CoV were bats in addition to dromedary camels that were suggested as a major intermediate host for MERS-CoV, therefore, the MERS infection was mainly spreading in Saudi Arabia and Arabian Peninsula [18-20]. However, some cases were reported all over the world [19,21-23]. According to WHO, the mortality rate of MERS-CoV was approximately 34%, which represents the highest mortality rate among coronaviruses infections (Table 1).

Coronavirus disease 2019 (COVID-19) pandemic

Coronavirus disease 2019 (COVID-19) has been named by the World Health Organization as a new worldwide pandemic caused by novel coronaviruses called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is one of the coronavirus family that highly contagious in humans and causes respiratory illness manifested mainly by shortness of breath, dry cough, and fever [24]. The first case of COVID-19 was discovered at a wholesale seafood market in Wuhan, Hubei province, in China by the end of December 2019, then spread all over the world [25]. Following the rapid community, regional and international spread associated with the quick rise of numbers in both cases and deaths, the WHO declared it as a pandemic on 11th March 2020 [26]. Currently, the disease spread worldwide in around 218 countries and territories with 15.7 million confirmed cases and more than 637 thousand deaths worldwide [27].

Epidemiology

Initially, COVID19 transmission was considered a strictly zoonotic disease with the liability of animal to human transmission. Since an association was established between those diagnosed patients and seafood and wet animal wholesale market in China. That consideration was corrected later with the confirmation of the human to human transmission among confirmed patients [28-30]. According to the current evidence, the 2019-nCOV virus is transmitted among humans through respiratory and droplets routs of infection (Figure 1) [31-35]. Droplet transmission occurs when the mucous membranes (mouth, nose, or conjunctiva) are exposed to the infected droplets (i.e. coughing, sneezing, or vomitus) through direct contact from close contact with an infected person or indirect contact with surfaces within the close environment of the infectious person [36,37]. The airborne route ensues aerosols producing procedures including cardiopulmonary resuscitation, invasive, and non-invasive ventilation procedures in addition to other invasive procedures as bronchoscopy, tracheostomy, and open suction [37,38]. Moreover, evidence suggests that the virus can invade the intestinal mucosa and subsequently can be excreted and isolated in faeces [39]. Based on the preliminary data, viral shedding can occur before the onset of symptoms with a mean duration of twenty days and the longest recorded duration of thirty-seven days [40]. The disease course of COVID19 varies among patients. Around 85-90% of patients develop mild or moderate symptoms with the remaining 10-15% who progress to viral pneumonia with severe lung affection and development of acute respiratory distress syndrome with an average calculated mortality rate that ranges between two to five percent [41-43]. The duration from the onset of disease symptoms to death ranged between one week to six weeks with a median duration of two weeks. This wide range could be attributed to many factors as the patient's age, immune status, and associated comorbidities [44,45].

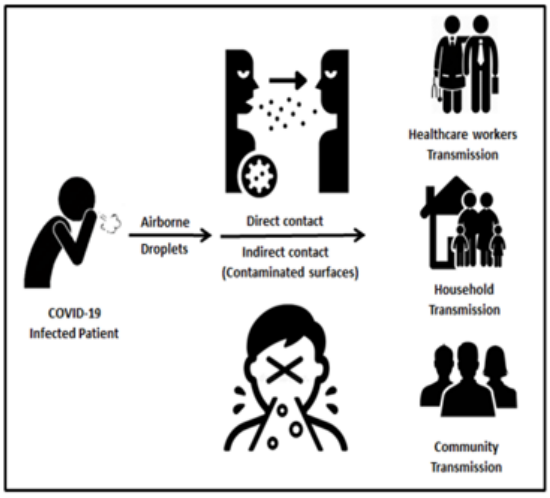

Figure 1: Modes of Transmissions of COVID-19 (According to WHO guidelines).

COVID-19 Pathogenesis

Pathophysiologic ally, COVID-19 begins with inhalation of the SARS-CoV-2 virus then binding to the epithelial cells in the nasal cavity resulting in viral replication and migration to respiratory tracts that is followed by the viral propagation within alveolar cells, resulting in increased viral replication.. Subsequently, this process followed by extensive viral invasion to cells that highly express ACE2, mainly lungs, heart, kidney, and gastrointestinal tract and eventually, the occurrence of cells apoptosis [46,47]. Although the mechanism of the pathogenesis of SARS-CoV-2 infection remains unclear and not fully explained, the mechanism of coronaviruses invasion to host cells involves five subsequent stages: attachment, penetration, biosynthesis, maturation, and release. The elementary (attachment) stage begins with viral binding to the functional (ACE2) receptors, then the occurrence of membrane fusion (penetration), followed by viral RNA replication inside the nucleus (biosynthesis), the formation of viral particles (maturation) and final stage is (release) of viral RNA into the nucleus [48,49]. The progressed deterioration of COVID-19 patients was attributed mainly to the subsequent process of an inflammatory storm due to immune-mediated inflammation, accompanied by an elevation in inflammatory markers and chemokine including interleukin (IL)-6, IL-10, granulocyte-colony stimulating factor (G-CSF), monocyte chemoattractant protein 1 (MCP1), macrophage inflammatory protein (MIP)1α, tumor necrosis factor (TNF)-α and C-reactive protein. Besides, there is a significant decrease in B cells, T cells, and natural killer (NK) cells. This process has an important role in the pathophysiology and increased mortality of COVID-19 [40,50]. The innate immunity response is initiated following the viral invasion. Particularly, airways epithelial cells, alveolar macrophages, and dendritic cells are the main target cells for triggering innate immunity response [51]. The subsequent inflammatory reactivation triggers the coagulation cascade by cytokines including IL-6 resulting in abnormality in the fibrinolytic system and formation of blood clotting (Figure 2) [52]. The pathogenesis of COVID-19 involves the stages of viral invasion including attachment, penetration, biosynthesis, maturation, and release. This causes abnormal cell function and reproduction. The consequence of this process leads to inflammatory reactivation and inflammatory storm resulting in cell apoptosis and hypercoagulation. Disseminated intravascular coagulation (DIC) was reported in over 70% of non-survivors of COVID-19. These deteriorating patients exhibit a hypercoagulation that was confirmed by elevated d-dimer and fibrinogen levels and abnormal levels of prothrombin time, fibrinogen, and thromboplastin time. Besides, a post-mortem examination showed thrombus formation in COVID-19 victims [53].

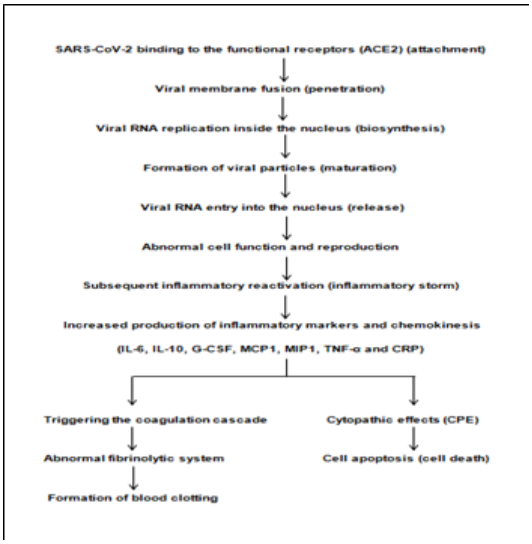

Figure 2: SARS-CoV-2 Pathophysiology.

Diagnosis of COVID-19

Clinical diagnosis

Given that the primary replication site for COVID-19 is the lower respiratory [54]. most patients present with cough, fever, dyspnea, fatigue, and myalgias with an incubation period that ranges between two to fourteen days with an average of five days [55]. Still, observations showed that many carriers do not express any symptoms [43,56]. Since most of the clinical presentation is non-specific, the World health organization developed surveillance criteria as shown in Table 2 In addition to the previously mentioned symptoms, COVID19 patients may develop a headache, hemoptysis, and diarrhea in addition to lymphopenia and dry or productive cough [44,64-66]. Recently, smell and taste dysfunctions have been recognized as warning signs for COVID19 infection even without the development of fever especially in young and immunocompetent patients [67]. It is worth noting that, symptoms alone cannot eliminate the possibility of infection by other beta coronaviruses that were

responsible for the former outbreaks in the last two decades [65,68]. However, some symptoms are suggestive of COVID19 infection such as the sore throat and cough as well as the gastrointestinal symptoms like diarrhea [30].

Table 2: World Health Organization surveillance criteria [55].

	Criteria
Contact	An individual exposed to any of the following experiences in 2 days duration before and 14 days after the onset of symptoms of a probable or confirmed case:
	a) Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes.
	b) Direct physical contact with a probable or confirmed case.
	c) Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment.
	d) Other situations as indicated by local risk assessments.
Suspect case	1) A patient with fever associated with at least one of the following acute respiratory illness:
	a) Cough
	b) Shortness of breath
	2) The patient is having a history of either one of the flowing:
	a) Travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days before the onset of symptoms.
	b) Contact with a confirmed or probable COVID-19 case in the last 14 days before the onset of symptoms
	c) Requiring hospitalization with the absence of an alternative diagnosis that fully explains the clinical presentation
Probable case	A suspect case having either one of the following conditions:
	a) testing for the COVID-19 virus is inconclusive
	b) testing could not be performed for any reason
Confirmed case	A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs, and symptoms.

Laboratory Diagnosis

Sample collection

In general, specimen collection, handling, or testing for laboratory diagnosis are critical steps for proper diagnosis and treatment. The improper sample collection, handling, or testing of clinical specimens for COVID-19 may lead to false-negative test results and inaccurate disease management. Therefore, strictly following the slandered guidelines and recommendations for sample collection would lead to better results and diagnosis. There are two targeted sites for COVID-19 samples collection, the first is the upper respiratory tract samples and the second is the lower respiratory tract samples. The upper respiratory tract samples include nasopharyngeal swab, oropharyngeal (Throat) swab, nasal mid-turbinate (NMT), anterior nares specimen, and nasopharyngeal wash/aspirate or nasal wash/aspirate. On the other hand, the lower respiratory tract samples include bronchoalveolar lavage, tracheal aspirate, pleural fluid, and lung biopsy. According to the Center for Diseases Control and Prevention (CDC), the golden standard for coronaviruses sampling including CODID-19 is the nasopharyngeal (NP) swab/oropharyngeal (OP) swabs [69]. A nasopharyngeal or oropharyngeal (Throat) swab specimen should be collected by an experienced healthcare professional. An (NP) swab has become the recommended swab as it is tolerated better by the patient and is safer for the operator. While in patients with pharyngitis as a dominant initial presenting symptom can be adequately sampled via the OP route [62]. The SARS-CoV-2 RNA was detected in 63% of NP swabs, which was significantly higher than the level in OP swabs (32%) [63]. In some cases, NPs/OPs/saliva may miss early infection as the main replication site may have shifted to the lower respiratory tract. Repeated swab or obtaining lower respiratory tract specimens may be important and required particularly if a patient has a clinical picture of COVID-19 pneumonia [65,66]. The lower respiratory tract specimens are collected from sputum sampling or Bronchoalveolar lavage (BAL) (Table 3) [70-71].

Table 3: The different types of Tests for SARS–CoV-2/COVID-19 and its potential uses.

Test type	Samples	Measure	Potential uses	Grantee
Detect viral RNA through nucleic acid amplification	NPs/OPs/ saliva/ BAL/sputum	Current or suspected infection SARS–CoV-2	Management and medical support to Patient.	Individuals with Current or suspected infection.
			Social distancing measures.	Health care provider
			Prevention and control	Public health.
Detect IgM, IgA, IgG, or total antibodies	Blood	Past exposure to SARS–CoV-2	Herd immunity.	An employee who could be returned to work.
			Mitigation strategies	workers on experimental therapy (vaccine)
			Detect susceptible individuals.	
			Facilitate contact tracing and surveillance.	

Molecular Diagnosis

Genetics of SARS-CoV2

The genomic sequence of the coronaviruses encodes four major structural compartment proteins, namely spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins. Functionally, the E and M proteins are essential in viral assembly, while the N protein is important for RNA synthesis. There are two subunits of S protein, the first is the S1 domain, which plays a crucial role in binding to the functional receptor and viral cell invasion, and the second is the S2 domain, which is responsible for mediating fusion of the viral and cellular membranes. Therefore, S protein is the main target for therapeutic and vaccination pathways [72,73].

Tests

The detection of viral RNA nucleic acid using real-time RT-PCR is the most currently accepted test for direct detection of SARS–CoV-2 infection [74-76]. Following collection, the specimens are placed into a liquid to release virus/viral RNA from the swabs into solution. Then, viral RNA is extracted from that solution and subsequently amplified (e.g., by reverse transcription-PCR). The main advantage of real-time RT-PCR assays is that amplification and analysis are done simultaneously in a closed system to diminish false-positive results associated with amplification product contamination [62,77].

Serological diagnosis

Serological methods have focused on detecting serum antibodies against S proteins from the coronavirus spike and N protein from nucleocapsid [78]. Antibodies to the N protein are mostly detected in COVID-19 patients [79,80]. suggesting that the N protein may be one of the immune dominant antigens in the early detection of COVID-19 [81]. Lateral flow assays have been developed for the rapid detection of antibodies (IgM and IgG) against COVID-19 [82]. Which provides a fast time to result and low-cost detection of SARS-CoV-2 but is likely to suffer from poor sensitivity early in infection [83-87]. Antigen detection may miss cases due to low infectious burden or sampling variability. Serological methods play an important role in the epidemiology of COVID-19 and in determining the immune status of asymptomatic individuals but are unlikely to play any role in screening or for the diagnosis of early infections [79,80,88]. However, serology may be useful for confirming the diagnosis of COVID-19 [89].

Radiological diagnosis

Although the confirmation of COVID-19 infection is primarily dependent on the application of reverse transcriptase-polymerase chain reaction (RT-PCR) (64% sensitivity), still, imaging modalities can play an important role in suspecting COVID-19 patietns [90]. The X-rays findings in COVID-19 patients range from no apparent lesions especially in the early stages of the disease to unilateral or bilateral or even diffuse lung opacities (Figure 3) [91,92].

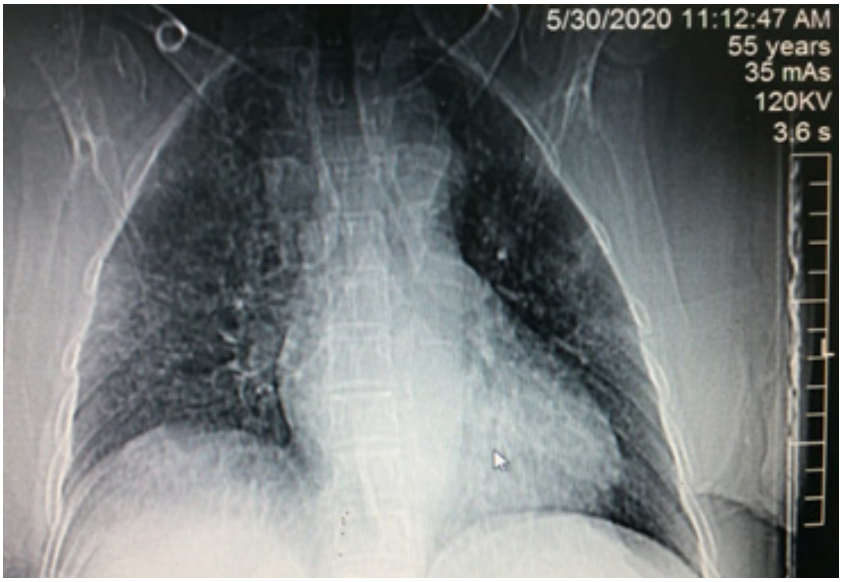

Figure 3: A 55- years-old male presented with fever, dry cough, and shortness of breath. Posteroanterior X-ray chest is showing diffuse lung opacities, suspecting of COVID-19.

On the other hand, computed tomography (CT) examination found to have superior diagnostic power to the ordinary radiographic techniques in COVID-19 patients. The CT findings progress with the disease course from normal examination in early symptomatic patients to focal ground-glass opacities in mild patients that may progress to a unilateral or bilateral diffuse ground-glass appearance in advanced cases (figure 4) [93-97]. Other associated lesions include bronchial dilation, linear opacities, and subpleural bands in addition to multiple subpleural peripheral ground-glass opacities in both lung fields. On the other hand, solid nodules, cavities, pleural effusion, and lymphadenopathy rarely develop [98,99]. However, dependence on the radiographic examination for the confirmation of COVID-19 infection has some limitations. the most important is the overlap between radiographic findings in COVID-19 infection and those findings in the other infiltrative pneumonia. Moreover, the limited availability of the advanced imaging techniques with the inconsistent use of the radiographic terminology in the reports limits the value of radiographic examination as a primary diagnostic tool for the current pandemic [100].

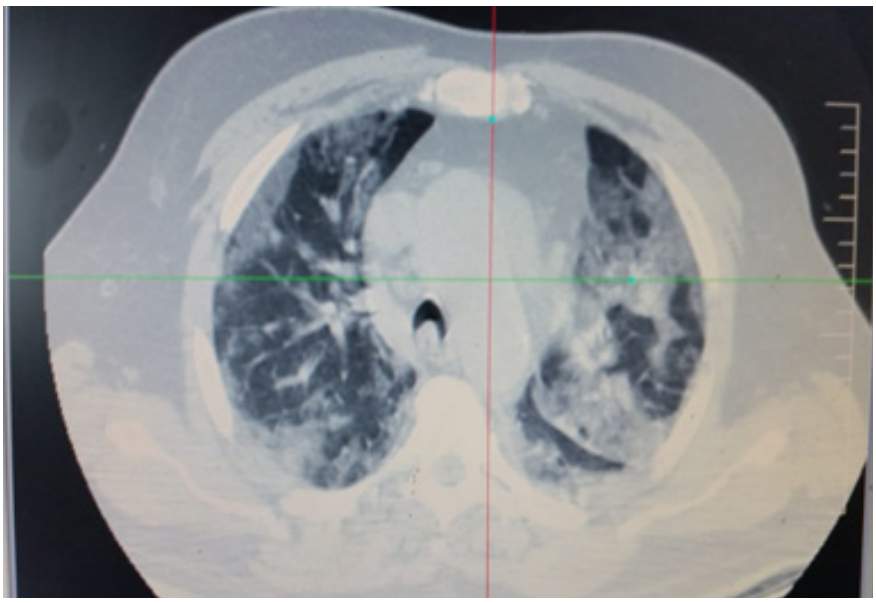

Figure 4: CT axial view of the same patient showing a diffuse ground glass of both lungs.

Forensic Investigations

An autopsy is of distinguished significance for the interpretation of the pathological changes and pathogenesis of deaths related to Coronavirus Disease and can provide a scientific basis for the measures of prevention and control of the pandemic. Even though, it is not advised to perform a forensic examination of confirmed or suspected COVID-19 deaths unless indicated for medicolegal reasons [101]. As the Coronavirus could survive in infected cadavers for a longer period due to the favorable conditions during refrigeration [102].

General rules for forensic pathology examination[103, 104]:

- The primary concern of forensic autopsy is to investigate the cause of death in medicolegal cases with the unconfirmed medical cause of death.
- The forensic medical authority should follow the guidelines of their national and local health departments when formulating work procedures and emergency plans for epidemic prevention and control.
- Autopsy sites should have protection protocols and security in place to guarantee personal and public safety.

Cadaver examiner

A senior forensic pathologist must perform the examination, for safety reasons, only one person to cut at a given time and limit the number of personnel working in the autopsy room [105].

Autopsy room

Autopsy room should be with sufficient and sustained negative pressure, air, and sewage discharge equipped with filtration or disinfection devices. If an autopsy room with negative pressure is not available, cadavers can be dissected in a disposable safety bag specially designed for postmortem examination of infectious diseases, it can completely isolate the infected body from forensic pathologists and surroundings. The examiner, from outside, performs the autopsy on the cadavers in the transparent bag using safety sleeves and gloves. If it is considered that the death is related to Coronavirus Disease (COVID-19), forensic examiners can choose either to perform a complete autopsy or a staged postmortem autopsy in which only diagnostic samples are taken and considering for subsequent autopsy after the results of these diagnostic tests being available. However, for the safety of the medical personnel, the staged technique is more recommended in suspected infection with coronaviruses if possible [106].

Clinical Features

There is no much differences in the assessment criteria for the possibility of COVID-19 infection in living patients or deceased with the exception that the timelines are given in the guidance refers to the time before death or the onset of related symptoms before death [107].

Pathological Findings in COVID-19

Although several case reports have been published recently on autopsy results, the information regarding the pathological findings in COVID-19 is limited [108,109]. Reports recognized most he macroscopic features of COVID-19 pathology being mainly in the chest in the form of pleurisy, pericarditis, lung consolidation, and pulmonary edema which lead to Increase Lung weight, purulent inflammation more typical of bacterial infection as a secondary infection [103]. Besides, the early histopathological findings in asymptomatic patients were in the form of edema, pneumocyte hyperplasia, focal inflammation, and multinucleated giant cell formation while no hyaline membranes were seen [108]. While in severe COVID-19 infection, marked histopathological findings include diffuse alveolar damage with exudates, predominant lymphocytic infiltration, and multinucleated giant cells were seen rather than a large typical pneumocytes [106]. Micro vesicular steatosis with mild inflammation was observed in the liver, although it is unknown whether this was due to the virus or iatrogenic. The features are much the same as those seen in SARS and MERS-coronavirus infections [110,111].

The Autopsy Procedures

Upon autopsy, the samples required to diagnose COVID-19 include a 5 mL of plain blood (no additive) for serology, upper respiratory, and digestive tract swabs (Nasopharyngeal Swab) and lower respiratory tract samples (Lung swab from each lung) by using synthetic swabs with plastic shafts [112]. The recommendation to take standard samples, such as respiratory tract swabs and tissue samples, and send them to local microbiology laboratory simultaneously to detect pathogens in the differential diagnosis [101]. Where possible, complete tissue histology

set from the upper airway, lung, and other major organs are also recommended along with other specific investigations [111]. Unfortunately, standard formalin-fixation inactivates known coronaviruses and SARS-CoV-2 [113]. Samples such as blood, urine, and cerebrospinal fluid, where appropriate, should be collected before opening the body cavity under sterile conditions to reduce contamination by using alcohol-containing disinfectant to clean the skin. Blood cultures should be taken from the subclavian vein, jugular vein, or left ventricle to avoid contamination from the bowel [114].

Prevention and Control

The COVID-19 has been found to have higher levels of transmissibility and pandemic risk than the SARS-CoV and MERS-CoV. The current applied Measures are aiming to protect general population groups from severe illness and fatal outcome by reducing transmission and enabling the reinforcement of healthcare systems [115.] The following public health measures to prevent or slow down the transmission and mitigate the impact of the pandemic should be applied at two levels: Community-level (Figure 5) and health care worker level [116]. At Community level, social distancing measures (including isolation of cases and quarantine of contacts; measures at, or closure of, workplaces and educational institutions; restrictions in movement and social gatherings) should be implemented proactively and with active community engagement in order to decrease the impact of the epidemic to avoid the overwhelming of the health care systems and permitting the healthcare systems to get ready to cope with the increased influx of patients. Moreover, Rigorous handwashing, respiratory etiquette, and the use of face masks are essential measures helping in minimizing the community transmission [117]. At the health care worker level, Contact, droplet, and airborne transmission are all relevant during airway maneuvers in infected patients, mostly during tracheal intubation. Personal protective equipment (PPE) is an important component for the protection of the medical staff and the patients from infection [118]. A number of organizations have produced different guidance on (PPE) which is broadly consistent, including the World Health Organization; the European Centre for Disease Control; Public Health England; and the European Society of Intensive Care Medicine and Society of Critical Care Medicine [119-122]. All organizations state that airborne precautions consist of fit-tested and fit-checked high filtration mask; goggles or visor; long-sleeved fluid repellent gown; and gloves.

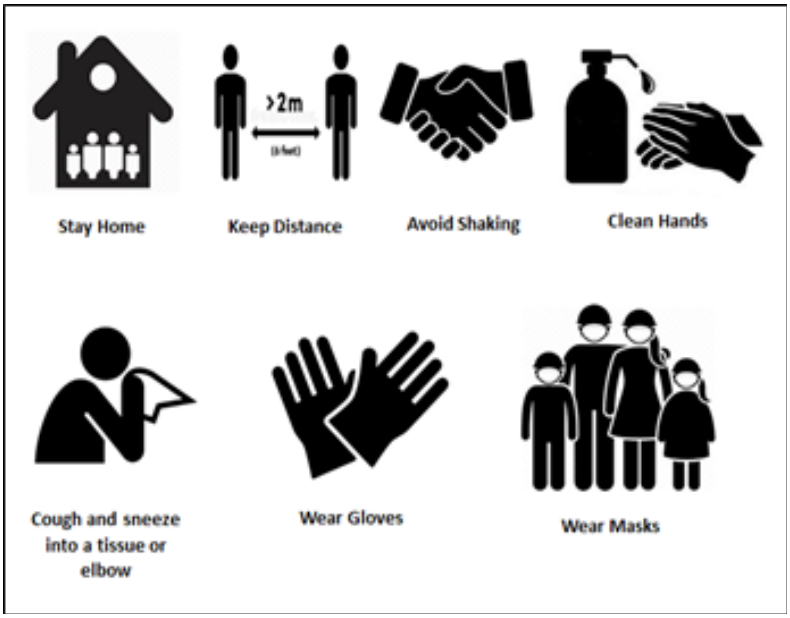

Figure 5: Precautions for Protection Against Coronaviruses (According to WHO preventive guidelines).

The Mask Efficiency

Fluid-resistant surgical facemasks are mostly used to protect against droplets. If the patient-worn it, it will prevent dispersal of large respiratory droplets which will protect staff against both droplet and contact transmission [123]. If the staff wore it, it would minimize droplet transmission, when within 1-2 m of the patient. Risk prevention by at least 80% is estimated [119]. The terms filtering facemask FFP2, FFP3, and N95 are used in reference to high performance filtering masks. Filtration is achieved by a combination of a web of polypropylene microfibers and electrostatic charge. There are three classes of protection, coherent with the European standard EN 149 + A1:2009 [124] each with an assigned protection factor which indicates the degree to which the mask will minimize the concentration of the hazardous substance.

For FFP1, FFP2 and FFP3 these are 4-, 10- and 20-fold, respectively [125]. The N95 masks prevent at least 95% of solid and liquid aerosol particles. The N, R, and P masks refer to their increasing resistance to oils and the number (95, 99, or 100) describes the minimal percentage of particles filtered under test conditions [126]. Personal mask fit-testing should be undertaken by each relevant member of staff before they are worn on clinical duty [127,128].

Treatment

So many hopes are focused on the current international efforts exerted to develop treatment protocols for COVID-19. So far, no treatment option nor a vaccine had been approved to be safe and effective for curing symptomatic patients nor minimizing the duration of the carrier state. The current challenges forced the clinical trials to test the efficiency of the off-label medications against severely symptomatic COVID-19 patients [129]. A broad-spectrum antiviral combination (oseltamivir, lopinavir, ritonavir, and ganciclovir) is currently used by the clinician to help in dipping the 2019-nCoV load to increase the chances of the host immunity to combat the infection [130]. On the other hand, the trial on interferon did not reveal a positive clinical impact on the patient rather than worsening the pulmonary lesions [98]. Besides, observational studies showed that the old antimalarial drug chloroquine and its analogue hydroxychloroquine demonstrated an in vitro inhibitory effect on the 2019-nCoV growth [131,132]. Moreover, initial studies showed improved outcomes and an increase in the virus clearance in those patients treated with chloroquine and hydroxychloroquine with higher safety profile and daily tolerable doses in the later [133]. On the other hand, a more recent multinational registry analysis included 96032 confirmed COVID-19 patients who received chloroquine or hydroxychloroquine either as a single therapy or in a combination of macrolides showed no benefit on the patient hospital outcome that was associated with an increase in the frequency of ventricular arrhythmia and decrease in-hospital survival [134]. In addition, trials were done to evaluate the effect of the antiviral drugs remdesivir and favipiravir on the patient outcome as well as the viral clearance that showed promising results [135,136]. Furthermore, therapeutics that demonstrated efficiency in treating the previous influenza pandemic were included in the trials to assess their effect on the patient outcome and viral load. Those pharmaceutical compounds include Lopinavir, Ritonavir, EIDD-2801, and peptide EK^{30}.

Vaccination

Observations on the immune response to COVID-19 exposure indicate that the virus can escape the host immune response through adaptation. This could help in clarifying the relatively higher incubation period in cases of COVID-19 in comparison to the influenza virus [137]. This creates an urgent need to develop a vaccine to increase the population resistance against the virus. Consequently, several research groups are working on the development of different types of vaccines that can withstand 2019-nCoV. These types include the recombinant-subunits containing viral epitopes, adenovirus-based vectors, and purified inactivated virus [138-140]. An ongoing study is conducted on ChAdOx1 nCoV-19 (a chimpanzee adenovirus-vectored vaccine expressing the SARS-CoV-2 spike protein). The primary results of the study revealed immune specific cellular and antibody responses against SARS-CoV-2 of 91% of the study group in 2 weeks and 4 weeks, respectively. With the administration of the dose, 100% of the included individuals expressed neutralizing antibodies against SARS-CoV-2 with no or minimal adverse reactions [141].

Conclusions and Future Prospective

The pandemic COVID-19 is one of the serious diseases in this century and has a high priority for governmental and health organizations worldwide. Up to date, no effective therapeutic antivirals for COVID-19 and researchers and scientists worldwide carrying out extensive research to discover the SARS-CoV-2 vaccine or successful antiviral. Meanwhile, medical practitioners are focusing to establish different protocols for medical management to cease or moderate disease progression. Medical autopsy of confirmed cases of COVID-19 can play a conspicuous role in the complete understanding of the disease and subsequently developing effective planes for management. However, restrict precautions should be applied during the preservation and performance of autopsy to protect the medical personnel. Besides, different authorities around the globe are enhancing the efforts to increase community awareness regarding the prevention management to reduce the virus spread. Finally, accelerated research and investigations in the fields of pathophysiology, pharmacology, and genetics of COVID-19 are progressing to develop targeted vaccinations and successful therapeutic regimens.

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