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Role of autopsy in COVID-19 patients

Vriti Pursnani, Amit Reche, Gaurav Majumdar, Prerna Gautam, Kumar Gaurav Chhabra*, Gargi Nimbulkar

Department of Public Health Dentistry, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Wardha, Maharashtra, India

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Abstract

Coronavirus disease 2019 had caused a pandemic leading to over 6M positive cases worldwide out of which 3.73 lac are demised (until when the article was written). Its first outbreak was seen in Wuhan, China. In the Indian scenario, we have a total of 2 lac cases out of which 5,679 have been deceased (until when the article was written). Due to the high transmissibility of this disease, the entire country is under lockdown to prevent the spread of the virus. The main etiology of this virus is the severe acute respiratory syndrome coronavirus-2(SARS-CoV-2). This affects the respiratory system leading to cough, shortness of breath, and fever. There have been cases with mild or no symptoms reported, but the cause of death is due to the virus. This helps us understand the diagnosis, epidemiology, symptoms, and pathophysiology about the virus, which can help in treatment modalities. An autopsy is one of the methods by which we can understand the systematic involvement other than the respiratory system. Various pathological, microbiological changes can occur in the other organs. Even though the person is deceased, the virus is highly infectious can cause the spread through body fluids. Proper care must be taken while handling the body and performing the procedure. This review article aims to focus on the autopsy findings found in various cases to study the disease pathophysiology of the SARS-CoV-2. This article also helps us understand the guidelines that have been put forward by WHO and CDC must be followed regarding the specification required in the autopsy room; PPE's to be worn, human waste and fluid disposal, body transportation. Proper personal hygiene must be maintained while handling the COVID-19 patients; this can lead to less susceptibility of acquiring the disease.

*Corresponding Author

Name: Kumar Gaurav Chhabra
Phone: 7976840339
Email: rajsushil.chhabra@gmail.com

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INTRODUCTION

We all are aware of the current situation that the world is facing. Every individual is in a state of complete distress and fear since there is no cure for this disease and it's a contagious disease. COVID'19 or Coronavirus is an infectious disease that affects the human's respiratory system mainly. The origin of this pandemic is said to be from Wuhan, China (Hui *et al.*, 2020). The transmission is due to inhalation of droplets or by coming in direct contact with the infected person or indirectly by coming in contact with the environment or object handled by an

infected person. Everyone till now is aware that the initial symptom starts with fever, difficulty in breathing, cough, fatigue, altered taste, and smell sensation and may progress to respiratory symptoms (Huang *et al.*, 2020). No treatment has been found until now, so the only treatment that could be done is by treating the patient symptomatically. Today the total people affected by COVID-19 are more than 49 lakh cases according to WHO (until till article is written). To deal with any disease, it is very important to know as to how a particular disease is affecting a human body, acknowledging the fact whether the disease has a uniform effect on every individual or there are variations or variations in the way the disease affects the body. So to conclude as to know how the virus is affecting the body, medical professionals are performing an autopsy on people who have demised because of coronavirus. An autopsy means "see for oneself", it is a detailed external and internal examination of the body, to either see the effect of a disease or to know the cause of death often used in crime investigations, etc. (Ayoub and Chow, 2008). An autopsy can reveal many important pieces of evidence and findings of the extent of damage the disease can cause and which all organs can be affected by it so that the treatment for the patients could be more specific and could be done in a better and effective way.

Etiology

Coronavirus is said to be an RNA virus having an envelope structure, and it consists of rod-like extensions from its surface can infect multiple hosts at a time (Holshue *et al.*, 2020). There was a high nucleotide similarity found in bat-like severe acute respiratory syndrome coronavirus (SARS-CoV) almost around 88% with corona'19. Therefore, it is proven that SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV are similar to COVID'19 (Ren *et al.*, 2020). The International Committee on Taxonomy of Viruses has put COVID'19 under the classification of SAR-CoV-2. Clinically COVID'19 belongs under the plague (Wang *et al.*, 2020).

Although the pathobiology of COVID'19 is not known as it has similarity with SAR-CoV therefore based on the studies of SAR-CoV, the disease can be put into three stages. First, the Asymptomatic state (Initial 1-2 days of infection), second is the Upper airway and conducting airway response (Next few days), third is the Hypoxia, ground-glass infiltrates, and progression to ARDS (Wu and McGoogan, 2020).

1^{st} phase- Asymptomatic phase

In this phase, the person doesn't show any type of signs or symptoms; although the virus levels are low still, the person is infectious. The person inhales the virus and it gets stuck in the nasal epithelium, especially the ciliary cells and the replication starts (Hoffmann *et al.*, 2020; Wan *et al.*, 2020). At this stage, the nasal swab is the most effective way to find out about coronavirus.

2^{nd} phase- Upper airway and conducting airway response

Since the individual is already affected and the virus has already entered the nasal passage, it travels through the respiratory passage, and the body's immune system is triggered due to which many cytokines and other cells get released (Tang *et al.*, 2005). One of which is CXCL10 interferon which reacts to SAR-CoV and influenza (Qian *et al.*, 2013). This helps in identifying the disease. In this phase, the individual will show some clinical symptoms. In 80% of the cases, the disease is limited to the upper respiratory and conducting airway (Wu and McGoogan, 2020) till this phase patients are been treated symptomatically and in a conservative way at home.

3^{rd}phase- Hypoxia, ground-glass infiltrates, and progression to ARDS

This is the ultimate phase, nearly about 20% of the cases proceed towards this phase towards the lungs and alveoli this may cause fatality and morbidity in some, the usual percentage is around 2% but it varies with age, as the morbidity is more commonly seen in elderly (Wu and McGoogan, 2020). In this, the virus affects the gas exchange units, in which the type II alveolar units are damaged (Weinheimer *et al.*, 2012). The viral particles are released in these units, which causes apoptosis of the cells, and then there is released of toxins that affect the neighbouring cells, and this spreads (Qian *et al.*, 2013). The pathologic conclusion states that there is diffuse alveolar damage with fibrin rich hyaline membranes and a few multinucleated giant cells (Xu *et al.*, 2020). Since the cells are undergoing apoptosis, the body will try to bring the damage back to normal and will start the process of healing, which will cause fibrosis and scar formation which will lead to various forms of ARDS. The healing will require tremendous innate and acquired immune response and epithelial regeneration.

The reason the elderly are more severely affected and more cases of mortality is seen in older ages is because their immune responses are much weaker and their mucocil**i**ary clearance is much slower (Ho *et al.*, 2001). There are many anti-viral drugs on trial for finding a cure for this disease. Though the pathogenesis is not very clear, this is based on the knowl-

edge so far collected.

Epidemiology

According to WHO, after the first case of coronavirus (COVID-19) on December 19, there has been a significant rise seen in no cases worldwide. The first outspread was seen in the seafood market named Huanan which is located in Wuhan, China, whereas the precise course of the first case of infection is still unknown (Lu *et al.*, 2020) Novel coronavirus or COVID-19 was named official by the World health organization after 29 December 2019 (Li *et al.*, 2020). This crucial virus predominantly attacks the human respiratory system. Severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV were included in the former epidemic of coronaviruses which was earlier specified as high risk to the health of the human community (Bogoch *et al.*, 2020; H. Lu., C. W. Stratton., Y. Tang et al., 2020). The COVID-19 started around December 2019. The first case was reported from 18 December 2019, where five patients were hospitalized. They had acute respiratory distress syndrome and among one of them died (Ren *et al.*, 2020). Till 2 January 2020, it was confirmed that 41 patients who were admitted in the hospital had laboratory-confirmedCOVID-19infection. It was observed that only one-third of them were having a disease such as diabetes, hypertension, etc. (Huang *et al.*, 2020).

Nosocomial infection was found to be the main reason for the spread of infection among these patients. It was found that the infection was spread through droplets or contact with the infected person. In china till 22 January 2020, 571 cases were reported in 25 provinces which included 17 death. Thereafter, 1975 cases were found with 56 deaths in mainland China (W. Wang., J. Tang., F. Wei et al., 2020). On 24 January 2020, china was having 5502 cases (Nishiura *et al.*, 2020). China had 7734 cases till 30 January 2020 and also it was spread to several countries such as the United States, The Philippines, India, Australia, Canada, Finland, France, Taiwan, Thailand, Vietnam, Malaysia, Nepal, Sri Lanka, Cambodia, Japan, Singapore, Republic of Korea, United Arab Emirates (Bassetti *et al.*, 2020). At first, it was found that infected travellers from china were the only reason for the global spread of COVID-19. Many countries, including Malaysia, Australia, Vietnam, Singapore, Japan, the united states of America, etc., have reported cases that are travel-associated. Sadly, after mid-February 2020 in South Korea, Iran, Italy, and Japan, it started spreading locally. On 18 February 2020, there were 31 cases in South Korea due to close contact from travelers. In South Korea, on 24 February 2020 resulted in 763 cases. Among them, 74.6% of cases were due to religious group Daegu metropolitan area that triggered the spread of disease domestically. The first confirmed case in the United States of America was reported first on 23^{rd} January 2020 from a traveller who came back from China. The SARS-CoV-2 positive patient was due to secondary transmission, the patient had not travelled from china and he was the husband of the index patient (Ghinai *et al.*, 2020). Number of COVID-19 cases were 395,926 on 7^{th} April 2020 and there were 12,757 deaths in the United States. There was a significant rise in no of cases in Italy. A total of 135,000 COVID-19 cases were noted with 17000 deaths on 7^{th} April 2020. After the united states of America, Italy is second in several COVID 19 cases but it is first in no of deaths. A group of travellers was quarantined from different countries in India on 2^{nd} March 2020. On 15^{th} March, many more were quarantined and most visas were suspended to India. On 11 March 2020 COVID 19 was declared a pandemic by WHO. Till 13^{th} March 2020, 5900 individuals were tested for SARS-CoV-2 despite 1.5 million traveller's to India (Venkatesan, 2020). It was 784,794 cases all over the world and 37,788 death by march 30,2020. It entered in India on January 30, 2020. There were about 1251 cases with 32 deaths in India by 30 march 2020. By 19^{th} May 2020, there are 96,169 cases from January 30, 2020, With 3,029 deaths and there are around 5000 cases per day in India according to the World health organization (WHO)Older age group above 60 years have an increasing number of mortality rate than that of younger age group. Household contacts are the main reason for infection in elderly people. Therefore, more attention should be given to this reason.

During the time of preparing this manuscript, there was 4,962,707cases with 3,26,459 deaths globally according to the World health organization (WHO).

SYMPTOMS

It has been reported that the symptoms may vary from mild to moderate. There can be severe conditions as well which may lead to death, though all the clinical signs and symptoms are not yet established. As observed by a medical professional, the arrival of symptoms in COVID-19 patients has roughly an incubation period of 5.2 days (Li *et al.*, 2020).

There is a span of 6 to 41 days that is an average of 14 days from the beginning of symptoms till death, which solely depends on the immunity and the age of the individual (W. Wang., J. Tang., F. Wei et al., 2020). After one week, Mid symptomatic patients show improvement, whereas it has been detected

that severe patients may lead to death as there is damage to the lungs alveoli, due to malfunctioning of the respiratory system. Pre-existing disorder such as hypertension, diabetes, cirrhosis, coronary heart disease, etc. were predominantly elderly patients (Huang *et al.*, 2020).

One of the most usual symptoms that are observed in patients of COVID-19 are fever, sore throat, cough, muscle ache, shortness of breath, nasal obstruction, and other symptoms include headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia (Huang *et al.*, 2020; Ren *et al.*, 2020). There many unusual features associated, such as acute respiratory distress syndrome, the incidence of ground-glass opacities, acute cardiac injury, and RNA aemia that can cause death. CT scan was also performed on these patients that revealed features of pneumonia (Huang *et al.*, 2020).

In the lungs rise of inflammation was observed, and in the subpleural region, ground-glass opacities were observed. An attempt was made to treat by inhalation interferon, but it also failed that resulted in pulmonary opacities. Results of Chest radiographs which was done on COVID-19 patients, showed hypoxemia with increased dyspnoea that was linked with infiltration of lungs (upper lobe) (Phan *et al.*, 2020).

There is an indistinguishable characteristic between beta coronavirus and coronavirus (COVID-19) which are dyspnea, bilateral ground-glass opacities (on chest CT scan), dry cough, and fever. But according to investigations, there are some exclusive features of this virus as it affects the lower airway such as rhinorrhoea, sneezing etc. (Holshue *et al.*, 2020). To eliminate a second possible route of infection investigation of faecal and urine (Zhang *et al.*, 2020) sample should also be taken into consideration as SARS-CoV-2 can transmit through the gastrointestinal tract as symptoms such as nausea, diarrhoea, and vomiting have been observed in suspected cases of COVID-19.

Also, there is enough evidence which provides information that acute gastritis and enteritis are caused by SARS-CoV-2 (Wan *et al.*, 2020). Previous studies had indicated that there this virus had the large capability of mutations which may cause increased transmissibility, decreased virulence and multiorgan infection (Jin *et al.*, 2020).

Thus there should be more advancements in diagnosis of various modes of transmission and strategies as an effect more to health care providers to control the spread of this disease (Rothan and Byrareddy, 2020).

AUTOPSY

As the decedents are bought in for autopsy, it is performed in a room that is isolated from the rest of the morgue. This room needs to have its ventilation, air condition to maintain the airflow and vacuum unit to isolate the aerosol, which is generated during electric bone cutting. All the equipment (swabs, culture bottles etc.) must be bought before starting the procedure to avoid leaving and re-entering the space to avoid contamination of the operating field.

The autopsy team must consist of highly experienced personnel which consist of a forensic pathologist, pathology technician and a circulator (if required).

The personal protective equipment (PPE'S) worn by the personnel are the head cap, protective eyewear, N-95 mask, scrub suits, autopsy dedicated shoes with shoe covers, long-sleeve waterproof grown (Tyvek suit), long-sleeved plastic apron, double gloves and cut gloves and powered air-purifying respirator with full face shield (PARP). Later, after the autopsy, the PPE's are disposed of and the scrubs worn under the PPE's are washed and sterilized in the laboratory. The autopsy tables with cleaned with disinfecting wipes and a clean towel which is discarded after use (Hanley *et al.*, 2020).

Initially, when the body is brought into the morgue, it is stored at 4°C and the autopsy should be done as soon as possible to prevent autolysis. A full-body autopsy is performed to evaluate every organ that could be affected due to the virus. Beginning from the thoracic cavity, dissection of the heart is done in the direction of the blood flow followed by dissection of organs like liver, spleen, kidney, large and small intestine inside the body. The exterior surface of these organs was examined thoroughly for any changes in the surface and further sections of these organs were taken for histological examination.

The skull was cut open using a hand saw to reduce the production of aerosol and the brain was removed from the cranium. In the case of lung, the swab was collected from the upper and bilateral lower respiratory tract as well as nasopharyngeal swab and then transported for real-time reverse transcriptase-polymerase chain react in (RRT-PCR) as well as sections of the tissue was taken for histologically examination.

There are other samples like blood, urine, cerebrospinal fluid that are taken before the autopsy in a sterile condition to avoid contamination. The blood drawn for these is taken from either the jugular vein or subclavian vein to avoid contamination of the sample from the bowel.

Systemic findings of few cases:

Respiratory system

The post-mortem radiographic examination shows bilateral ground-glass opacities.

On histological examination, "classical hallmark of diffused alveolar damage (DAD) can be seen that is mild interstitial thickening due to oedema, focal pneumocyte hyperplasia, and scattered hyaline membranes."

On open examination, the lung parenchyma was heavy with bluish-red coloration suggestive of capillary congestion and prominent mucosal oedema within the airspaces, bronchi and bronchioles were noticed focally.

A patchy to the diffused area is seen which indicated severe suppurative bronchopneumonia infiltrates. Mucus plugging of the airway and "tracheobronchitis / severe mucus tracheitis" could be observed.

Other findings like patchy and sparse interstitial leucocytes, in some cases, moderate lymphoid inflammatory infiltrate was found without the trace of viral RNA, oedematous parenchyma and alveolar haemorrhage in relation with peripheral and central pulmonary embolism.

Fibrin microthrombus was detected in small alveolar capillaries (Menter *et al.*, 2020).

Renal findings

The majority of autopsies noticed signs of shock in this system. These findings were observed in different cases. Histologically, "diffuse acute tubular injury with widened tubular lamina, flattened tubular epithelium and interstitial oedema". Acute pyelonephritis was observed with the corresponding lung findings, showed multiple foci of bacteria and polymorphonuclear casts in the lumen of tubules. Chronic inflammatory infiltrates with tubular atrophy and interstitial fibrosis. Arterionephrosclerosis, oncocytoma (renal mass) have also be noticed in a few cases. Transmission electron microscopy, virus RNA with electron-dense granules were observed in the cytoplasm of the "renal proximal tubule" and activated podocytes and endothelial cells were also noticed. In patients with diabetes, characteristic features of diabetic nephropathy have been noted (Hanley *et al.*, 2020).

Cardiovascular system

In hypertensive patients, myocardial hypertrophy is one of the commonest features observed. In aged patients, cardiac amyloidosis was diagnosed by the presence of ATTR amyloid during the autopsy. Most commonly amyloid deposits were found in the pulmonary vessels. In some cases, atherosclerosis of the aorta has also been observed (Menter *et al.*, 2020).

Other systemic findings

Multifocal hepatic necrosis, mild sinusoidal dilation, steatosis, acute splenitis. Analysis of the brain only revealed mild hypoxic conditions and no necrosis or inflammatory infiltrates were observed. Pre-existing conditions like arteriosclerosis, intima fibrosis of the arteries, vascular scarring due to hypertension, testicular hypertrophy, nodular thyroid, muscular dystrophy, liver cirrhosis, prostatic hyperplasia have been contributing factor in the cause of death along with COVID 19 (Menter *et al.*, 2020).

Post-autopsy protocol

After the autopsy, using the standard procedure, the body is closed back and cleaned with disinfectants. The body is wrapped and taped tightly in a clean shroud and transferred to a clean body bag where it can be stored until the funeral. The outer surface of the bag and the body table is cleaned using disinfectants to avoid the spread of the virus. The body fluids and the other contaminated liquids are cleaned using absorbent materials. The soiled absorbent materials, contaminants, fluids were disposed in a bag and marked as infectious. The PPE's were disposed of in the regular medical waste and human waste was discarded as routine pathological waste. The remaining re-usable instruments were thoroughly wiped using the disinfectants and then autoclaved for the next use. After the PPE's is removed, maintain personal hygiene by washing hands thoroughly with soap and alcohol-based hand rub (60%), if required. Avoid touching your face and belonging with the soiled to prevent the spread of infection (Lacy *et al.*, 2020).

Body disposal

The body after it has been identified needs to be transported. This is done by the body bagging method. There is no specification provided by the WHO or CDC regarding the disposal of COVID 19 positive body. PPE should be worn at all times in case of any fluid leak from the bag. If there is a chance of a fluid leak, cotton packing is done of the orifice, a double body bag is used and a plastic shroud can also be used. The body can either be buried or cremated according to state requirements and should be buried 1.5 – 3m deep (should be at least 2m above groundwater table) (Lacy *et al.*, 2020).

CONCLUSION

SARS-CoV-2 the pathogen which causes COVID-19, is highly infectious. It has originated from Wuhan, China in December. Due to the increase in cases and death rate day by day, the pandemic has caused havoc in the world. However, we are not completely aware of the pathophysiology of SARS-CoV-2. The scientist, doctors, and researchers are conducting clinical trials to check the efficiency of the medicines as well as a vaccine against this virus. In this article, along with the etiology, pathophysiology, epidemiology, symptoms and the autopsy findings of various cases helps us to study the pathology of the disease, different changes the organ system undergoes when it comes in contact with the virus. Proper autopsy room, scene safety, waste, and body handling have been explained for better management of the deceased and safety of the personnel. Hopefully, the remedy against this deadly virus is found soon, which can put a stop to this pandemic situation.

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Conflict of Interest

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