A meta-analysis of 2019 novel corona virus patient clinical characteristics and comorbidities

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Abstract

Introduction

Being a new variant of coronavirus, detailed information regarding the virulence, its clinical characters, high risk individuals are yet to be defined. This study was done with the objective of finding out clinical features of corona infection and also studies what are the comorbidities that are associated with it.

Methods

This is a single arm meta-analysis in which relevant data were derived from searches in PubMed. It includes study papers which were written in English language and their completely published article is found. Seven articles published from 24th Jan to 16th March, 2020 are included in this study.

Results

The total number of patients was 1786 with 1044 males and 742 females with male to female ratio of 1.4:1. The median age of patients was 41 years). Fever was present in 88.8% cases. Dry Cough in 68% followed by fatigue in 33%. Hypertension (15.8%) is the most common comorbidity followed by cardio and cerebrovascular condition (11.7%).

Conclusion

Patients often presented with symptoms of fever, dry cough, lethargy and fatigue, muscle pain, productive cough. Similarly, patients with previous history of HTN, DM, COPD, cardio and cerebrovascular condition, immune-deficient states are at high risk of developing into the severe COVID-19 infection.

Introduction

Novel Corona Virus, also known as 2019-nCOV[1] has been identified as the cause of outbreak of respiratory illness which originated in Wuhan Hubei Province, China and has spread to other parts of the world. This variant of corona virus is named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2)by World Health Organization.[2] At present, there are 8,96,450 confirmed cases with 45,525 deaths.[3] In recent times, two variants of Corona Virus Severe Acute Respiratory Syndrome

(SARS) and Middle East Respiratory Syndrome (MERS) were found to cause respiratory illness in animals and human being. The knowledge regarding this new variant is limited and studies regarding this virus are going all around the world. In this study, I have analyzed multiple studies which incorporate clinical findings in patients which were present in COVID–19 diagnosed patients. This will identify the clinical features which are commonly present in these patients and can act as a prospective detail which can be used for diagnosing patients who are suspected to be suffering from the condition.

Methods

Data for this meta-analysis were identified by searches of PubMed and references from relevant articles using the search terms ''novel corona virus", ''Covid-19'', and ''clinical features of novel corona virus''. Total of hits were 1029. Only articles published in English between 24th Jan and 16th March, 2020 were included. 10 research papers were found which had description of clinical features. 7 papers which were published in English language were included. 2 papers were excluded from the study as one of the papers was found to be retracted and remaining two were published in language other than English and had only abstracts. Following 7 studies were included in this meta-analysis.

(Table 1)

Table 1: List of research articles used for this meta-analysis

Name of research paper	Authors	Patient details (Age and Sex) (male-M, Female-F)	Journal publishe
Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study	Chen N et al[1]	Total patients- 99 Age group-21-82 years M-67, F-32	The Lancet
Clinical features of patients infected with 2019 novel	Huang C et al[4]	Total patients- 41 Age group-41-58 years M-30, F-11	The Lancet

coronavirus in Wuhan, China			
Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19):A multi-center study in Wenzhou city, Zhejiang, China	Yang W et al[5]	Total patients-149 Age group-31-59 years M-81, F-68	Journal of Infect
Clinical Characteristics of Coronavirus Disease 2019 in China	Guan W et al[6]	Total patients-1099 Age group-0-65+ years M-640, F-459	New England Medicine
Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China	Wang D et al [7]	Total patients-138 Age group-42-68 years M-75, F-63	Journal of Am Association
Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China	Wang Z et al[8]	Total patients-69 Age group-35-62 years M-32, F-37	Clinical Infectio
Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort	Zhou F et al[9]	Total patients-191 Age group-46-67 years M-119, F-72	The Lancet

study			

Results
Demographics and Clinical Characteristics

We obtained data regarding demographics including their age and sex distribution. The total number

of patients was 1786 with 1044 males and 742 males with a male to female ratio of 1.4:1. The median

age of patients were 41 years(interquartile range-0 to 82 years of age). Fever was present in 88.8%

cases. The second most common symptom was dry cough present in 68% cases. Fatigue was present

in 33.1% cases. Productive cough was present in 28.5%cases followed by muscle pains in 14.4%

cases. Diarrhea(4.4%) ,Nausea or vomiting (4.1%), Rhinorrhea(3.2%) Chest and abdominal

pain(0.15%) were among the least common cases. The clinical characteristics of patients are shown in

Table 2.

Table 2: Clinical characteristics of patients with COVID-19

Clinical characteristics	Number	Percentage
Fever	1587	88.8%
Dry cough	1215	68%
Fatigue	591	33.1%
Productive Cough	510	28.5%
Shortness of Breath	303	17%
Muscle pain	257	14.4%
Sore throat	203	11.4%
Headache	183	10.2%
Diarrhea	78	4.4%
Nausea and Vomiting	74	4.1%
Rhinorrhea	57	3.2%
Chest pain	3	0.16%
Abdominal pain	2	0.11%

Similarly, multiple comorbidities were found among patients of COVID-19. Though 7 studies are

included in this meta-analysis. Only six of them are included here as one did not provide information

regarding co-morbidities with a total of 1717 patients. Hypertension (15.8%) is the most common comorbidity in patients suffering from COVID-19 infection. Other cardiovascular and cerebrovascular conditions were present in 11.7% patients followed by endocrine disorder primarily diabetes in 9.4% patients. The comorbidities of patients are shown in Table 3.

Table 3: Pre-existing comorbidities in patients with COVID-19

Comorbidities	Number	Percentage
Hypertension(HTN)	272	15.8%
Cardiovascular and Cerebrovascular diseases	200	11.7%
Endocrine system(Diabetes)	161	9.4%
Co-existing infection(HIV and Hepatitis B)	25	1.5%
Malignancy	25	1.5%
Respiratory system(COPD and others)	24	1.4%
Renal disorders	14	0.8%
Immunodeficiency states	2	0.01%

Discussion

COVID-19, new variant of Corona Virus, is an enveloped virus with helical nucleo-capsid that contains single stranded RNA and have distinctive club-shaped surface projections that give appearance of a solar corona to the virion named for Crown like spikes proteins around the lipid envelope.[9] Though, exact genetic composition and its variation has not be decrypted. Multiple of published studies show that Novel corona Virus(COVID-19) is sufficiently different from SARS corona virus and is hence a new variant of beta-coronavirus. This novel corona virus might be linked to a zoonotic pathogen. It has been said that this virus might have originated from a zoonotic pathogen as the virus isolated from the affected patient showed the similar corona virus sequence   EPI_ISL_402131which is also found in Rhinolophus affinis, an Asian bat predominantly found in China. At least 96% similarity was found between corona virus genome and that of bat relative, however, similarity with the human strain of SARS is much lower of around 80%.   Although zoonotic origin of virus is seen, animals sold at the sea food market in Wuhan might represent an intermediate host facilitating the emergence of virus in humans.[10,11,12,13,34,36,37,38]

In this study, it has been found that fever and cough(both dry and productive), fatigue, shortness of breath and muscle aches were found to be the major symptoms in patients who were diagnosed to be suffering from COVID-19. One of the published retrospective study by Yang *et al*[14], showed that fever, cough and shortness of breath were major symptoms in patients of COVID-19 pneumonia. Centre for disease control(CDC) also listed these symptoms to be the major symptoms.[15] Another studies showed that fever, cough and vomiting were among the most common symptoms.[16] Similar findings were shown in multiple of other studies.[17,18,19,20,21,28,29,30,31,32,33,35,]

Similarly, this study shows that the extent of disease severity is largely dependent in patient comorbid conditions. This study shows that Hypertension(HTN), other cardiovascular and cerebrovascular diseases, diabetes mellitus(DM), respiratory disorders like Chronic Obstructive Pulmonary Disease(COPD), other concurrent infections and immunodeficiency states are among major co-morbidities present in individuals suffering fromCOVID-19. In a systematic review by Yang J *et al*[22], HTN,DM, cardiovascular and cerebrovascular conditions, COPD, malignancy and immunosuppressed states were shown among others as the important risk factors. Angiotensin Converting Enzyme inhibitors which is generally used in HTN has warranted a specific concern [42], however, substantial findings are yet to be found. Angiotensin converting enzyme 2 (ACE2) receptors have been shown to be the entry point into human cells for SARS-CoV-2, the virus that causes COVID-19. In a few experimental studies with animal models, both angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) have been shown to upregulate ACE2 expression in the heart. Though these have not been shown in human studies, or in the setting of COVID-19.[23] Multiple of published reports show that Diabetes[39,40,41], Hypertension[43,44,45,46,47]and Cardiovascularconditions[45,46,47] , Immunosuppressed states[48,49,50,51], gastric conditions are among the most common co-morbidities that leads to increased infection, virulence and fatality when an individual is affected by Novel Corona Virus.[22,24,]

Conclusion

Novel Corona Virus is the recent outbreak of new form of Corona Virus whose exact determinants are

yet to be found. But it is certain that it causes variety of clinical conditions which manifests in the form of fever, cough, shortness of breath, muscle pain and fatigue, abdominal pain, nausea and vomiting. It is also found that milder forms may be found in previously healthy individuals as compared to those who had pre-existing conditions like hypertension, diabetes, arrhythmias, COPD, immunodeficiency states and concurrent infections.

References

1.   Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., et al (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30211-7/fulltext [Accessed 7 Feb. 2020].

2.   Naming the coronavirus disease (COVID-19) and the virus that causes it [Internet]. Who.int. 2020 [cited 3 April 2020]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it

3.   Novel Coronavirus (2019-nCoV) situation reports [Internet]. Who.int. 2020 [cited 3 April 2020]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/

4.   Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet [Internet]. 2020 [cited 15 March 2020];395(10223):497-506. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext

5.   Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19):A multi-center study in Wenzhou city, Zhejiang, China. Journal of Infection [Internet]. 2020 [cited 15 March 2020];. Available from:

https://www.sciencedirect.com/science/article/pii/S0163445320300992

6. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J et al. Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine [Internet]. 2020 [cited 15 March 2020];. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2002032

7. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA [Internet]. 2020 [cited 15 March 2020];. Available from: https://jamanetwork.com/journals/jama/fullarticle/2761044

8. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. Clinical Infectious Diseases [Internet]. 2020 [cited 17 March 2020];. Available from: https://academic.oup.com/cid/advancearticle/doi/10.1093/cid/ciaa272/5807944

9. Oie.int. (2020). *Questions and Answers on 2019-nCoV Acute Respiratory Disease: OIE - World Organisation for Animal Health*. Available at: https://www.oie.int/scientific-expertise/specific-information-and-recommendations/questions-and-answers-on-2019novel-coronavirus/ [Accessed 7 Feb. 2020].

10. Healthcare-in-europe.com. (2020). *New coronavirus: largest meta-analysis yet answers important questions*. Available at: https://healthcare-in-europe.com/en/news/new-coronavirus-largest-meta-analysis-yet-answers-important-questions.html [Accessed 7 Feb. 2020].

11. Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., et al. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet*. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30251-8/fulltext [Accessed 7 Feb. 2020].

12. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P et al. Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. Cell Host & Microbe [Internet]. 2020 [cited 18 March 2020];27(3):325-328. Available from: https://www.ncbi.nlm.nih.gov/pubmed/32035028

13. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The Lancet [Internet]. 2020 [cited 18March2020];395(10224):565-574.Availablefrom: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30251-8/fulltext

14. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine [Internet]. 2020 [cited 18 March 2020];. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30566-3/fulltext

15. Cdc.gov. (2020). *Symptoms of Novel Coronavirus (2019-nCoV) | CDC*. Available at: https://www.cdc.gov/coronavirus/2019-ncov/about/symptoms.html [Accessed 7 Feb. 2020].

16. Liu W, Zhang Q, Chen J, Xiang R, Song H, Shu S et al. Detection of Covid-19 in Children in Early January 2020 in Wuhan, China. New England Journal of Medicine [Internet]. 2020 [cited 18 March 2020];. Available from: https://www.nejm.org/doi/full/10.1056/NEJMc2003717?query=featured_home

17. Holshue M, DeBolt C, Lindquist S, Lofy K, Wiesman J, Bruce H et al. First Case of 2019 Novel Coronavirus in the United States. New England Journal of Medicine [Internet]. 2020 [cited 18 March 2020];382(10):929-936. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2001191

18. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. New England Journal of Medicine [Internet]. 2020 [cited 18 March 2020];382(8):727-733. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2001017

19. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. New England Journal of Medicine [Internet]. 2020 [cited 18 March 2020];382(10):970-971. Available from: https://www.nejm.org/doi/full/10.1056/NEJMc2001468

20. Leung C. Clinical features of deaths in the novel coronavirus epidemic in China. Reviews in Medical Virology [Internet]. 2020 [cited 18 March 2020];. Available from: https://onlinelibrary.wiley.com/doi/10.1002/rmv.2103

21. Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected Coronavirus Disease 2019 in two emergency departments outside of Hubei, China. Journal of Medical Virology [Internet]. 2020 [cited 18 March 2020];. Available from: https://doi.org/10.1002/jmv.25763

22. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. International Journal of Infectious Diseases [Internet]. 2020 [cited 18 March 2020];. Available from: https://www.ncbi.nlm.nih.gov/pubmed/32173574

23. HFSA/ACC/AHA Statement Addresses Concerns Re: Using RAAS Antagonists in COVID-19 - American College of Cardiology [Internet]. American College of Cardiology. 2020 [cited 18 March 2020]. Available from: https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19

24. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S et al. Risk Factors Associated With Acute

Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Internal Medicine [Internet]. 2020 [cited 18 March 2020];. Available from: https://www.ncbi.nlm.nih.gov/pubmed/32167524

25. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clinical Research in Cardiology [Internet]. 2020 [cited 18 March 2020];. Available from: https://link.springer.com/article/10.1007%2Fs00392-020-01626-9

26. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?. The Lancet Respiratory Medicine [Internet]. 2020 [cited 18 March 2020];. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30116-8/fulltext

27. Wang T, Du Z, Zhu F, Cao Z, An Y, Gao Y et al. Comorbidities and multi-organ injuries in the treatment of COVID-19. The Lancet [Internet]. 2020 [cited 18 March 2020];. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30558-4/fulltext

28. Jiang F, Deng L, Zhang L, Cai Y, Cheung C, Xia Z. Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19). Journal of General Internal Medicine [Internet]. 2020 [cited 3 April 2020];. Available from: https://link.springer.com/article/10.1007/s11606-020-05762-w

29. Sun P, Lu X, Xu C, Sun W, Pan B. Understanding of COVID-19 based on current evidence. Journal of Medical Virology [Internet]. 2020 [cited 3 April 2020];. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25722

30. Shi F, Yu Q, Huang W, Tan C. 2019 Novel Coronavirus (COVID-19) Pneumonia with Hemoptysis as the Initial Symptom: CT and Clinical Features. Korean Journal of Radiology [Internet]. 2020 [cited 3 April 2020];21. Available from:

https://www.kjronline.org/DOIx.php?id=10.3348/kjr.2020.0181

31.   Han Y, Yang H. The transmission and diagnosis of 2019 novel coronavirus infection

disease (COVID-19): A Chinese perspective. Journal of Medical Virology [Internet].

2020 [cited 3 April 2020];. Available from:

https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25749

32.   Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early Clinical and CT

Manifestations of Coronavirus Disease 2019 (COVID-19) Pneumonia. American Journal

of Roentgenology [Internet]. 2020 [cited 3 April 2020];:1-6. Available from:

https://www.ajronline.org/doi/full/10.2214/AJR.20.22961

33.   Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients

Dying in Relation to COVID-19 in Italy. JAMA [Internet]. 2020 [cited 3 April 2020];.

Available from: https://jamanetwork.com/journals/jama/fullarticle/2763667

34.   Rothan H, Byrareddy S. The epidemiology and pathogenesis of coronavirus disease

(COVID-19) outbreak. Journal of Autoimmunity [Internet]. 2020 [cited 3 April

2020];:102433. Available from:

https://www.sciencedirect.com/science/article/pii/S0896841120300469?via%3Dihub

35.   Rodriguez-Morales A, Cardona-Ospina J, Gutiérrez-Ocampo E, Villamizar-Peña R,

Holguin-Rivera Y, Escalera-Antezana J et al. Clinical, laboratory and imaging features

of COVID-19: A systematic review and meta-analysis. Travel Medicine and Infectious

Disease [Internet]. 2020 [cited 3 April 2020];:101623. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102608/

36.   Shereen M, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin,

transmission, and characteristics of human coronaviruses. Journal of Advanced

Research [Internet]. 2020 [cited 3 April 2020];24:91-98. Available from:

https://www.sciencedirect.com/science/article/pii/S2090123220300540

37. COVID-19 coronavirus epidemic has a natural origin [Internet]. ScienceDaily. 2020 [cited 3 April 2020]. Available from: https://www.sciencedaily.com/releases/2020/03/200317175442.htm

38. Weston S, Frieman M. COVID-19: Knowns, Unknowns, and Questions. mSphere [Internet]. 2020 [cited 3 April 2020];5(2). Available from: https://msphere.asm.org/content/5/2/e00203-20

39. Bloomgarden Z. Diabetes and COVID-19. Journal of Diabetes [Internet]. 2020 [cited 3 April 2020];12(4):347-348. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/1753-0407.13027

40. Gupta R, Ghosh A, Singh A, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes & Metabolic Syndrome: Clinical Research & Reviews [Internet]. 2020 [cited 3 April 2020];14(3):211-212. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102582/

41. Muniyappa R, Gubbi S. COVID-19 Pandemic, Corona Viruses, and Diabetes Mellitus. American Journal of Physiology-Endocrinology and Metabolism [Internet]. 2020 [cited 3 April 2020];. Available from: https://journals.physiology.org/doi/abs/10.1152/ajpendo.00124.2020

42. Marin G. Facts and reflections on COVID-19 and anti-hypertensives drugs. Drug Discoveries & Therapeutics [Internet]. 2020 [cited 3 April 2020];. Available from: https://www.jstage.jst.go.jp/article/ddt/advpub/0/advpub_2020.01017/_article

43. Lippi G, Wong J, Henry B. Hypertension and its severity or mortality in Coronavirus Disease 2019 (COVID-19): a pooled analysis. Polish Archives of Internal Medicine [Internet]. 2020 [cited 3 April 2020];. Available from: https://www.mp.pl/paim/issue/article/15272

44. Leung C. Clinical features of deaths in the novel coronavirus epidemic in China.

Reviews in Medical Virology [Internet]. 2020 [cited 3 April 2020];. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/rmv.2103

45.   Guo T, Fan Y, Chen M, Wu X, Zhang L, He T et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiology [Internet]. 2020 [cited 3 April 2020];. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7101506/

46.   Chen T, Wu D, Chen H, Yan W, Yang D, Chen G et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ [Internet]. 2020 [cited 3 April 2020];:m1091. Available from: https://www.bmj.com/content/368/bmj.m1091.long

47.   Madjid M, Safavi-Naeini P, Solomon S, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System. JAMA Cardiology [Internet]. 2020 [cited 3 April 2020];. Available from: https://jamanetwork.com/journals/jamacardiology/fullarticle/10.1001/jamacardio.2020.1286

48.   Guillen E, Pineiro G, Revuelta I, Rodriguez D, Bodro M, Moreno A et al. Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation?. American Journal of Transplantation [Internet]. 2020 [cited 3 April 2020];. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15874

49.   D'Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic. Liver Transplantation [Internet]. 2020 [cited 3 April 2020];. Available from: https://aasldpubs.onlinelibrary.wiley.com/doi/abs/10.1002/lt.25756

50.   Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R et al. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. Annals of Oncology [Internet]. 2020 [cited 3 April 2020];.

Available from: https://linkinghub.elsevier.com/retrieve/pii/S0923-7534(20)36383-3

51. Ritchie A, Singanayagam A. Immunosuppression for hyperinflammation in COVID-19: a double-edged sword?. The Lancet [Internet]. 2020 [cited 3 April 2020];395(10230):1111. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140-6736(20)30691-7