The universal spread of novel virus named coronavirus disease 2019 (COVID-19) also known as 2019-nCoV, Middle East Respiratory Syndrome and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) declared by the world health organisation (WHO). This virus has dived in to multiorgan, with clinical manifestations of fever, sore throat, dry cough, dyspnoea, chest pain, nausea, vomiting, diarrhoea and muscle pain. As novel coronavirus been categorised as HG3 infection which has highest with inhalation and by skin surface contact. As previous pandemics have occurred like SARS and MERS special attention to autopsy had been given to prevent exposure to the healthcare workers. Similar attention should be given to the autopsy protocols and underlying pathology for COVID-19 infection so as to better understanding of the disease for further control and treatment guidelines. Thus, herein we bring and summarise review of literature for understanding.

**Keywords:** Autopsy, COVID-19, forensic pathology

**Background**

The coronaviruses are ribonucleic acid (RNA) virus that are source of various critical, widespread and fatal universal infections including the Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The WHO declared the outbreak in January 2020, an outbreak of serious coronavirus infection (COVID-19) also known as 2019-nCoV and SARS-CoV-2. The outbreak was originated from the city in China named Wuhan. This continues to unfurl across 26 nations leading to a worldwide pandemic.

Basically, these viruses of Corona-viridae family are enveloped, non-segmented, positive sense single-stranded RNA genome viruses responsible for significant mortality and morbidity in the past. The subfamily of these viruses known as Ortho-coronavirinae. These further have four genera: Alpha, beta, delta, and gamma. Importantly, alpha and beta CoV are known to affect the mammals. The SARS-CoV-2 pathogen has been reported to share similarities with SARS-CoV as per its genomic sequence, biological and clinical behaviour is concerned. Structurally, these have surface glycoprotein, envelope protein, matrix and nucleocapsid protein as major structural proteins. The surface glycoproteins are arranged in spikes. Reportedly, the glycoprotein binds the receptor binding domains of the enzyme. There are many enzymes which act as entry point but Angiotensin Converting enzyme-2 (ACE-2) is the important and vastly studied. However, many tissues has this enzyme like respiratory tract, liver, kidney, brain, lymphoid rich tissues like: gastrointestinal tract, lymph nodes, thymus and spleen. The most commonly reported symptoms/presentation include fever, sore throat, dry cough, dyspnoea, chest pain, shortness of breath nausea, vomiting, diarrhoea and musculoskeletal involving muscles and joint pain.

The infections at workplace (laboratories) are explained and regulated by Health and Safety Executive (HSE). In the UK, a committee named Advisory Committee on Dangerous Pathogens (ACDP) categorises these infections as a health hazard to the microbiologists/mortuary staff and those involved in the clinical and research microbiology activities into four groups (HG1–HG4) Table 1. The main categorization of these groups is according to three considerations.
The Autopsy Risk and Handling

For the autopsy handling and related risks guidelines have been issued by Royal College of Pathologists (RCPPath) for the 1) Approach to COVID-19 patients, 2) improve the facilities (state of mortuary and equipment) of the mortuaries to reduce the likelihood of dangerous infections, 3) to prepare SOP to cover anticipated infections, 4) to provide personal protective equipment (PPE) kits and safe handling of the dead bodies, 5) preventive prophylaxis of the staff and reduce the risk of the mortuary staff to minimal using and following these guidelines. The risk of contracting HG3 infections in mortuary are highest with inhalation followed by skin surface contact. The Control of Substances Hazardous to the Health Regulations (COSHH) guidelines for practitioners outlines the risk assessment in each case. Prior to autopsy, it is important to include all the clinical notes, the hospital file and laboratory records including positive serologies and direct information from clinicians, for the risk assessment to the healthcare workers.

The Autopsy Room and Other Pre-Requisite

Recommendation for the cautious working, there should be an ideally separate, fully equipped, well ventilated high risk suite of which a pathologist should be an integral part; as autopsy is the most important time to visualise the internal organs and withdraw additional samples if required. All the key tools/material must be gathered prior to the post-mortem examination (e.g. vials, containers, electric bone saws, etc.) so as to minimise/negate the need to enter the working space again and again. Shoes worn during the autopsy should remain inside. Proper shower rooms with hygienic products and clean towels should be available. Blunt ended scissors, blunt ended PM 40 blades will minimise many sharp injuries. Only one examiner working at one time in the body will also be helpful in preventing taking duplicate samples or missing samples due to miscommunication. Organs which require fixation should be properly sliced and shall sent to pathology laboratory in formalin. Needles need to discarded in sharp bins without resheathing. A list of minimum PPE in case of suspected coronavirus case should be given to the deployed staff. Table 2: After assessing the risk in each case for COVID-19 infection, the decision to proceed for detailed post mortem examination or a limited one (to obtain samples/swabs to confirm COVID-19), or staged post-mortem (in which samples are taken to assess COVID-19 infection) and a further sampling if required should be considered and recommended. However, the utility of a limited autopsy (single organ sampling or needle sampling) remains an issue of debate especially in concern to autopsy practice in countries with lack of resources, limited mortuary facilities and staff. The limited autopsies can provide useful information in systemic infection where samples from blood, liver, spleen can be taken. However, if the infections are focal or localised then use of minimally invasive autopsies should be deterred. To summarise, a nasal swab is preferred method for COVID-19 diagnosis, but it should be aided with blood samples and autopsy samples.

Pathology in COVID-19 Autopsies

As discussed earlier the previous pandemics caused by the coronavirus families (MERS-CoV and SARS) were studied for their detailed pathology by performing autopsies. In the year 2004, Chong PY, et al. postmortem in six with probable SARS, eight with suspected SARS and subjected tissues to light microscopy and immune-fluorescence. On gross examination, patients confirmed as SARS showed multiple hemorrhagic infarcts in both lungs, subpleural hemorrhages, red and gray hepatization along-with organizing thrombi in the pulmonary arteries. On microscopic examination, majority of patients had acute phase diffuse alveolar damage and hyaline membrane formation. On autopsy, main pulmonary artery or segmental pulmonary arteries showed pulmonary emboli. In one of the patient’s thrombi even extended to the para-ovarian and para-uterine veins. Infarction of multiple organs showed widespread intravascular fibrin thrombi including heart, spleen and kidneys. In addition, liver showed wide-spread centrilobular necrosis, steatosis and periportal inflammation.

The first autopsy of MERS was done in UAE which showed diffuse alveolar damage on histopathology of lung. Exudative-phase with diffuse alveolar damage with sluffing of the bronchiolar epithelial layer, widespread hyaline membranes

Table 1: Advisory Committee on Dangerous Pathogens (ACDP): Hazard categorisation

| Category | Hazard categorisation |
|----------|-----------------------|
| Category 1 | No transmission to the humans. |
| Category 2 | May spread to humans and occupational hazards |
| Category 3 | Cause severe diseases in human and significant occupational hazard. Contagious to other humans. |
| Category 4 | Cause severe diseases in human and significant occupational hazard. Non-contagious to other humans. |

Table 2: List of PPE for mortuary staff

| PPE | |
|------|---|
| Whole Body Surgical Suit | |
| Scrub head cap | |
| Face Glass Shield | |
| Plastic apron | |
| Surgical Scrub | |
| Rubber Boots | |
| Protective neoprene gloves | |

Previously, while the majority coronavirae were categorised as HG2, MERS and SARS were categorised as HG3 pathogens with the latest addition of SARS-CoV-2. As discussed earlier the previous pandemics caused by the coronavirus families (MERS-CoV and SARS) were studied for their detailed pathology by performing autopsies. In the year 2004, Chong PY, et al. postmortem in six with probable SARS, eight with suspected SARS and subjected tissues to light microscopy and immune-fluorescence. On gross examination, patients confirmed as SARS showed multiple hemorrhagic infarcts in both lungs, subpleural hemorrhages, red and gray hepatization along-with organizing thrombi in the pulmonary arteries. On microscopic examination, majority of patients had acute phase diffuse alveolar damage and hyaline membrane formation. On autopsy, main pulmonary artery or segmental pulmonary arteries showed pulmonary emboli. In one of the patient’s thrombi even extended to the para-ovarian and para-uterine veins. Infarction of multiple organs showed widespread intravascular fibrin thrombi including heart, spleen and kidneys. In addition, liver showed wide-spread centrilobular necrosis, steatosis and periportal inflammation.

The first autopsy of MERS was done in UAE which showed diffuse alveolar damage on histopathology of lung. Exudative-phase with diffuse alveolar damage with sluffing of the bronchiolar epithelial layer, widespread hyaline membranes
and deposition of fibrin in the alveoli were the predominant pulmonary histologic pattern. Also, edematous fluid in alveoli with dense inflammatory infiltrate comprising acute and chronic inflammatory cells, along with hyperplasia of type 2 pneumocytes and rare multinucleated cells was also reported. However, none of the viral inclusions were reported. Further, viral antigens illustrated with IHC and double staining showed localization of antigens to type 2 pneumocytes and syncytiot cells. Ng et al. [8] thus highlighted that direct cytoplasmic effects in the pneumocytes, suggesting development of respiratory system symptoms. These pathological features of MERS-CoV are also shared by SARS-CoV, highlighting the widespread alveolar damage.

Similarly, the autopsies of patients with confirmed cases of SARS-CoV-2 infection can provide us with important details and comprehension about the novel disease and its course. In the recent case report by Xu et al. [9] in 2020 in COVID-19 biopsy samples from multiple organs including heart, lungs and liver. They reported cellular fibro-myxoid exudates with bilateral diffuse alveolar damage (DAD), type 2 pneumocyte sluffing and thick hyaline membrane formation which are features of acute respiratory distress syndrome (ARDS). Similar findings were reported, in addition many of the cells showed viral cytopathic effects. Viral inclusions were not found.

During early 2020 in USA, two autopsies of a 77 year and 42 year males of confirmed cases of SARS-CoV-2 (on nasopharyngeal swabs) were conducted. On external examination, bilateral lungs were heavy with diffuse consistency. Microscopic examination revealed DAD with hyaline membrane formation, the interstitium showed patchy infiltrate with lymphocytes and edema in alveoli. Bronchi and bronchioles showed chronic inflammatory infiltrate (acute bronchopneumonia).

The pathogenesis of SARS coronavirus was shown to be very complex involving mainly epithelial cells leading to alveolar damage along with edema and hyaline membrane organization with mononuclear cell infiltration comprised of macrophages, multinucleated giant cells. The other organs reportedly infected include mucosa of intestine, tubular epithelial cells of kidneys, neuronal system. The organs are mainly affected by indirect injury. Another recent pathological study was conducted on four cases for postmortem core biopsies. Three of the four cases showed hyaline membrane formation, vascular congestion, pneumocyte injury, infiltration by mononuclear cells and giant cells. Whereas, one of the cases in addition also showed intra-alveolar fibrin cluster formation, type 2 pneumocyte hyperplasia, fibrinoid necrosis of the small vessels and features of broncho-pneumonia. In the largest study by Edler C., on patients dying of novel coronavirus from March to April 2020, included 80 patients in which 74 patients were diagnosed antemortem and rest (6) were diagnosed postmortem. It was concluded that characteristic of COVID-19, the lungs were heavy due to edema, probably due to retained fluid. Histologically, few cases showed widespread alveolar damage with hyperplasia of type 2 pneumocytes, few fibroblasts, proteinaceous exudates, hyaline membrane with advanced changes of squamous metaplasia and fibrosis. In addition, the small pulmonary arteries also showed infiltration by lymphocytes and plasma cells with advanced stages there is destruction of alveolar septae, fibrosis and lymphocytic infiltrate.

Elsoukkary SS, et al. [10] showed in their study 84% of the patients had both macroscopic and microscopic thrombi on autopsy examination along with raised D-dimer levels (69%). Also showed thrombi in other vital organs most frequently in lungs in 78% and cardiovascular system in 25%. Macroscopically pulmonary thrombi were detected in 34% cases.

A very few studies are done on full body autopsies due to risk of infection and other measurements done for infection control. Falasca L, et al. [11] did full body autopsies in COVID-19 patients. They have shown findings in the spleen and bone marrow also. Vital changes are noted including lymph node and megakaryocytic hyperplasia. Furthermore, they have given stress on use of immunohistochemical and electron microscopic analysis for further analysis.

**Conclusion**

Thus, to conclude, there is a need to understand the underlying pathology of the novel coronavirus. Recently published literature mainly shows that the coronavirus mainly plays a role in the pathogenesis by attacking the respiratory system and also leading to widespread thrombosis. More studies on autopsies are required to know more about the pathological changes in various other organs. Full body autopsies have provided detailed analysis of every organ along with bone marrow examination. Furthermore, use of immunohistochemistry and electron microscopy must be added to learn the disease pathogenesis at molecular level. Safety precautions to be undertaken and are of utmost importance for infection control. More studies and microbiological analysis on the formalin fixed specimens to assure the pathologist about inactivation of 2019-nCoV.

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**Conflicts of interest**

There are no conflicts of interest.

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