



Research Article

Human Body: The Secret Chamber of SARS-CoV-2

Sandra SN¹, Anjali Rajendran², Merlin K Regi³, Sheeba P⁴, Feebarani John⁵

^{1,2,3,4,5}Department of Zoology, Vimala College (Autonomous), Thrissur, Kerala, India.

DOI: <https://doi.org/10.24321/0019.5138.202215>

I N F O

Corresponding Author:

Anjali Rajendran, Department of Zoology, Vimala College (Autonomous), Thrissur, Kerala, India.

E-mail Id:

aspiringresearchers3@gmail.com

Orcid Id:

<https://orcid.org/0000-0002-0126-3270>

How to cite this article:

Sandra SN, Rajendran A, Regi MK, Sheeba P, John F. Human Body: The Secret Chamber of SARS-CoV-2. Special Issue - COVID-19 & Other Communicable Disease. 2022;98-102.

Date of Submission: 2021-09-23

Date of Acceptance: 2021-11-26

A B S T R A C T

Background: A larger number of people have been affected with COVID-19 and the number of survivors is increasing day by day. Recently many reports on health issues have been arising from various corners of the world. This raises the question of whether SARS-CoV-2 has a long term impact on our health conditions or will it persist in the human body. This work peeps into such concerns of COVID-19 survivors.

Objective: This study focuses on the persistence and sequelae of SARS-CoV-2 in COVID-19 survivors.

Methods: A survey was conducted among COVID-19 survivors of Kerala, India to analyse the long term health impacts of COVID-19. 294 COVID-19 survivors participated in the survey and Google form was the key tool used in the study. The results obtained were compared with published research papers and articles to check for the probability of persistence of SARS-CoV-2.

Results: SARS-CoV-2 poses long term health issues for survivors. Majority of the participants (64.2%) reported that they have neurological, reproductive and musculoskeletal symptoms. The present study on the mode of entry of virus and immune-privileged sites in the human body, when compared to reported works earlier suggests that the chance of persistence of SARS-CoV-2 in the human body is higher as this virus has a noticeable potency to infect immune-privileged sites.

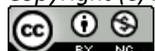
Conclusion: Most of the survivors face numerous difficulties even after laboratory tests shows them negative for COVID-19 and hence the question 'whether the human body will act as a reservoir for SARS-CoV-2' cannot be neglected. Further studies are to be conducted in this regard and emphasis should be on establishing more post-COVID clinics.

Keywords: COVID-19, SARS-CoV-2, Persistence, Post-COVID Symptoms, Immune-privileged Site, ACE2 Receptor

Introduction

COVID-19 a newly emerged pandemic caused by SARS-CoV-2 has become a nightmare to the whole world. SARS-CoV-2

is a highly virulent single-stranded RNA virus belonging to the family Coronaviridae.¹ It was first reported from Wuhan, on 31 December 2019 and is spreading its wings



since then.² Nearly 162,000,000 cases have been reported globally and around 3,376,555 people have lost their lives.³

Once infected with SARS-CoV-2 the person may show various symptoms such as cough, headache, nasal obstruction, fever, and loss of smell etc.^{4,5} Cases, where patients are asymptomatic, have also been reported.⁶ The current focus is on recovery from COVID-19 without giving due emphasis to its future complications. Recent reports suggest that various symptoms such as fatigue, dizziness, chest pain, continue to persist even after recovery from COVID-19.⁷ These indicate that there is a high chance of persistence of SARS-CoV-2 in the human body.

The prevalence of SARS-CoV-2 is the current area of investigation. The duration, type and severity of post COVID symptoms in COVID-19 survivors are studied by scientists around the world. The present study aims to inspect various post COVID symptoms in survivors and the chance of persistence of SARS-CoV-2 in the human body.

Materials and Method

The prime aim of the online survey was to collect relevant data regarding post COVID symptoms among COVID-19 survivors in Kerala. The survey was conducted through Google form and was open to all COVID-19 survivors of Kerala who tested COVID negative, for at least one week before taking part in the survey. The form was circulated through various online platforms and 294 COVID-19 survivors took part in the survey. It was a completely anonymous survey conducted solely for research work. No one can trace who entered the data by any means to make data entry sincere. None of the personal details of the participants were collected.

Questionnaire Design and Survey Dissemination

Questions consisted of socio-demographic profile and COVID and post-COVID history. Specifically, the participants were asked to state their gender to understand whether any gender-specific variations are there or not. For the age specifications, the participants were divided into 7 age groups ranging between (i) 0-10 years, (ii) 10-20 years, (iii) 20-30 years, (iv) 30-40 years, (v) 40-50 years and (vi) above 60 years. The participants were also asked about their location/district to understand their locality for the soundness of the survey. The duration taken for recovery and the duration after testing COVID negative were also taken and later was divided into four categories: (i) 1 week, (ii) 2 weeks, (iii) 3 weeks, (iv) more than three weeks.

The common COVID-19 and post-COVID-19 symptoms were assessed objectively. Apart from the symptoms given in the question, the participants were also asked to specify if they experienced any other COVID-19 and post COVID-19 symptoms. The enlisted COVID-19 symptoms in the questionnaire were: (i) fever, (ii) cough, (iii) headache,

(iv) pneumonia, (v) breathing difficulty, (vi) throat pain, (v) tiredness and the post COVID symptoms given in questionnaire were: (i) eye itching or eye redness, blurred vision, (ii) headaches, fatigue, dizziness, (iii) loss of taste, (iv) itching, (v) painful inflammation at genital part, painful urination, lower abdominal pain, discharge from the penis, (vi) shortness of breath or other difficulties in newborn of COVID-19 survivors, (vii) joint pain, (viii) muscle pain, (ix) disturbed menstrual cycle, (x) discomfort in the chest and burning sensation in the chest. Participants without any noticeable post COVID symptoms were also spotted by assigning a separate option "no post COVID symptoms" in the survey. The survey was open to all who tested COVID negative for at least 1 week before the day of taking part in it. Illustrative statistics were carried out for all questions in the survey.

Results

Table 1 manifests the socio-demographic characteristics of all COVID-19 survivors who took part in the survey. Out of the 294 participants, 141 were females and 153 were males. Majority of the participants (83 participants) were between 21-30 years followed by 11-20 years (60 participants) and 31-40 years (48 participants).

Table 1. Participant's Demographic Profile (n=294)

Characteristics	Number (%)
Age categories (years)	
0-10	10(3.4)
11-20	60(20.4)
21-30	83(28.2)
31-40	48(16.32)
41-50	42(14.3)
51-60	36(12.2)
Above 60	15 (5.1)
Gender	
Male	153(52.1)
Female	141(47.9)

Table 2. Post-recovery Period

Post-recovery period	Participants n(%)
1 week	86 (29.25)
2 weeks	65 (22.10)
3 weeks	36 (12.24)
More than 3 weeks	107 (36.39)

Table 2 indicates the post-recovery period i.e. how long has it been after testing negative for COVID-19. Of all the respondents, majority (107) tested negative for more than 3 weeks before taking part in the survey, followed by 86 of

them who turned out COVID negative before 1 week and 65 of them tested negative 2 weeks before taking part in the survey.

Table 3 illustrates the COVID-19 symptoms that were experienced by the participants. Majority of them experienced fever (179,60.88%), followed by headache (150,51.02%) and tiredness (144,48.97%). Other symptoms reported were cough (105), throat pain (93), breathing difficulty (57) and pneumonia (6). 43 of the total participants were reported asymptomatic i.e. they experienced no COVID-19 symptoms.

Table 3. COVID-19 Symptoms in the Participants

Symptoms	Participants n (%)
Fever	179 (60.88)
Cough	105 (35.7)
Headache	150 (51.02)
Pneumonia	6(2.00)
Breathing difficulty	57(19.38)
Throat pain	93(31.63)
Tiredness	144 (48.97)
Asymptomatic	43 (14.6)

Table 4. Prevalence of Post-COVID-19 Symptoms among COVID-19 Survivors

Characteristics	Participants n (%)
Neurological symptoms	
Eye itching/redness/blurred vision	13 (4.4)
Headache/fatigue/dizziness	95(32.3)
Loss of taste	76(25.9)
Loss of smell	3(1.0)
Sleeping disorders	2(0.68)
Musculoskeletal symptoms	
Joint pain	50(17)
Muscle pain	58(19.7)
Reproductive symptoms	
Disturbed menstrual cycle**	7(4.9)
Discharge from penis/lower abdominal pain/painful inflammation at genital part/painful urination*	9 (5.8)
Integumentary symptoms	
Itching	12 (4.1)

*percentage of males only.

**percentage of females only.

Table 4 display the post-COVID symptoms of the participants i.e. the symptoms which prolong even after the recovery

from COVID-19. It was surprising to find that many of the participants do experience post COVID symptoms which points to their deteriorating health conditions.

Data shows that majority of the participants experienced neurological signs such as headache/ fatigue/ dizziness (95) and loss of taste (76). 13 participants reported eye itching/ redness/ blurred vision. Loss of smell (3) and sleeping disorders (1) were also reported by the respondents. Musculoskeletal symptoms included muscle pain in 58 and joint pain in 50 respondents. 7 females had disturbed menstrual cycle and 9 males had painful inflammation at genital part/ discharge from penis/ lower abdominal pain/ painful urination which signifies reproductive regularities. 12 participants complained about itching, which is an integumentary symptom.

Discussion

The present study revealed that many of the COVID-19 survivors experience post COVID symptoms. Recent studies have proven that SARS-CoV-1 and SARS-CoV-2, of family Coronaviridae exhibit many similar features; both use their S protein to recognise and bind with the ACE2 receptor in host epithelial and endothelial cells and thereby gain access to the cell.^{8,9} Hence, ACE2 receptor is the potential therapeutic target that paves the route for this pandemic as this receptor is widespread over the organ systems.

According to the present survey, 64.2% of the COVID-19 survivors had CNS symptoms including dizziness, headache, dysgeusia, hyposmia and insomnia. Dizziness and insomnia were reported in a similar study conducted by Fernández-de-Las-Peñas C et al.¹⁰ Davidob et al. reported headache in COVID-19 survivors during the post-COVID period.¹¹ It has been found that there is high expression of ACE2 receptors in the brain.¹² As stated earlier, ACE2 being the key entry receptor it's evident that SARS-CoV-2 have neuro-invasive potential. Though our whole body is protected by the immune system, immune-privileged sites are impotent to cope with the attack of the pathogen. The central nervous system (CNS) of human beings is one among them.¹³ Due to high expression of ACE2 receptor in the CNS, it becomes susceptible to invasion by SARS-CoV-2. The virus causes inflammation there taking advantage of the immune-privileged nature of CNS,¹³ as it is not much prone to the attack of immune system. Hence, the possibility of persistence of SARS-CoV-2 in the nervous system cannot be ruled out.

Viruses like hepatitis virus, human immunodeficiency virus and mumps virus are known to enter the testis and cause viral orchitis which often leads to testicular tumour and infertility.¹⁴ The researchers conducted on previous SARS outbreaks have described the correlation between members of family Coronaviridae and orchitis. Even though SARS-

CoV-2 virus has not been detected in testis,¹⁵ testicular damage has been widely reported.¹⁶ In the survey, 5.8% of respondents complained of testicular and lower abdominal pain. Shastri A et al. (2020) observed high expression of ACE2 receptors in testis.¹⁷ A study also suggests high expression of ACE2 in sertoli cells, spermatogonia and leydig cells, indicating severe effects on spermatogenesis and the existence of orchitis in males.¹⁸ Testis, have high expression of ACE 2 receptor, the prime entry receptor of SARS-COV-2. Testis is also an immune privileged site; i.e it is less accessible to the immune system. The chance of testis acting as a viral reservoir was also stated in the work of Shastri et al and Fijak et al.^{17,19} Thus the authors hypothesis that SARS-COV-2 persist in human body cannot be neglected.

Moreno-perez O et al., reported persistence of dyspnoea 34.4% and 11.1% in global assessment and specialized evaluation respectively. After discharge, 50.9% of the individuals had post-COVID symptoms [visual loss (5.4%), skin problems (8.3%), and headache (17.8%)]. In specialist evaluation, it was found that neurological symptoms improved within 16-18 weeks after its onset.²⁰ According to a study, out of the 100 assessed patients, with a mean of 48 days post-discharge from the hospital in the United Kingdom, 72% of ICU patients and 63% of non-ICU patients reported fatigue, followed by breathlessness (65% ICU patients and 42.6% non-ICU patients) and psychological distress (46.9% ICU patients and 23.5% non-ICU patients).²¹

Tenforde MW et al. escorted a study by analysing the post COVID symptoms of 274 outpatients via telephone calls. Symptoms such as cough (43%) and fatigue (35%) were found unresolved on the date of interview.²² Carfi A et al. examined COVID-19 symptoms persisting in Italian patients with a mean of 60 days since its commencement and observed that a high proportion of the individuals had persistent symptoms such as fatigue (53.1%), joint pain (27.3%) and chest pain (21.7%). Symptoms such as red eyes, headache and sore throat were identified in a range between 0-20%.²³

Limitations of the Study

Several limitations popped out in our study. Proper clinical verification of the post-COVID symptoms was not possible as we couldn't collaborate with any hospital or post-COVID treatment centres. We could propose the probability of persistence only theoretically. The sample size was less compared to the number of survivors as many were reluctant to participate in the survey which might be due to the social stigma.

Conclusion

This study probed into life after COVID-19 and the probability of persistence of SARS-CoV-2 in the human body. It reveals

that COVID-19 survivors face many health issues even after testing negative for COVID-19 and hence the probability of persistence of SARS-CoV-2 in the human body can't be neglected. Further studies are required to establish the probability of persistence of SARS-CoV-2.

Acknowledgement

The authors are grateful to the Principal, Vimala College (Autonomous), Trissur for the constant support, guidance and encouragement throughout the work. No financial aid was provided for this work.

Conflict of Interest: None

References

1. Payne S. Family *Coronaviridae*. *Viruses*. 2017;149-58.
2. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY, Yuan ML, Zhang YL, Dai FH, Liu Y, Wang QM, Zheng JJ, Xu L, Holmes EC, Zhang YZ. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020 Mar;579(7798):265-9. [PubMed] [Google Scholar]
3. World Health Organisation [Internet]. WHO Coronavirus (COVID-19) Dashboard; [cited 2021 May 15]. Available from: <https://covid19.who.int/>
4. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, Huet K, Plzak J, Horoi M, Hans S, Rosaria Barillari M, Cammaroto G, Fakhry N, Martiny D, Ayad T, Jouffe L, Hopkins C, Saussez S; COVID-19 Task Force of YO-IFOS. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. *J Intern Med*. 2020 Sep;288(3):335-44. [PubMed] [Google Scholar]
5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020 Feb;395(10223):497-506. [PubMed] [Google Scholar]
6. Zhou R, Li F, Chen F, Liu H, Zheng J, Lei C, Wu X. Viral dynamics in asymptomatic patients with COVID-19. *Int J Infect Dis*. 2020 Jul;96:288-90. [PubMed] [Google Scholar]
7. Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y, Dong W. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect*. 2021 Jan;27(1):89-95. [PubMed] [Google Scholar]
8. Datta PK, Liu F, Fischer T, Rappaport J, Qin X. SARS-CoV-2 pandemic and research gaps: understanding SARS-CoV-2 interaction with the ACE2 receptor and implications for therapy. *Theranostics*. 2020 Jun;10(16):7448-64. [PubMed] [Google Scholar]
9. Ortega JT, Serrano ML, Pujol FH, Rangel HR. Role of

- changes in SARS-CoV-2 spike protein in the interaction with the human ACE2 receptor: An *in silico* analysis. EXCLI J. 2020 Mar;19:410-7. [PubMed] [Google Scholar]
10. Fernández-de-Las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, Cuadrado ML, Florencio LL. Defining post-COVID symptoms (post-acute COVID, long COVID, persistent post-COVID): an integrative classification. Int J Environ Res Public Health. 2021 Mar;18(5):2621. [PubMed] [Google Scholar]
 11. Davido B, Seang S, Tubiana R, de Truchis P. Post-COVID-19 chronic symptoms: a post infectious entity? Clin Microbiol Infect. 2020 Nov;26(11):1448-9. [PubMed] [Google Scholar]
 12. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol. 2020 Jun;92(6):552-5. [PubMed] [Google Scholar]
 13. Forrester JV, McMenamin PG, Dando SJ. CNS infection and immune privilege. Nat Rev Neurosci. 2018 Nov;19(11):655-71. [PubMed] [Google Scholar]
 14. Dejuq N, Jégou B. Viruses in the mammalian male genital tract and their effects on the reproductive system. Microbiol Mol Biol Rev. 2001 Jun;65(2):208-31. [PubMed] [Google Scholar]
 15. Ding Y, He L, Zhang Q, Huang Z, Che X, Hou J, Wang H, Shen H, Qiu L, Li Z, Geng J, Cai J, Han H, Li X, Kang W, Weng D, Liang P, Jiang S. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. J Pathol. 2004 Jun;203(2):622-30. [PubMed] [Google Scholar]
 16. Xu J, Qi L, Chi X, Yang J, Wei X, Gong E, Peh S, Gu J. Orchitis: a complication of severe acute respiratory syndrome (SARS). Biol Reprod. 2006 Feb;74(2):410-6. [PubMed] [Google Scholar]
 17. Shastri A, Wheat J, Agrawal S, Chatterjee N, Pradhan K, Goldfinger M, Kornblum N, Steidl U, Verma A, Shastri J. Delayed clearance of SARS-CoV2 in male compared to female patients: high ACE2 expression in testes suggests possible existence of gender-specific viral reservoirs. medRxiv:20060566v1 [Preprint]. 2020. Available from: <https://www.medrxiv.org/content/10.1101/2020.04.16.20060566v1>. [Google Scholar] Access date: 13 June 2021
 18. Cardona Maya WD, Du Plessis SS, Velilla PA. SARS-CoV-2 and the testis: similarity with other viruses and routes of infection. Reprod Biomed Online. 2020 Jun;40(6):763-4. [PubMed] [Google Scholar]
 19. Fijak M, Bhushan S, Meinhardt A. Immunoprivileged sites: the testis. Methods Mol Biol. 2011 Jun;677:459-70. [PubMed] [Google Scholar]
 20. Moreno-Pérez O, Merino E, Leon-Ramirez JM, Andres M, Ramos JM, Arenas-Jiménez J, Asensio S, Sanchez R, Ruiz-Torregrosa P, Galan I, Scholz A, Amo A, González-de-la-Aleja P, Boix V, Gil J; COVID19-ALC Research Group. Post-acute COVID-19 syndrome. Incidence and risk factors: a Mediterranean cohort study. J Infect. 2021 Mar;82(3):378-83. [PubMed] [Google Scholar]
 21. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, Walshaw C, Kemp S, Corrado J, Singh R, Collins T, O'Connor RJ, Sivan M. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. J Med Virol. 2021 Feb;93(2):1013-22. [PubMed] [Google Scholar]
 22. Tenforde MW, Kim SS, Lindsell CJ, Billig Rose E, Shapiro NI, Files DC, Gibbs KW, Erickson HL, Steingrub JS, Smithline HA, Gong MN, Aboodi MS, Exline MC, Henning DJ, Wilson JG, Khan A, Qadir N, Brown SM, Peltan ID, Rice TW, Hager DN, Ginde AA, Stubblefield WB, Patel MM, Self WH, Feldstein LR; IVY Network Investigators; CDC COVID-19 Response Team; IVY Network Investigators. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network — United States, March–June 2020. MMWR Morb Mortal Wkly Rep. 2020 Jul;69:993-8. [PubMed] [Google Scholar]
 23. Carfi A, Bernabei R, Landi F; Gemelli against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA. 2020 Aug;324(6):603-5. [PubMed] [Google Scholar]