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Autopsy findings in COVID-19 Infection: Study of case series of autopsies at tertiary health care centre.

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ABSTRACT- On 11th march 2020, The World Health Organisation had declared COVID- 19 as a Pandemic. The virus engulfed the entire world causing disease ranging from no to minimal symptoms to full blown respiratory and multiorgan systemic infection. Many deaths were reported due to COVID 19 infection. The autopsy on COVID 19 deceased could be useful to add more information about pathophysiology in different vital organs during the course of COVID 19 infection. The present study reports a series of autopsy findings conducted upon the deceased which were either diagnosed COVID-19 positive before death by rapid antigen test and RT-PCR or which turned out to be incidentally positive after death while conducting rapid antigen test before commencement of autopsy. The gross and histopathological examination findings were discussed in the present study.

KEYWORDS- COVID 19, Autopsy, Histopathological Examination.

INTRODUCTION

The entire world has been racing against time to fight Corona virus while million of humans have died and are still dying of it. Late 2019 observed an outbreak of SARS- Corona virus causing the Novel Corona Virus Disease (COVID-19). Coronaviruses are single, positive-stranded non segmented RNA viruses, round or oval in shape and are enveloped.[1] Corona virus related different pandemics include Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Corona Virus Disease 2019 (COVID-19). It is frequently associated with acute respiratory infections in humans and animals. It can be detected in respiratory tract secretions, as well as found in faeces, serum, and urine of the patients.[1,2,3] Trans-respiratory droplets and contact transmission are the main routes of transmission of this virus.[4] Coronaviruses gain entry into cells via the angiotensin-converting enzyme 2 (ACE2), which is expressed in multiple tissue types.[5] Autopsy along with pathology can serve as an important tool in providing scientific and theoretical basis for pathological changes, pathogenesis and cause of death in COVID-19 deaths in context of pandemic control. To observe pathological changes underlying the severe respiratory distress syndrome and immune dysfunction in critically ill COVID-19 patients, the systematic autopsy was carried out on 9 deceased died due to COVID 19 infection with their comprehensive pathological analyses. Our findings provide new evidence on pathological changes associated with COVID-19 disease.

MATERIAL AND METHODS- This is a retrospective and descriptive study carried out at Tertiary Medical teaching institute in Western Maharashtra, India from March 2020 to August 2021.
The cases in which medicolegal autopsies were performed on deceased in known COVID 19 infection during the study period were included. All those cases diagnosed as COVID positive based on nasopharyngeal swab for COVID 19 Infection either by RT-PCR technique or by Rapid Antigen Test were considered for study.

INCLUSION CRITERIA-
Medicolegal autopsies performed on known cases of COVID 19 Infection and during autopsy samples of vital organs preserved for histopathological examination
EXCLUSION CRITERIA-
Medicolegal autopsies performed on known case of COVID 19 Infection but samples of vital visceral organs were not preserved for histopathological examination.

Before commencement of autopsy, the information about clinical profile was obtained by perusal of indoor case reports, police inquest and information provided by accompanying relatives. The complete medicolegal autopsy was performed in all the selected cases and the standard autopsy protocols laid down by Indian Council of Medical Research were followed during autopsy. The gross findings of vital visceral organs on naked eye examination were noted during autopsy and the samples of vital visceral organs were preserved in 10 % formalin at room temperature for 72 hours before macroscopic analysis and processing for histological examination. Tissue samples were processed using hematoxylin and eosin staining (H&E), and special stains wherever necessary.

OBSERVATIONS -

Patient's demographic and clinical information was extracted from case records of 9 patients who died due to COVID-19 and were autopsied.

Table-1-shows Gross and Microscopic findings of organs in COVID-19 patient.

Sr No	Age And Sex	Cause of death	Day of death from COVID Detection	Course of illness	Gross findings of all organs	Microscopy findings of all organs
1	34 years, Female	Head injury with COVID 19 Infection	RAT Positive 1 Day before death	No symptoms and signs related with COVID 19 Infection History of assault with multiple skull vault fractures and subarachnoid haemorrhage noted	**Lungs** - Oedema and congestion present	**Lungs** - focal intra-alveolar haemorrhages and diffuse pulmonary oedema
2	27 years, Male	Septicaemia in an operated case of head injury with COVID 19 Infection	RAT Positive on the day of death and 37 days after admission	History of assault and operated case of craniotomy with type 1 respiratory failure	**Lungs** – Greyish white Pulmonary oedema	**Lungs** - Alveolar wall destruction, focal hyaline membrane Formation, diffuse pulmonary oedema suggestive of Pneumonia with lung fibrosis
3	39 years, Male	Lobar pneumonia with bronchitis with COVID 19 Infection	RAT POSITIVE 21 days before death during the course of treatment	COVID negative LRTI- Day 1- 4 Aspiration pneumonia-day 5 Fever, breathlessness – 5 days before death K/C/O psychosis and chronic alcoholic	**Lungs** - Bilateral lower zone consolidation seen **Heart –** Atherosclerotic changes present in coronaries. **Liver, Kidneys, Cerebrum and cerebellum** showed no significant COVID related changes.	**Lungs –** diffuse pulmonary oedema, bronchioles and alveoli Showed polymorphonuclear cell infiltration and focal alveolar wall destruction suggestive of lobar pneumonia with bronchitis. **Heart –** all coronary arteries showed patent lumen. **Liver**- centrilobular congestion **Kidney –** focal tubular infarct **Cerebrum and cerebellum** showed no significant COVID related changes.
4	43 years, Male	Pulmonary thrombo-embolism with COVID 19 Infection	RAT Positive 21 days before death	Brought dead with history of Fever, body ache - 3 days before death	**Lungs –** oedema **Heart –** Atherosclerotic changes present in coronaries **Liver, Kidneys, Cerebrum and cerebellum** showed no significant COVID related changes.	**Lungs**- Diffuse pulmonary oedema, blood vessel showed thrombus and focal intra-alveolar haemorrhagic infiltrate in alveolar septae and focal fibrosis suggestive of Pulmonary thromboembolism **Heart**- Left circumflex artery shows grade 2 atherosclerosis 20% narrowing of lumen. Left anterior descending shows grade 3 atherosclerosis 30% narrowing of lumen. **Liver -** diffuse fatty change suggestive of fatty liver **Kidneys** showed partial autolysis changes **Cerebrum and cerebellum** showed no significant COVID related changes.
5	30 years, Female	Pneumonia with hyaline membrane disease with Bilateral pulmonary consolidation with COVID 19 infection	RAT Positive 3 days before death and 19 days after admission	High grade fever, abdominal pain, burning micturition- since 3 days – **Day 1** Septic and cardiogenic shock, bilateral pyelonephritis, AKI- **Day 4** Atypical streptococci pneumonia- **Day 5** Quadriparesis- **Day 14** MODS- **Day 21**	**Lungs**- whitish areas of consolidation in all lobes **Heart**- Subendocardial yellowish chalky white band throughout the circumference of left ventricle **Liver** showed nutmeg appearance **Kidneys** showed wedge shaped pale whitish area.	**Lungs –** pulmonary oedema, congestion, focal intra-alveolar haemorrhage and destruction of alveolar walls, hyaline membrane formation, pulmonary vessel showed fibrin thrombi suggestive of Pneumonia with hyaline membrane disease **Heart**- Right coronary artery, left circumflex artery, left anterior descending shows grade 2 atherosclerosis with patent lumen, area of myocardiolysis and calcification **Liver**- centrilobular sinusoidal haemorrhagic necrosis and focal fatty change suggestive of chronic passive venous congestion of liver **Kidneys –** congestion, large area of infarct suggestive of Renal infarction. **Cerebrum and cerebellum** showed no significant COVID related changes.

					Cerebrum and cerebellum showed no significant COVID related changes.	
6	27 years, Male	Coronary athero-sclerosis with bilateral pulmonary consolidation in a diagnosed case of COVID 19 Infection	RTPCR positive 11 days before death	Brought dead Fever and bodyache - **11 Days**	**Lungs-** soft to firm in consistency, cut surface showed congestion and oedema	**Lungs** showed alveolar destruction and patchy pulmonary oedema along with focal intra-alveolar haemorrhage and pigment laden microphages.
7	69 years, Female	Pneumonia with hyaline membrane disease and coronary artery disease with diabetic ketosis, urosepsis, AKI, DM with HTN with COVID 19 Infection	RAT Positive on the day of death, 9 days after admission	Vomiting on food intake- day 1 Urinary incontinence- day- 7 Drowsiness Diabetic ketoacidosis with Acute Kidney Injury K/C/O Diabetes Mellitus TYPE 2- 12 Years, Diabetic nephropathy- 1 Year, Cough, dyspnoea- 1 day before death	**Lungs** – firm **Heart-** changes of atherosclerosis in coronaries present **Liver, Kidneys, Spleen, Cerebrum and Cerebellum** showed no significant COVID related changes	**Lungs** – showed congestion, pulmonary oedema, haemosiderin laden macrophages, focal granuloma, multiple focal areas of intra-alveolar inflammatory infiltrate of polymorphs, few lymphocytes and macrophages with hyaline membrane formation suggestive of Pneumonia with hyaline membrane Disease **Heart-** Left anterior descending shows grade 6 atherosclerosis with Thrombo-embolism with 95% narrowing of lumen suggestive of coronary artery disease. **Liver**-focal fatty changes and increased portal to portal fibrosis. **Spleen -** congestion
8	46 years, Female	Pulmonary consolidation and coronary atherosclerosis with COVID 19 Infection	RAT Positive on the day of death, 20 days after admission	Brought dead with history of assault No signs and symptoms related with COVID	**Lungs-** spongy, firm, mild pulmonary oedema **Heart-** changes of atherosclerosis in coronaries present **Liver, Kidneys, Spleen, Cerebrum and Cerebellum** showed no significant COVID related changes	**Lungs-** congestion, patchy pulmonary oedema, at places focal alveolar damage seen. **Heart-** right coronary artery and left circumflex artery patent lumen. left anterior descending – grade 5 atherosclerosis with 20% narrowing of lumen. **Liver –** congestion, focal fatty change, focal mononuclear infiltration. **Spleen, cerebrum and cerebellum** showed no significant COVID related changes.
9	57 Year, Male	Coronary artery disease with healed myocardial infarction with COVID 19 Infection	RAT Positive 17 days before death.	Brought dead with history of fever and breathlessness for two days before death	**Lungs-** congestion **Heart-** Atherosclerotic changes present in coronaries. **Liver**-nutmeg appearance **Kidneys, spleen, Cerebrum and cerebellum** showed no significant COVID related changes.	**Lungs –** congestion **Heart -** left anterior descending artery - showed grade IV (Calcific) AT with 60% narrowing of lumen. s/s/s multiple patchy areas of fibrosis surrounded by hypertrophied myocardium to all wall suggestive of CAD with healed myocardial infarction **Liver showed** centrilobular haemorrhagic necrosis **Kidney-** ischemic scars,1 piece showed moderate interstitial mononuclear infiltrate with focal fibrosis **Spleen, cerebrum and cerebellum** showed no significant COVID related changes.

In our study, out of 9 cases, 5 were male and 4 were female with mean age of 41.3 years (age range 27- 69 years). In 3 cases, nasal swab was found to be RAT Positive incidentally after their death. The history of symptoms and signs related to COVID 19 infection before death was observed in 5 cases while 4 cases had no such history. Regarding past co-morbidities, only 1 case had diabetes mellitus type-2 with diabetic nephropathy. On histopathological examination, typical COVID related findings were observed in 8 cases while in 1 case, typical findings were not observed in other organs but heart showed atherosclerotic changes with coronary narrowing.

Lungs being the primary organ to be affected in COVID 19 infection in 8 cases showed increased volume, were firm, edematous and congested with diffuse pleural thickening and pleural effusion. Cut surface showed consolidation of lobes and red congested areas, firm with thickening of the interstitial septa and pulmonary edema. Haemorrhage with odema was observed in 3 cases. Alveolar wall destruction was present in 4 cases. Hyaline membrane formation was observed in 3 cases. Features suggestive of pneumonia were seen in 4 cases. Pulmonary thrombo-embolism was seen in 2 cases. Bronchitis was present in 1 case. Fibrosis was observed in 2 cases.

The heart in 4 cases showed increased size and weight, hypertrophy and dilation of the left and right atria and ventricles. The myocardium appeared pale and flabby. Atherosclerotic changes in coronaries were observed in 4 cases. Mononuclear cells infiltrating – myocarditis characterized by mononuclear, predominantly lymphocytic, infiltrate, and was associated with focal myocytes necrosis and calcification seen in 1 case.

Macroscopic inspection of liver of all deceased showed parenchymal congestion. The main findings at histological level were sinusoidal congestion and extravasation of red blood cells. Haemorrhagic necrosis was present in 2 cases. Chronic passive venous congestion was present in 1 case. Portal triad showed increased lymphocytic inflammatory infiltrate in 1 case as portal fibrosis and mononuclear infiltrate in 1 case.

Both the kidneys of 6 deceased had normal shape with reduced volume and size and outer surfaces showed reddish depressions. Histological examination showed interstitial fibrosis, mainly in 3 cases with swollen glomerular endothelial cells. Chronic tubular and renal infarct were observed in 2 cases. Ischaemic scar and mononuclear infiltrate with focal fibrosis was present in 1 case.

The spleen of 6 deceased had normal shape but reduced in volume and size. The splenic white pulps of 1 case showed lymphoid hypoplasia with congested red pulp.

DISCUSSION

Histopathology is a branch of medical science that deals with the microscopic examination of diseased cells and tissues to study about the manifestations of a disease. The histopathology laboratory plays a significant role in defining the cause of death and diagnosing a lesion. It also helps us to understand a disease's pathogenesis, its dynamics and could be an essential tool for diagnosis, surveillance and research. Our study aims to seek the role of histopathological examination in post-mortem examination of COVID 19 deceased and also to provide a clear picture of the histopathological features of different body organs in Severe Acute Respiratory Syndrome. The autopsy on COVID 19 Positive cases has been done with the aim of harvesting organs necessary to establish and describe the changes observed in this infection.

Zhu Z. et al, reported that the lungs of patients who died of COVID-19 had diffuse alveolar injury with fibrinous mucinous exudation in both lungs. The epithelial cells of alveoli were exfoliated with the hyaline membrane formation and pulmonary oedema was observed.[6] Xiao S. et al, described the nonspecific histopathological findings in lungs including pulmonary oedema, vascular congestion, prominent proteinaceous exudates, focal inflammation along with multinucleated giant cells.[7] Tian S. et al, studied the histopathological findings of lungs showing the pulmonary tissue was characterized by diffuse alveolar damage along with hyaline membrane formation and type II pneumocytes were activated. Presence of inflammatory infiltration (mononuclear cells) was also observed.[8] Carsana L. et al reported that all of their cases showed features of exudative and proliferative phases of diffuse alveolar damage and hyaline membrane formation with intra alveolar odema in lungs. The predominant pattern of lung lesions was diffuse alveolar damage.[9] Hanley B. et al carried out a study of autopsy in suspected COVID-19 cases. They observed that macroscopic findings included pleurisy, lung consolidation, pulmonary odema. Lung weight was increased. Microscopically pulmonary odema, multinucleated giant cells formation with no hyaline membrane were observed.[10] Maiese A. et al reported that lungs generally appeared heavy and edematous. Histologically, the most commonly observed pathological finding was both exdudative and proliferative diffuse alveolar damage in different stages, with hyaline membrane formation, inflammatory cell infiltration and small vessel congestion.[11] Stoyanov G. et al carried out a study which revealed contraction of lungs towards hilus, cyanotic and severely increased weight. Lungs were diffusely consolidated without any visible thrombi in the vasculature. Histology of lungs revealed evidence of alveolar hyaline membranes, interstitial pneumonia, diffuse zones of hemorrhages. Other changes observed were microthrombi, diffuse endothelitis with degenerative and necrotic changes.[12]

The present study of autopsy evaluation of 9 deceased with COVID-19, also observed that histologically the most frequent pathological finding was diffuse alveolar damage with hyaline membrane formation and inflammatory cell infiltration. Presence of thrombi in the microvessels of the lung was also a prominent finding. The heart showed atherosclerotic changes in coronaries, mononuclear cells infiltration suggestive of myocarditis characterized by predominantly lymphocytic infiltrate and was associated with focal myocytes necrosis and calcification. The liver showed sinusoidal congestion, extravasation of red blood cells along with haemorrhagic necrosis and chronic passive venous congestion. Both the kidneys showed interstitial fibrosis and swollen glomerular endothelial cells. Chronic tubular and renal infarct were also observed. The spleen showed lymphoid hypoplasia with congested red pulp.

Most of the authors studied histopathological changes only in lungs of the deceased died from COVID. The present study also considered other visceral organs including lungs and their changes histologically. Our study describes the systemic target of the infection of mostly respiratory system followed by cardiovascular, renal and hepatic system. Though this study has limitations in the form of small number of cases from a single centre, the knowledge and information about pathological changes in different visceral organs and their analysis may greatly

contribute to analysing the interactions between human host and the coronavirus, thus making a way for more accurate therapeutic approach against COVID 19 Infection.

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Legends

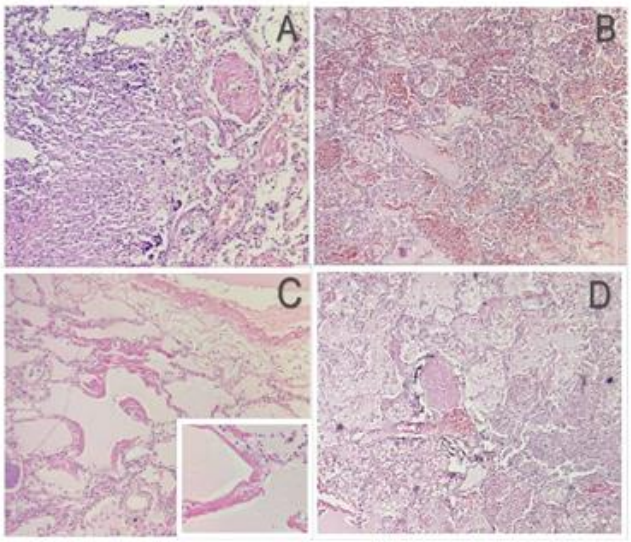

Figure 1

- **A-** H and E stain photograph showing Giant cells along with thrombosed vessel.
- **B-** H and E stain photograph showing intra alveolar haemorrhages.
- **C-** H and E stain photograph showing hyaline membrane with edema, Inset showing high power view of hyaline membrane
- **D-** H and E stain photograph showing thromboemboli along with intra alveolar polymorphs- Pneumonia

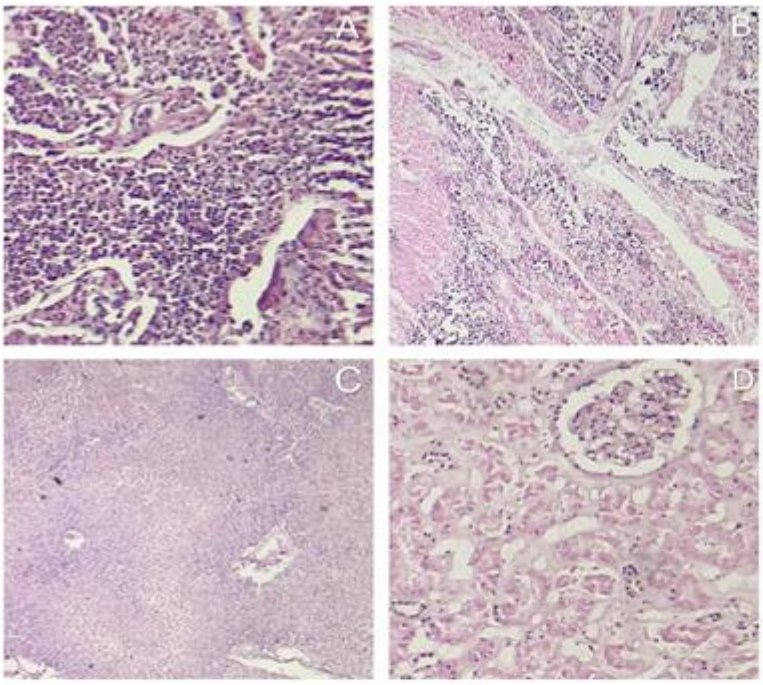

Figure 2-

- **A-** H and E stain section (High power view) photograph showing intra alveolar inflammatory infiltrate of lymphocytes and polymorphs- Pneumonia
- **B-** H and E stain section showing necrosis and calcification of myocardium.
- **C-** H and E stain section showing chronic passive venous congestion changes in liver.
- **D-** H and E stain section showing acute tubular necrosis of kidney.