ORIGINAL: Investigating the prevalence of liver, heart, and kidney injuries caused by COVID-19 in patients hospitalized at Imam Sari Hospital

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ABSTRACT

Introduction: COVID-19 has been associated with multiple organ injuries, contributing to increased morbidity and mortality in hospitalized patients. This study aimed to investigate the prevalence of cardiac, renal, and hepatic injuries among deceased and ICU-admitted COVID-19 patients at Imam Sari Hospital.

Methods: A total of 600 patients were included in this cross-sectional study. Demographic data and clinical histories were collected. The presence of organ injuries was determined by a medical team based on laboratory findings and CT scans. Statistical analyses were performed using SPSS version 26, with a significance level set at 0.05. Descriptive statistics and appropriate inferential tests (independent sample t-test, Pearson Chi-square) were used to analyze the data.

Results: The mean age of patients was 51.83 ± 16.70 years, with most patients (42.3%) aged 61–75. Males comprised 53% of the sample. The prevalence of cardiac, renal, and hepatic injuries was 32.0%, 13.7%, and 3.7%, respectively. Older age was significantly associated with all three types of injuries ($P < 0.05$). No significant association was found between gender and organ injury prevalence. Mortality rates were significantly higher among patients with cardiac (45.8% vs. 5.4%), renal (57.3% vs. 12.2%), and hepatic (36.4% vs. 17.6%) injuries compared to those without these injuries ($P < 0.05$ for all).

Conclusion: Cardiac, renal, and hepatic injuries are prevalent among severe COVID-19 cases, especially in older patients, and are strongly linked to increased mortality. Gender does not appear to influence the risk of these injuries. These findings highlight the importance of early detection and management of organ dysfunction in COVID-19 patients to improve clinical outcomes.

Introduction

In December 2019, a group of patients with pneumonia of unknown causes was identified in Wuhan, China. The cause of this disease was diagnosed as infection with a novel coronavirus(1). This virus was named 2019-nCoV by the World Health Organization (WHO) and was recognized as the third coronavirus infecting humans after Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), causing severe pneumonia(2). On February 11, 2020, WHO chose the short name COVID-19 for this disease(3). On February 22, 2020, the number of cases in China was reported as 76,396, with 11,477 in critical condition and 2,348 deaths(4). The high infectivity and transmission power, even during the asymptomatic phase, led to the spread of this virus to other geographical regions and its transformation into a global pandemic. Over more than three months, 177 countries worldwide reported 266,037 cases and 11,184 deaths due to this virus(5,6).The main symptoms of COVID-19 infection were reported as fever, dry cough, and fatigue. Some patients exhibited symptoms such as nasal congestion, runny nose, and diarrhea, while patients in critical condition suffered from oxygen deficiency (hypoxia) and severe shortness of breath. In very severe cases, acute respiratory distress syndrome, septic shock, and multiple organ damage including heart, liver, and kidney were observed(4). Although the respiratory system is the primary organ involved in this infection, multiple organ failure is considered the cause of death in COVID-19 patients. Some reports indicate a 33% incidence of multiple organ failure in infected patients, with 3-7% of this related to kidney failure(7).Kidney dysfunction leads to obstruction in the excretion of waste products and metabolites, disrupting acid-base balance and electrolyte homeostasis in the body. Therefore, kidney injury endangers the patient's life. Timely identification of kidney damage plays a crucial role in interventions for its improvement. For this purpose, factors such as blood creatinine and urea, and urinary creatinine, microalbumin, and microglobulin are used to assess kidney function and determine kidney injury caused by coronavirus infection(4).Dehydration is the main mechanism causing kidney dysfunction in infected patients, with high fever and reduced fluid intake in elderly individuals being the causes, leading to decreased glomerular filtration and acute kidney injury. Cytokine storm syndrome, hypoxia, and viral invasion of tubular, glomerular, and interstitial kidney cells are other causes of kidney failure in this disease(8). Kidney involvement in coronavirus infection has

complex causes and is directly related to mortality in infected patients.On the other hand, acute myocardial injury is the most common cardiovascular disorder in COVID-19. Various definitions for acute myocardial injury have been proposed, including elevated cardiac enzymes and abnormalities in electrocardiograms. Among these, an increase in cardiac troponin I (cTnI) above the reference limit is the most commonly used definition. Elevated cTnI has been observed in 8-12% of cases. The cause of acute myocardial injury is viral myocarditis due to direct viral attack on the heart or systemic inflammation, with direct myocardial injury by the virus observed in 35% of autopsied heart samples(9).Reports have shown that MERS-CoV can cause acute myocarditis and heart damage. Since the pathogenicity of this virus and SARS-CoV are similar, acute myocarditis has also been observed in some SARS-CoV patients. For instance, in 5 out of 41 COVID-19 patients in Wuhan, China, increased cardiac troponin I (cTnI >28 pg/ml) was reported, with 4 of these 5 patients transferred to the intensive care unit (ICU) due to myocardial injury. Blood pressure levels in treated ICU patients were significantly higher than in untreated ICU patients. Another report showed that myocardial injury markers (creatine kinase myocardial band, CK-MB) were significantly higher in ICU-admitted patients compared to

non-ICU patients (18 U/l vs. 14 U/l). These studies indicate that myocardial injury is more frequent in patients with severe disease symptoms(4,10).According to the China National Health Commission (NHC), 11.8% of deceased cases without prior cardiovascular disease had severe cardiac injury with markedly increased cTnI or cardiac arrest. Therefore, cardiovascular symptoms are highly prevalent in COVID-19 patients and may be associated with inflammatory responses and immune system disorders(11).Liver injury in these patients is related to direct viral attack on liver cells. Between 2-10% of patients exhibited symptoms such as diarrhea and presence of viral RNA in stool and blood samples, indicating viral exposure to the liver. The presence of the virus at low titers in liver tissue has been confirmed. Gamma-glutamyl transferase is a diagnostic biomarker for cholangiocyte cell injury. Some studies reported increased levels of this enzyme in 54% of infected patients and increased alkaline phosphatase in 8.1% of patients(12). Angiotensin-converting enzyme 2 (ACE-2) is highly expressed on cholangiocyte cells, and it seems the virus uses ACE-2 positive cells to impair liver function(13).Despite these interpretations, pathological analysis of liver tissue from deceased patients did not observe viral entry into liver tissue. It is also possible that liver injury in these patients results from

the toxic effects of drugs used in treatment, hypoxia related to pneumonia, and cytokine storm. Liver injury in patients with moderate severity is transient and can return to normal(12).Further analyses have shown that acute multiple organ injury is higher in severely ill COVID-19 patients, which can be attributed to ACE-2 expression in organs such as liver, heart, kidney, brain, and gastrointestinal tract besides lung cells(14). The present study investigated the prevalence of multiple organ injury in COVID-19 patients in the city of Sari.

Material and methods

Study Design and Participants

This retrospective study was conducted by reviewing the medical records of 600 adult patients diagnosed with COVID-19 who were admitted to Imam Hospital in Sari. The study population included patients hospitalized in both the general wards and the Intensive Care Unit (ICU), as well as those who died due to the disease. Over the course of one year, a total of 600 adult patients were enrolled in this study.For each patient, a comprehensive questionnaire was completed, collecting detailed demographic and clinical information. The variables recorded included age, gender, pregnancy status, and history of underlying medical conditions such as diabetes, thyroid disorders, kidney, heart, and lung diseases. Additionally, severe medical conditions were documented, including leukemia, cancer, acquired immunodeficiency syndrome (AIDS), acute myocardial infarction during hospitalization, acute pulmonary embolism (considering long-term history of pulmonary embolism, prolonged bed rest, and blood coagulation disorders), stroke, and acute pancreatitis. Lifestyle factors such as smoking and tobacco use, specific medication use, duration of hospitalization, admission and discharge dates, cause of admission, type of COVID-19 treatment administered, blood pressure, and presenting symptoms were also recorded.

Upon admission, all patients underwent diagnostic procedures including chest computed tomography (CT) scans or throat swab sampling for real-time polymerase chain reaction (RT-PCR) testing to confirm COVID-19 infection. Based on clinical manifestations, chest CT findings, or RT-PCR results, diagnosis was established. Patients presenting with fever or suspected respiratory infection, along with at least one of the following clinical signs—respiratory rate exceeding 30 breaths per minute, severe respiratory distress, or oxygen saturation below 93% on room air—were classified as having severe disease.

Assessment of organ damage was performed by a multidisciplinary team of physicians. Laboratory evaluations included measurement of blood urea and creatinine

levels to assess kidney injury, and liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin to evaluate hepatic damage. Cardiac injury was assessed by measuring creatine kinase, lactate dehydrogenase, and troponin levels using the Pars Azmun kit. This study was approved by the Central Institutional Ethics Committee. Given the retrospective nature of the study and the use of existing medical records without interference in patient treatment, the requirement for documented informed consent was waived. this study was written according to Hilinski ethics roles and approved by ethics department (IR.MAZUMS..REC.1400.9091)

Statistical Analysis

Statistical analyses were conducted to compare clinical and laboratory variables among three groups of patients: those who died, those admitted to the ICU, and those hospitalized in general wards. For continuous variables such as liver enzymes, urea, and creatinine levels, analysis of variance (ANOVA) was used when data followed a normal distribution. In cases where normality assumptions were not met, non-parametric equivalents were applied. Categorical variables were analyzed using the chi-square test to assess the goodness of fit. The proportions of categorical variables were compared using either the chi-square test or Fisher's exact test, depending on the data distribution and sample size. A p-value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software, version 16.

Result

The study investigated the prevalence of liver, cardiac, and renal injuries caused by COVID-19 in deceased and ICU-admitted patients at Imam Sari Hospital, involving 600 patients. Statistical analysis was conducted using SPSS version 26, with a significance level set at 0.05%. Descriptive statistics included mean, standard deviation, median, confidence interval, frequency, and percentage, while appropriate inferential tests were applied as detailed below.

General Study Information

The demographic characteristics of participants are shown in Table 1. The mean age was 51.83 ± 16.70 years. The age group 61 to 75 years constituted the largest portion at 42.3%. The youngest participant was 18 years old and the oldest was 75 years. The median age was 57 years and the mode was 31 years. With 95% confidence, the mean age in the population was between 50.49 and 53.17 years. Males made up 53% of patients and females 47%. Among patients, 31.5% had

diabetes, 19.2% obesity, 6.3% had a history of kidney disease, and 16.3% had a history of cardiovascular disease. The mortality rate was 18.3%.

Table 1. The demographic characteristics of participants

Characteristic	Value
Mean Age (years)	51.83
Age Group 61-75 (%)	42.3
Minimum Age	18
Maximum Age	75
Median Age	57
Mode Age	31
95% CI Mean Age	50.49 - 53.17
Male (%)	53
Female (%)	47
Diabetes (%)	31.5
Obesity (%)	19.2
History of Kidney Disease (%)	6.3
History of Cardiovascular Disease (%)	16.3
Mortality Rate (%)	18.3

Prevalence of Cardiac, Renal, and Hepatic Injuries

The frequency and percentage of cardiac, renal, and hepatic injuries were determined by a medical team based on laboratory factors and CT scans, as shown in Table 2. Cardiac injuries were present in 32.0% of patients, renal injuries in 13.7%, and hepatic injuries in 3.7%.

Table 2. The frequency and percentage of cardiac, renal, and hepatic injuries

Injury Type	Frequency (%)
Cardiac Injury	32.0
Renal Injury	13.7
Hepatic Injury	3.7

Prevalence of Injuries by Age

Table 3 presents the mean age, standard deviation (SD), and standard error (SE) of

patients with and without cardiac, renal, and hepatic injuries. The mean age of patients with cardiac injury was 58.21 ± 13.36 years, compared to 51.45 ± 16.77 years for those without. For renal injury, the mean age was 61.69 ± 10.91 years versus 52.33 ± 16.38 years without injury. For hepatic injury, the mean age was 58.21 ± 13.36 years versus 53.24 ± 16.16 years without injury. Independent sample t-tests showed that mean age was significantly higher in patients with cardiac, renal, and hepatic injuries (P values 0.001, 0.003, and 0.000, respectively).

Table 3 .presents the mean age, standard deviation (SD), and standard error (SE) of patients with and without cardiac, renal, and hepatic injuries

Injury Type	Mean Age (years)	SD (years)
Cardiac Injury	58.21	13.36
No Cardiac Injury	51.45	16.77
Renal Injury	61.69	10.91
No Renal Injury	52.33	16.38
Hepatic Injury	58.21	13.36
No Hepatic Injury	53.24	16.16

Prevalence of Injuries by Gender

Tables 4 to 6 show injury prevalence by gender. Among patients with cardiac injuries, 53.1% were male and 46.9% female; among those without cardiac injuries, 52.9% were male and 47.1% female. Pearson Chi-square tests showed no significant association between cardiac injury and gender (P = 0.966).

Tables 4. injury prevalence by gender

Gender	Cardiac Injury (%)	No Cardiac Injury (%)
Male	53.1	52.9
Female	46.9	47.1

For renal injuries, 52.4% of injured patients were male and 47.6% female; among non-injured, 53.1% male and 46.9% female. No significant association was found between renal injury and gender (P = 0.913).

Tables 5. injury prevalence by gender

Gender	Renal Injury (%)	No Renal Injury (%)
Male	52.4	53.1
Female	47.6	46.9

For hepatic injuries, 50.0% of injured patients were male and 50.0% female; among non-injured, 53.1% male and 46.9% female. No significant association was found between hepatic injury and gender (P = 0.774).

Tables 6. injury prevalence by gender

Gender	Hepatic Injury (%)	No Hepatic Injury (%)
Male	50.0	53.1
Female	50.0	46.9

Prevalence of Injuries by Mortality

Tables 7 to 9 display injury prevalence by mortality status. Among patients with cardiac injuries, 45.8% died and 54.2% survived; among those without cardiac injuries, 5.4% died and 94.6% survived. There was a significant association between cardiac injury and mortality, with higher death rates in injured patients (P = 0.000).

Tables 7. injury prevalence by mortality status

Mortality Status	Cardiac Injury (%)	No Cardiac Injury (%)
Dead	45.8	5.4
Alive	54.2	94.6

Among patients with renal injuries, 57.3% died and 42.7% survived; among those without renal injuries, 12.2% died and 87.8% survived. Renal injury was significantly associated with higher mortality (P = 0.000).

**Tables 8. injury prevalence by mortality status**

Mortality Status	Renal Injury (%)	No Renal Injury (%)
Dead	57.3	12.2
Alive	42.7	87.8

Among patients with hepatic injuries, 36.4% died and 63.6% survived; among those without hepatic injuries, 17.6% died and 82.4% survived. Hepatic injury was also significantly associated with mortality (P = 0.026).

Tables 9. injury prevalence by mortality status

Mortality Status	Hepatic Injury (%)	No Hepatic Injury (%)
Dead	36.4	17.6
Alive	63.6	82.4

These findings indicate that cardiac, renal, and hepatic injuries are prevalent in COVID-19 patients, with higher age correlating with increased injury rates. While gender did not significantly influence injury prevalence, these injuries were significantly associated with increased mortality.
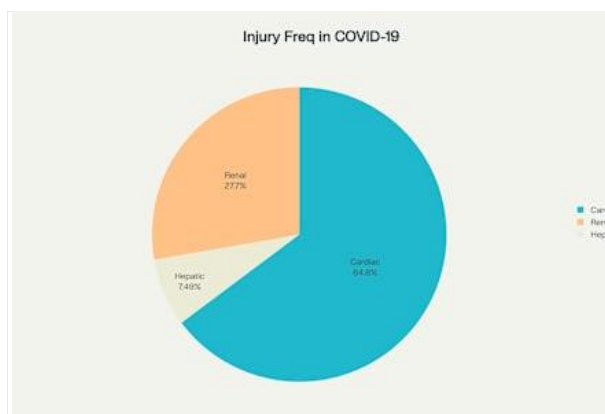
Figure1 .injury Frequency in COVID-19

Discussion

In December 2019, a group of patients with pneumonia of unknown causes was identified in Wuhan, China. The cause of this disease was diagnosed as infection with a novel coronavirus(1). This virus was named 2019-nCoV by the World Health Organization (WHO) and was recognized as the third coronavirus infecting humans after Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), causing severe pneumonia(2). The China National Health Commission (NHC) reported that 11.8% of deceased cases without a history of cardiovascular disease had severe heart injury accompanied by a significant increase in cardiac troponin I (cTnI) or cardiac arrest. Therefore, cardiovascular symptoms are highly prevalent in COVID-19 patients and may be associated with inflammatory responses and immune system disorders(11).

Liver injury in these patients has also been observed due to direct viral attack on liver cells. It is also possible that liver injury results from the toxic effects of drugs used during treatment, hypoxia related to pneumonia, and cytokine storm. Liver injury in patients with moderate severity is transient and can return to normal(12). Further analyses have shown that acute multiple organ injury is more frequent in severe COVID-19 patients, which can be attributed to ACE-2 expression on organs such as liver, heart, kidney, brain, and gastrointestinal tract in addition to lung cells(14). In the present study, the prevalence of multiple organ injury in COVID-19 patients in the city of Sari was investigated. First, the results of this study were examined,

followed by comparison with other studies. The results showed that 32% of patients had cardiovascular injuries, 13.7% had kidney injuries, and 3.7% had liver injuries. Additionally, the mean age of patients with heart, kidney, and liver injuries was significantly higher. The results showed no significant association between heart, kidney, liver injuries and gender. One of the most important findings was a significant association between heart injuries and mortality, with death being significantly higher in patients with heart injuries. Similarly, a significant association was found between kidney injuries and mortality, with death significantly higher in patients with kidney injuries. The same significant association was observed between liver injuries and mortality(11).

Comparing the present study with others, on March 16, 2020, Yichun Cheng and colleagues examined the prevalence of acute kidney injury (AKI) in hospitalized COVID-19 patients in Wuhan, China, and evaluated the association between death and markers related to kidney dysfunction. This prospective cohort study included 701 patients with a median age of 63 years (range 50-71), including 367 men and 334 women, hospitalized in a tertiary teaching hospital. Proteinuria was observed in 43.6% and hematuria in 26.7% of patients. Elevated serum creatinine, blood urea nitrogen, and glomerular filtration rate (GFR) below 60 ml/min/1.73m² were reported in 14.4%, 13.1%, and 13.1% of patients, respectively. During the study period, AKI occurred in 5.1% of patients. In the present study, the overall incidence of kidney problems was 13.7%, which is higher than Cheng's study, possibly due to considering all kidney problems generally. Kaplan-Meier analysis demonstrated that patients with kidney involvement were at higher risk of death. Cox regression identified serum creatinine (hazard ratio [HR]: 1.2, 95% CI: 1.36-3.26), urea (HR: 3.97, CI: 0.57-6.14), AKI stages 1 to 3, proteinuria, and hematuria as independent risk factors for mortality after adjusting for age, sex, leukocyte count, underlying diseases, and disease severity. This study highlighted the high prevalence of kidney disease in hospitalized COVID-19 patients, which is associated with increased mortality(15). The present study also identified kidney disorders as an independent risk factor for death, consistent with Cheng's findings.

Another study by Aurelio Sonzogni, published on March 11, 2020, analyzed liver biopsy samples from 48 deceased COVID-19 patients with severe pulmonary symptoms and respiratory failure in two major hospitals in northern Italy. None of the patients had clinical signs or liver dysfunction during or before hospitalization. Functional tests were

available for all patients. All liver samples showed at least minimal inflammatory features. Histological images revealed vascular changes including increased portal vein branches with lumen dilation, complete or partial thrombosis of portal and sinusoidal vessels. COVID-19 virus was detected in 15 out of 22 patients examined by in situ hybridization. Preliminary results suggested that liver damage is not a major concern in this disease and that the liver is not the primary target of inflammation(16). Contrary to Sonzogni's findings, liver injuries were observed in 3.7% of patients in the present study, with mortality significantly higher in patients with liver damage. Differences in study methods may explain these discrepancies.

In another study by Yichun Cheng published on February 20, 2020, the prevalence and incidence of abnormal urinalysis and kidney dysfunction were investigated in hospitalized COVID-19 patients in Wuhan. Hematuria, proteinuria, serum creatinine concentration, and other clinical factors were evaluated alongside AKI incidence and its association with mortality. Among 710 hospitalized patients, 12.3% died, 44% had proteinuria and hematuria, and elevated creatinine and urea levels were observed in 15.5% and 14.1%, respectively. AKI occurred in 3.2% of patients during the study. Kaplan-Meier

analysis confirmed that patients with kidney injury had a higher risk of death. This finding aligns with the present study, which also showed that 13.7% of patients had kidney disorders associated with increased mortality(15).

Manish Bansal reported that many COVID-19 patients had a history of cardiovascular disease or developed cardiac injury during illness. Respiratory abnormalities are the main hallmark of coronavirus infection, while cardiovascular injury is less common. Acute cardiac injury is characterized by elevated cardiac troponin levels and occurs in 8-12% of patients. Direct viral involvement of cardiomyocytes and systemic inflammation are the most common causes of myocardial injury. A history of cardiovascular disease and acute cardiac injury contribute to severe outcomes(17). The present study found cardiac injury in 32% of patients, associated with increased mortality, consistent with Bansal's findings.

Another study by Ajay Kumar Mishra MD examined laboratory parameters indicating cardiac injury in 273 COVID-19 patients. The role of cardiac injury markers such as creatine kinase myocardial band (CK-MB), myoglobin, and cardiac troponin I in disease outcomes was assessed. Elevated levels of these enzymes in venous blood correlated with disease severity and poor recovery. Both ischemic and non-ischemic myocardial injury

were observed. Cytokine storm, hemophagocytic lymphohistiocytosis, viral myocarditis, stress cardiomyopathy, and hypoxia were identified as causes of non-ischemic myocardial injury(18). This study also found cardiac injury in 32% of patients, linked to increased mortality, consistent with the present study.

Conclusion

Overall, it can be concluded that 32% of patients suffered cardiovascular injuries, 13.7% had kidney injuries, and 3.7% had liver injuries. Additionally, the mean age of patients with heart, kidney, and liver injuries was significantly higher.

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Authorship

all authors meet the ICMJE authorship criteria.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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References

1.Saldanha M, Reddy R, Vincent MJ. Title of the article: paranasal mucormycosis in COVID-19 patient. Indian Journal of Otolaryngology and Head & Neck Surgery. 2021:1-4.

2.Kondapavuluri SK, Anchala VKR, Bandlapalli S, Gorantla R, Danaboyina AR, Kondapavuluri BK, et al. Spectrum of MR imaging findings of sinonasal mucormycosis in post COVID-19 patients. The British Journal of Radiology. 2021;94(1127):20210648.

3.Al-Tawfiq JA, Alhumaid S, Alshukairi AN, Temsah M-H, Barry M, Al Mutair A, et al. COVID-19 and mucormycosis superinfection: the perfect storm. Infection. 2021;49:833-53.

4.Mishra N, Mutya VSS, Thomas A, Rai G, Reddy B, Mohanan AA, et al. A case series of invasive mucormycosis in patients with COVID-19 infection. Int J Otorhinolaryngol Head Neck Surg. 2021;7(5):867-70.

5.Said Ahmed WM, Elsherbini AM, Elsherbiny NM, El-Sherbiny M, Ramzy NI, Arafa AF. Maxillary mucormycosis osteomyelitis in post COVID-19 patients: a series of fourteen cases. Diagnostics. 2021;11(11):2050.

6.Jagtap SV, Jagtap SS, Nagar V, Varshney K. Invasive mucormycosis in post COVID-19 infection: case report with review. IP Arch Cytol Histopathol Res. 2021;6(2):135-9.

7.Walsh TJ, Gamaletsou MN, McGinnis MR, Hayden RT, Kontoyiannis DP. Early Clinical

and Laboratory Diagnosis of Invasive Pulmonary, Extrapulmonary, and Disseminated Mucormycosis (Zygomycosis). Clinical Infectious Diseases. 2012;54(suppl_1):S55-S60.

8. Chennamchetty VK, Adimulapu S, Kola BP, Padua M, Ambika C, Verma M, et al. Post-COVID pulmonary mucormycosis-a case report. IP Indian J Immunol Respir Med. 2021;6(1):62-6.

9. Daniel J. Education and the COVID-19 pandemic. Prospects. 2020;49(1):91-6.

10. DeRoo SS, Pudalov NJ, Fu LY. Planning for a COVID-19 vaccination program. Jama. 2020;323(24):2458-9.

11. Fauci AS, Lane HC, Redfield RR. Covid-19—navigating the uncharted. Mass Medical Soc; 2020.

12. Velavan TP, Meyer CG. The COVID-19 epidemic. Tropical medicine & international health. 2020;25(3):278.

13. Andreadakis Z, Kumar A, Román RG, Tollefsen S, Saville M, Mayhew S. The COVID-19 vaccine development landscape. Nature reviews Drug discovery. 2020;19(5):305-6

14. Cao X. COVID-19: immunopathology and its implications for therapy. Nature reviews immunology. 2020;20(5):269-70.

15. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the treatment of Covid-19. New England Journal of Medicine. 2020;383(19):1813-26.

16. Klopfenstein T, Kadiane-Oussou N, Toko L, Royer P-Y, Lepiller Q, Gendrin V, et al. Features of anosmia in COVID-19. Médecine et Maladies infectieuses. 2020;50(5):436

17. Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: common findings in COVID-19 patients. The Laryngoscope. 2020;130(7):1787-.

18. Haynes BF, Corey L, Fernandes P, Gilbert PB, Hotez PJ, Rao S, et al. Prospects for a safe COVID-19 vaccine. Science translational medicine. 2020;12(568).

19. Weissleder R, Lee H, Ko J, Pittet MJ. COVID-19 diagnostics in context. Science translational medicine. 2020;12(546).

20. Shi Y, Wang G, Cai X-p, Deng J-w, Zheng L, Zhu H-h, et al. An overview of COVID-19. Journal of Zhejiang University-SCIENCE B. 2020;21(5):343-60.

21. Ahmad T, Khan M, Haroon THM, Nasir S, Hui J, Bonilla-Aldana DK, et al. COVID-19: Zoonotic aspects. Travel medicine and infectious disease. 2020;36:101607.

22. Watkins J. Preventing a covid-19 pandemic. British Medical Journal Publishing Group; 2020.

23. McKibbin W, Fernando R. The economic impact of COVID-19. Economics in the Time of COVID-19. 2020;45(10.1162).

24. Graham BS. Rapid COVID-19 vaccine development. Science. 2020;368(6494):945-6.

25. South AM, Diz DI, Chappell MC. COVID-19, ACE2, and the cardiovascular consequences. American Journal of Physiology-Heart and Circulatory Physiology. 2020;318(5):H1084-H90.

26. Nambiar M, Varma SR, Damdoum M. Post-Covid COVID-19, a fatal sequel to the pandemic in India. Saudi Journal of Biological Sciences. 2021;28(11):6461-4.

27.Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease COVID-19.: a deadly addition to the pandemic spectrum. The Journal of Infection deasise. 2021;135(5):442-7.

28.Saad RH, Mobarak FA. The diversity and outcome of COVID-19. A case report. International Journal of Infections Case Reports. 2021;88:106522.