Original Article

Histopathology of Corona virus

Clinical Characteristics and Histopathology of Corona Virus Disease 2020

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ABSTRACT

Objective: To investigate the clinical and histopathological characteristics of corona virus disease.
Study Design: Systamatic Review
Place and Duration of Study: This study was conducted at the Watim Medical and Dental College from Jan 2021 to June 2021.
Materials and Methods: All the articles published in 2020 at Google Scholar and PubMed were searched from to gather the information about the clinical and histopathological characteristics of corona virus disease. The articles published in English language only were included in this study. The terms like "clinical features of COVID-19", "COVID-19", "Histopathology of corona virus" and "Histology of COVID-19" were searched. I^2 and Egger's test was used to analyze the data about the clinical characteristics of the patients.
Results: The most common comorbidities related to COVID-19 are hypertension in 16 % cases and cardiovascular and cerebrovascular diseases in 12 % of the cases. The histopathological changes were most evident in the lungs. According to the percentage the most common lungs findings were congestion and diffused alveolar damage with 97.8 %. Corona virus disease also effects other organs and systems like CVS; myocardial hypertension, nervous system; hypoxic injury, digestive system; segmental dilatation and stenosis, liver; steatosis, kidney; acute tubular injury, immune system; coagulation abnormalities among many other.
Conclusion: TMultiple dysfunction caused by corona virus disease can occur due one of the following reasons: to direct viral attack, systemic inflammation, injury to the immune system or shock.
Key Words: COVID-19, Clinical features, Histopathology, Histopathological features, corona virus disease.

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INTRODUCTION

The COVID-19 virus that causes the corona virus disease was first identified in China, Wuhan, in December of 2019. This variant was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2). This virus effected the people worldwide to such an extent that it was declared pandemic by World Health Organization [1]. Currently this virus has caused almost 4.3 million deaths worldwide.
We had encountered the virus of this family previously also. In 2002, SARS-CoV caused an outbreak and infected over 8 thousand people[2].

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Then in 2012, MERS-CoV cause another outbreak [3]. But the outbreak of 2019 has been more severe and dangerous than the previous two outbreaks. This variant of the corona virus is highly contagious and difficult to deal with [4]. It rapidly spreads from the infected person to the non-infected and increases the number of infected people further [5].
The research on the clinical features of this virus is in progress. In one of such researches, meta-analysis was done to sum up the clinical features of COVID-19[6]. This study reported that the most common symptoms of COVID-19 were fever, myalgia, sore throat and fatigue. The case fatality rate was 4.3 %. This study also reported 96.6 % prevalence of abnormal chest CT scan.[6] Some of the studies indicated that the geographical region can cause a difference in the clinical outcomes of the COVID-19 virus. One of the study reported that the patients in Wuhan endured more severe illness and abnormalities than the patients outside Wuhan. [7]
On the other hand, the histopathological features of this virus are also not fully known yet. This is because the autopsies and biopsies of the cases of COVID-19 patients are not sufficient. Even though the clinical features of the disease shows that it mainly effects the

lungs and the respiratory tract, there are indications present that this virus can cause multiple organ dysfunction which can then cause death of the patient. [8]
In the light of the above mentioned information, it is important that we investigate the clinical and histopathological characteristics of corona virus disease to treat and control it in a better way.

MATERIALS AND METHODS

Google Scholar and PubMed were searched to gather the information about the clinical and histopathological characteristics of corona virus disease. The articles published in English language only were included in this study. The terms like "clinical features of COVID-19", "COVID-19", "Histopathology of corona virus" and "Histology of COVID-19" were searched. I^2 test was used to analyze the heterogeneity of different studies related to the clinical features of COVID-19. 25 % value meant low heterogeneity, 50 % meant moderate heterogeneity and 75% meant high heterogeneity. If the heterogeneity was more than 75%, subgroup analysis was done. Age, region, sex and comorbidity variables were included in subgroup analysis. Egger's test was used to analyze the publication bias, if more than three studies are used to analyze the data related to the clinical characteristics. Histopathological features were observed after either autopsy or biopsy of the COVID-19 patient.

RESULTS

In this study, 26 articles with the total number of 2100 patients were included. 1100 were male and 1000 were females. 89 % of the patients had fever, 69 % had non-productive cough and 35 % had fatigue.

Table No.1: Analysis of the clinical characteristics of corona virus disease

Clinical characteristic	Prevalence %	I^2 %	Egger's test
Fever	89 %	96 %	< 0.001
Non-productive cough	69 %	80 %	0.147
Fatigue	35 %	86 %	0.971
Myalgia	29 %	90 %	0.008
Productive cough	27 %	92 %	0.561
Dyspnea	25 %	84 %	0.158
Chills	15.5 %	76 %	0.396
Chest pain	15 %	89 %	0.155
Headache	14.8 %	74 %	0.452
Sore throat	13.4 %	67 %	0.558
Diarrhea	9.5 %	83 %	0.006
Dizziness	8.7 %	51 %	0.239
Nausea / vomiting	4.7 %	49 %	0.873
Rhinorrhea	4.6 %	0 %	0.025
Hemoptysis	3 %	64 %	0.047
Nasal congestion	2.8 %	3 %	0.228

Myalgia was present in 29 % of the patients, dyspnea in 25 % of the patients, chest pain in 15 % patients, chills in 15.5 % patients, headache in 14.8 % patients, sore throat in 13.4 % patients, productive cough in 27 % patients, dizziness in 8.7 % patients, diarrhea in 9.5 % patients, rhinorrhea in 4.6 % patients, nausea/ vomiting in 4.7 % patients, hemoptysis in 3 % patients and nasal congestion in 2.8 % patients. This analysis of the clinical characteristics of corona virus disease is shown in Table 1.
Table 1 also showed the results of Egger's test. Publication bias was present in fever, diarrhea, hemoptysis, myalgia and rhinorrhea.
The most common comorbidities related to COVID-19 are hypertension in 16 % cases and cardiovascular and cerebrovascular diseases in 12 % of the cases. Diabetes mellitus was present in 10 % of the patients, infections like hepatitis and HIV in 1.7 % of the patient, cancer in 1.7 % of the patients, respiratory disorders in 1.6 % of the patients, renal disorders in 0.7 % of the patients and immunodeficiency disorders in 0.02 % of the patients. These results are shown in Table 2.

Table No.2: Comorbidities related to corona virus disease

Comorbidities	Percentage
Hypertension	16 %
Cardiovascular and Cerebrovascular diseases	12 %
Diabetes mellitus	10 %
Infections i.e. hepatitis	1.7 %
Cancer	1.7 %
Respiratory disorders	1.6 %
Renal disorders	0.7 %
Immunodeficiency disorders	0.02 %

Table 3 shows the histopathological finding in lungs. Lungs are most commonly affected organ in case of corona virus disease [8]. This table 3 shows that congestion was described in 97.8 % patients, diffused alveolar damage was described in 97.8 % patients, microthrombi in 82.6 % patients, pneumocyte changes in 95.6 % patients, superimposed pneumonia in 91.3 % patients, vasculitis in 60.9 % patients, paucity of lymphoid cells in 69.6 % patients and proteinaceous exudate in 32.6 % patients. According to the percentage the most common lungs finding is congestion and diffused alveolar damage with 97.8 %.

Table No.3: Histopathological finding in lungs

Histological changes	Percentage
Congestion	97.8
Diffuse alveolar damage	97.8
Microthrombi	82.6
Pneumocyte change	95.6
Superimposed pneumonia	91.3
Vasculitis	60.9
Paucity of lymphoid cells	69.6
Proteinaceous exudate	32.6

Table 4 shows the histopathological findings in different organs and systems of the human body. Diffused alveolar damage is the most common histopathology of lungs in corona virus disease. Histological observation in many studies have reported vascular congestion, diffused alveolar damage, microthrombi, pulmonary embolism, mononuclear inflammation and pneumonia[9-16]. Effects on nervous system included mild hypoxic injury[14]. Liver's pathology included steatosis, nuclear granulation, mild lobular mononuclear inflammation, mild lobular and portal activity and sinusoidal dilatation[10,12,13,16]. Myocardial hypertension, fibrosis, mild mononuclear inflammation and edema was observed in the histology of cardiovascular system[10,14,16]. Effects on the digestive system included segmental stenosis and dilatation, focal/mild edematous mucosa infiltrated by mononuclear inflammatory cells, ACE2 receptors down regulation and esophageal mucous lesion [17, 18]. Immune system also showed histopathological changes i.e. T cell lymphopenia, increased neutrophil- lymphocyte ratio, coagulation abnormalities, high level of cytokines and tissue infiltration by macrophages[19-21]. Corona virus effected the kidneys in many ways: diffuse proximal tubular injury, up regulation of ACE2 receptors, collapsing glumerulopathy, focal interstitial mononuclear inflammation, loss of brush borders, hemosiderin granules, distal tubules and collecting ducts cellular swelling, cystic tubules, fibrosis, tubular atrophy, necrosis, microthrombi, epithelial detachment and pigmented casts.

Table No.4 Histopathological findings in different organs and systems

System	Reported findings	Source
Respiratory	Vascular congestion	16, 12, 15, 9, 14, 10, 13
	Diffused alveolar damage	16, 12, 15, 9, 14, 10, 13
	Microthrombi	16, 12, 15, 14
	Pulmonary embolism	16, 14
	Mild mononuclear inflammation	16, 12, 15, 9, 14, 10, 13
	No mucus plug	16, 12, 15, 9, 14, 10, 13
	Secondary bacterial pneumonia	16, 12, 14, 10
	No eosinophilic or neutrophilic infiltration	16, 12, 15, 9, 14, 10, 13
Nervous system	No inflammation	14
	Mild hypoxic injury	14
	No necrosis	14
Liver	Steatosis	16, 12, 10, 13
	Nuclear granulation	10
	Mild lobular mononuclear inflammation	10
	Mild lobular and portal activity	13
	Sinusoidal dilatation	10
	Myocardial hypertension	16, 14, 10
Cardiovascular system	Fibrosis	10
	Mild or absent mononuclear inflammation	16, 12, 13
	Edema	10
Digestive system	Segmental stenosis and dilatation	18
	Focal/mild edematous mucosa infiltrated by mononuclear inflammatory cells	17
	ACE2 receptors down regulation	17
	Esophageal mucous lesion	17
Immune system	T cell lymphopenia	20, 21
	Increased neutrophil-lymphocyte ratio	20, 21
	Coagulation abnormalities	20, 21
	High level of cytokines	19, 20, 21
	Tissue infiltration by macrophages	20, 21
Kidney	Diffuse proximal tubular injury	14, 22, 23
	Up regulation of ACE2 receptors	23
	Collapsing glumerulopathy	22
	Focal interstitial mononuclear inflammation	14, 22, 23
	Loss of brush borders	23
	Hemosiderin granules	23
	Distal tubules and collecting ducts cellular swelling	23
	Cystic tubules	14, 22
	Interstitial edema or fibrosis	14, 22
	Tubular atrophy	14
	Acute pyelonephritis	23
	Necrosis	23
	Microthrombi	14, 23
	Epithelial detachment	23
	Pigmented casts	23
System	Reported findings	Source
Respiratory	Vascular congestion	16, 12, 15, 9, 14, 10, 13

DISCUSSION

In this study, the clinical characteristics of corona virus disease included fever, non-productive cough, fatigue, myalgia, productive cough, dyspnea, chills, chest pain, headache, sore throat, diarrhea, dizziness, nausea / vomiting, rhinorrhea, hemoptysis and nasal congestion. The major symptoms were fever, non-productive cough and fatigue. In another study, the major symptoms of corona virus disease were fever, cough and dyspnea. One of the study reported that fever, cough and vomiting were the most common clinical characteristics.

The most common comorbidities related to COVID-19 were hypertension and cardiovascular and cerebrovascular diseases in our study. Another study reported hypertension, diabetes mellitus and cardiovascular disorders as some of the risk factors of

corona virus disease. A different study also established that comorbidities i.e. hypertension, diabetes mellitus, increased the risk of severe illness due to COVID-19 virus.

Our study also established that this virus induced histological changes in lungs, digestive system, cardiovascular system, respiratory system, liver, kidneys and nervous system. The histopathological changes were most evident in the lungs. These results are similar to some of the other studies[8].

In our study the microthrombi was majorly observed in kidney and lungs. This is similar to many other studies[24-26]. This indicates that the COVID virus attacks endothelial cells more than other cells. It can cause complications like hypoxemia.

The main strength of this study is that it provides a comprehensive review of clinical and histopathological characteristics of corona virus disease. At the same time, this study has some limitations. Details of the clinical characteristics and histopathological findings is not given. The prevalence of histopathological findings is also not included in this study. Duration of illness and autopsy and biopsy details are also absent in this study.

As the pandemic caused by the corona virus disease continues, it is very import to understand its clinical and histopathological features to understand it in a better way. Doing research on this virus is our only solution right now.

CONCLUSION

The most common symptoms of COVID-19 are fever, non-productive cough, fatigue, myalgia and dyspnea among many other. Patients who suffer from hypertension, cardiovascular and cerebrovascular diseases, diabetes mellitus, infections, cancer, respiratory disorders, renal disorders and immunodeficiency disorders are at higher risk of COVID-19. The most common histopathological characteristic of corona virus disease is mild mononuclear inflammatory cell infiltration. In lungs and kidneys microthrombi was majorly observed. Diffused alveolar damage is the most common histopathology of lungs in corona virus disease. Multiple dysfunction caused by corona virus disease can occur due one of the following reasons: to direct viral attack, systemic inflammation, injury to the immune system or shock.

Author's Contribution:

Concept & Design of Study:	Momina Khadija Abbasi
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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