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Are Children Essentially Immune to COVID? - A Review

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ABSTRACT

Aim: The study aims to find whether children are essentially immune to COVID-19.

Introduction: Immune is the resistance to a particular infection or toxin owing to the presence of antibodies or sensitized white blood cells. The novel coronavirus has been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), whereas the disease associated with it is referred to as COVID-19. The diagnostic methods that are involved exclusively are RNA detection by reverse transcription-polymerase (RT-PCR) of secretions through nasopharyngeal and throat swabs and in stool samples.

Materials and Method: In this review, various articles were searched through search engines like Google Scholar and Pubmed using keywords like immunity in children, resistance, COVID-19 in adults, COVID-19 in children, asymptomatic, less susceptible and milder symptoms. Over 70 articles were collected and reviewed thoroughly.

Results and Discussion: Like adults, children exposed to the coronavirus can be infected with it and display signs of Covid-19. At the beginning of the pandemic, it was assumed that children are not getting infected with the coronavirus, but now it is clear that the amount of infection in children is the same as in adults. It is just when they do get the infection they show much milder symptoms. However, young children, particularly infants were vulnerable to infection. Children frequently do not have a notable disease, raising the possibility for facilitators of viral infection transmission.

Conclusion: From this review, we can conclude that children are also susceptible to COVID 19 on the exposure to the virus and they are not essentially immune to COVID-19.

Key Words: Immune, Resistance, COVID-19, Children, Less susceptible, Milder symptoms

INTRODUCTION

Immune is the resistance to a particular infection or toxin owing to the presence of antibodies or sensitized white blood cells. The outbreak of the coronavirus disease 2019 (COVID-19) emerged in Wuhan City, China, in late 2019 and has now reached pandemic status. The novel coronavirus has been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), whereas the disease associated with it is referred to as COVID-19. The envelope has club-shaped glycoprotein spikes that give the virus a crown-like or coronal appearance. COVID-19 is primarily transmitted through

respiratory droplets and contact routes. Coronaviruses typically cause mild upper respiratory tract infections; however, SARS-CoV-2, severe acute respiratory syndrome coronavirus (SARS-CoV), and Middle East respiratory syndrome coronavirus (MERS-CoV) have all been associated with severe illness and death. Common symptoms reported in adults with COVID-19 are fever, dry cough, and fatigue; severe cases have been associated with dyspnoea¹. Laboratory observation of bilateral ground-glass opacities² on chest CT³. Symptoms in children include flu-like syndrome, fluctuating fever, pneumonia, and upper respiratory signs like cough, sore throat, stuffy nose, sneezing, and rhinorrhea⁴.

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The basic reproduction number of SARS-CoV-2 in the early outbreak in China was estimated to be two⁵. The diagnostic methods that involved exclusively RNA detection by reverse transcription-polymerase (RT-PCR) of secretions through nasopharyngeal and throat swabs and in stool samples⁶. The RNA in nasopharyngeal and throat swab samples has been shown to become undetectable within 6–22 days of illness onset in children⁷. The shorter period of excretion of virus in asymptomatic patients and there is no available sampling series⁸. An analysis from China has shown that children younger than 10 years account for only 1% of COVID-19 cases,⁹ which was similar to the proportion for SARS-CoV and MERS-CoV epidemics^{10,11}. There have been reports about etiological treatment with the antiviral activity of chloroquine, a well-known antimalarial treatment¹², and remdesivir which had been tried against the Ebola virus¹³. According to the epidemiology of COVID-19 among children in China, young children particularly young infants were vulnerable to COVID 19¹⁴. Compared with the adults' cases, the severity of children's COVID-19 cases was milder, and the case fatality rate was much lower¹⁵.

Like adults, children exposed to the coronavirus can be infected with it and display signs of Covid-19. At the beginning of the pandemic, it was assumed that children are not getting infected with the coronavirus, but now it is clear that the amount of infection in children is the same as in adults¹⁶. It is just when they do get the infection they get much milder symptoms. The study aims to analyze whether children are essentially immune to COVID-19.

COVID-19 in adults

The clinical severity of COVID-19 was higher among adults aged greater 65 years old¹⁷. Almost half the 425 cases were in adults 60 years of age and 93% represented signs and symptoms reported in China¹⁸. Human pathogenic coronaviruses; severe acute respiratory syndrome coronavirus [SARS-CoV] and [SARS-CoV-2] bind to their target cells through angiotensin-converting enzyme 2 (ACE2), which is expressed by epithelial cells of the lung, intestine, kidney, and blood vessels^{19,20}. The expression of ACE2 is substantially increased in patients with type 1 or type 2 diabetes²¹, as they are treated with angiotensin II type-I receptor blockers (ARBs) and ACE inhibitors. Similarly, hypertension is also treated with ACE inhibitors and ARBs, which results in an upregulation of ACE2. In consequence, the increased expression of ACE2 would facilitate infection with COVID-19. Hence the patients with diabetes, high blood pressure, and chronic illness are at higher risk²². In patients with severe disease, dyspnoea, central cyanosis, and oxygen saturation were observed²³. In COVID-19 patients, increased liver enzymes, inflammatory markers²⁴, and hypocalcemia were observed clinical characteristics²⁵. The C-reactive protein and procalcitonin were also increased. According to WHO, preg-

nancy was not a risk for severe COVID-19 disease, but there will be an impact on fetal distress²⁶. Smoking²⁷ was not the major feature of the pathogenesis of COVID-19 in adults²⁸. The high prevalence of comorbidities with confirmed cases was about 26%²⁹ and those who died from COVID-19 had a higher prevalence of about 67.2%³⁰.

COVID-19 in children

Children showed relatively milder illness and a better prognosis than adults³¹. The deaths in children were extremely rare. More than 90% of the children diagnosed showed mild or were asymptomatic. Only one child died in the age group 10-19 years and no child aged 0-9 years died³², in China. In the U.S 1.6%-2.5% were children in COVID-19 cases but no child needed intensive care as they showed milder symptoms³³. In the neonatal cases, the youngest to be diagnosed was a 30 hours old baby³⁴. According to Simon, the immune system undergoes substantial changes from birth to adulthood³⁵. Angiotensin-converting enzyme 2 (ACE 2) was known as a cell receptor for SARS-CoV. Recent evidence indicates that children were less sensitive to 2019-nCoV because of the maturity and function of ACE 2 in children may be lower than that in adults³⁶. Additionally, children often experience respiratory infection Respiratory Syncytial Virus (RSV), that may have increased the levels of antibody against the virus than adults³⁷. The immature immune system creates cytokine storms that help in fighting against the viral disease³⁸. The inflammatory markers in children with COVID 19 were low³⁹. Many children diagnosed did not have any symptoms or radiographic features⁴⁰. Children were less susceptible as they were involved in fewer outdoor activities or international travel⁴¹. The number of confirmed cases in the United States, China, Italy, and Spain among persons aged <18 were 2%³³, 2.2%⁴², 1.2%⁴³, and 0.8%⁴⁴ respectively. Among the cases in children reported from China, most had exposure to household members with confirmed COVID-19. Mother-to-child transmission of COVID-19 during pregnancy is uncommon. However, after birth, a newborn can be infected⁴⁵ after being in close contact with an infected mother or other caregivers⁴⁶. Several problems, such as preterm birth, have been reported in babies born to mothers with COVID-19 positive late during their pregnancy⁴⁷.

Table 1: The given table shows the percentage of children less than 18 years of age affected by COVID 19 in different countries. From the table, it is evident that children are less susceptible than adults.

| Countries | % of Children Affected from Covid 19 |
|---------------|--------------------------------------|
| United States | 2% |
| China | 2.2% |
| Italy | 1.2% |
| Spain | 0.8% |

Asymptomatic carriers

Children show mild symptoms to COVID⁴⁸ and only a few children were hospitalized⁴⁹. Patients with less serious illness play an important role in the transmission of the disease⁵⁰. Incubation time for onset of symptoms is 3 days but it can be as long as 24 hours⁵¹. The asymptomatic carriers from initial and throughout disease exhibit disease transmission¹³.

SARS in children

Compared to adults, teenagers SARS was less aggressive during the clinical course in children⁵². The children were observed with abnormal chest radiographs³⁷. Children had mild symptoms⁵³ as young children had higher lymphocytes than adults⁵⁴. The constitutional symptoms were chills and myalgia⁵⁵. There were no fatal cases reported in children⁵⁶ but the children showed mild abnormalities⁵⁷. From positive children, there was no transmission to parents⁵⁸. Osteonecrosis was reported in children who had treatment with steroids⁵⁹.

Children immunity to viral diseases

Infants and young children are typically at high risk for admission to hospital after respiratory tract infection with viruses such as respiratory syncytial virus and influenza virus⁶⁰. Immaturity of the respiratory tract and immune system is thought to contribute to severe viral respiratory disease in this age group⁶¹. Acute Lower Respiratory Tract Infection (ALTI) is also one of the common infections and it is the leading cause of morbidity and mortality in children aged less than 5 years worldwide⁶². In children, Influenza A virus attains innate immunity during their childhood⁶³. An immune response is adapted in all stages of life to maximize survival⁶⁴. Deficient immune system response to viral infections causes the prognosis of the disease in children⁶⁵. Therefore the absence of pediatric patients⁶⁶ severe COVID-19 has perplexed clinicians, epidemiologists, and scientists.

CONCLUSION

The review demonstrates whether children are essentially immune to Covid-19. But children of all ages were sensitive to COVID-19, and there was no significant gender difference. Clinical manifestations of children's COVID-19 cases were less severe than those of adult patients. However, young children, particularly infants, were more vulnerable to 2019-nCoV infection. Children frequently do not have a notable disease, raising the possibility that children could be facilitators of viral transmission. It is important to be safe by staying at home, maintaining social distance, and proper hygiene. It is also important to boost the immune system and follow a proper diet. The future scope of this research is to create awareness among people of all age group are susceptible to COVID 19 and to understand that there no age and sex differences in transmission of COVID 19.

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REFERENCES

1. Bokadia GS, Sneha. Bokadia G, Brundha MP, Ariga P. Current knowledge about lung cancer among middle-aged nonmedical males a questionnaire-based survey [Internet]. Vol. 11, Research Journal of Pharmacy and Technology. 2018. p. 2565. Available from: <http://dx.doi.org/10.5958/0974-360x.2018.00474.2> access on 24/04/2020
2. Mp B, Brundha MP, Nallaswamy D. Hide and seek in pathology- A research on game-based histopathology learning [Internet]. Vol. 10, International Journal of Research in Pharmaceutical Sciences. 2019. p. 1410-4. Available from: <http://dx.doi.org/10.26452/ijrps.v10i2.606>
3. Brundha MP, Sai Vignesh S. Myeloid sarcoma [Internet]. Vol. 3, International Journal of Clinicopathological Correlation. 2019. p. 41. Available from: http://dx.doi.org/10.4103/ijpcpc.ijpcpc_11_19
4. Kumar MDA, Ashok Kumar MD, Brundha MP. Awareness about nocturia-A questionnaire survey [Internet]. Vol. 9, Research Journal of Pharmacy and Technology. 2016. p. 1707. Available from: <http://dx.doi.org/10.5958/0974-360x.2016.00344.9>
5. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. The basic reproduction number of novel coronavirus (2019-nCoV) estimation based on exponential growth in the early outbreak in China from 2019 to 2020: A reply to Dhungana. *Int J Infect Dis*. 2020 May;94:148-50.
6. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* [Internet]. 2020 Jan;25(3). Available from: <http://dx.doi.org/10.2807/1560-7917.ES.2020.25.3.2000045>; access on 24/04/2020
7. Download citation of Awareness about personal protective equipment in hospital workers (sweepers and cleaners) – Research [Internet]. ResearchGate. [cited 2020 Jun 6]. Available from: https://www.researchgate.net/publication/309120844_Awareness_about_personal_protective equipments_in_hospital_workers_sweepers_and_cleaners_-_Research; access on 24/04/2020
8. Morand A, Fabre A, Minodier P, Boutin A, Vanel N, Bosdure E, et al. COVID-19 virus and children: What do we know? [Internet]. Vol. 27, Archives de Pédiatrie. 2020. p. 117-8. Available from: <http://dx.doi.org/10.1016/j.arcped.2020.03.001>; access on 24/04/2020
9. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China [Internet]. Vol. 323, JAMA. 2020. p. 1239. Available from: <http://dx.doi.org/10.1001/jama.2020.2648>; access on 24/04/2020
10. Denison MR. Severe acute respiratory syndrome coronavirus

- pathogenesis, disease, and vaccines: an update. *Pediatr Infect Dis J*. 2004 Nov;23(11 Suppl): S207–14.
11. Al-Tawfiq JA, Kattan RF, Memish ZA. Middle East respiratory syndrome coronavirus disease is rare in children: An update from Saudi Arabia. *World J Clin Pediatr*. 2016 Nov 8;5(4):391–6.
 12. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the newly emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020 Mar;30(3):269–71.
 13. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents*. 2020 Mar;55(3):105924.
 14. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study [Internet]. Vol. 395, *The Lancet*. 2020. p. 507–13. Available from: [http://dx.doi.org/10.1016/s0140-6736\(20\)30211-7](http://dx.doi.org/10.1016/s0140-6736(20)30211-7); access on 24/04/2020
 15. Tang C, Zhang K, Wang W, Pei Z, Liu Z, Yuan P, et al. Clinical Characteristics of 20,662 Patients with COVID-19 in mainland China: A Systematic Review and Meta-analysis [Internet]. Available from: <http://dx.doi.org/10.1101/2020.04.18.20070565>; access on 24/04/2020
 16. Feroz J, Brundha MP. Awareness of stye. *International Journal of Pharmaceutical Sciences Review and Research*. 2016 Jan 1;40(1):30–2.
 17. Zhang G, Zhang J, Wang B, Zhu X, Wang Q, Qiu S. Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a retrospective analysis [Internet]. Available from: <http://dx.doi.org/10.21203/rs.3.rs-17712/v1>; access on 24/04/2020
 18. Brüssow H. Faculty Opinions recommendation of Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia [Internet]. Faculty Opinions – Post-Publication Peer Review of the Biomedical Literature. 2020. Available from: <http://dx.doi.org/10.3410/f.737281536.793571806>; access on 24/04/2020
 19. Timothy CN, Samyuktha PS, Brundha MP. Dental pulp Stem Cells in Regenerative Medicine – A Literature Review [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology*. 2019. p. 4052. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00698.x>; access on 24/04/2020
 20. A Comparative Study- The Role of Skin and Nerve Biopsy in Hansen’s Disease. 2015 [cited 2020 Jun 10]; Available from: <https://www.semanticscholar.org/paper/A-Comparative-Study-The-Role-of-Skin-and-Nerve-in/32987df6dde8c273cbd62e9c7d11d7ff9a7d82a4>
 21. Preetika S, Brundha MP. Awareness of diabetes mellitus among the general population [Internet]. Vol. 11, *Research Journal of Pharmacy and Technology*. 2018. p. 1825. Available from: <http://dx.doi.org/10.5958/0974-360x.2018.00339.6>
 22. Fang L, Karakoulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? [Internet]. Vol. 8, *The Lancet Respiratory Medicine*. 2020. p. e21. Available from: [http://dx.doi.org/10.1016/s2213-2600\(20\)30116-8](http://dx.doi.org/10.1016/s2213-2600(20)30116-8)
 23. Yao XH, Li TY, He ZC, Ping YF, Liu HW, Yu SC, et al. [A pathological report of three COVID-19 cases by minimal invasive autopsies]. *Zhonghua Bing Li Xue Za Zhi*. 2020 May 8;49(5):411–7.
 24. Brundha MP, Padma Shri VP, Sundari S. Quantitative Changes of Red Blood cells in Cancer Patients under Palliative Radiotherapy-A Retrospective Study [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology*. 2019. p. 687. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00122.7>; access on 24/04/2020
 25. Harsha L, Brundha MP. Prevalence of dental developmental anomalies among men and women and its psychological effect in a given population. *Res J Pharm Biol Chem Sci*. 2017 Jan 1;9(6):869–73.
 26. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records [Internet]. Vol. 395, *The Lancet*. 2020. p. 809–15. Available from: [http://dx.doi.org/10.1016/s0140-6736\(20\)30360-3](http://dx.doi.org/10.1016/s0140-6736(20)30360-3)
 27. Hannah R, Ramani P, Brundha MP, Herald. J. Sherlin, Ranjith G, Ramasubramanian A, et al. Liquid Paraffin as a Rehydrant for Air Dried Buccal Smear [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology*. 2019. p. 1197. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00199.9>
 28. Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Apr 30;382(18):1708–20.
 29. 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. *Lancet*. 2020 Feb 15;395(10223):497–506.
 30. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [Internet]. Vol. 395, *The Lancet*. 2020. p. 1054–62. Available from: [http://dx.doi.org/10.1016/s0140-6736\(20\)30566-3](http://dx.doi.org/10.1016/s0140-6736(20)30566-3); access on 24/04/2020
 31. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults [Internet]. Vol. 109, *Acta Paediatrica*. 2020. p. 1088–95. Available from: <http://dx.doi.org/10.1111/apa.15270>; access on 24/04/2020
 32. 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 Feb 7; Available from: <http://dx.doi.org/10.1001/jama.2020.1585>; access on 24/04/2020
 33. Team CC-19 R, CDC COVID-19 Response Team, Bialek S, Gierke R, Hughes M, McNamara LA, et al. Coronavirus Disease 2019 in Children — United States, February 12–April 2, 2020 [Internet]. Vol. 69, *MMWR. Morbidity and Mortality Weekly Report*. 2020. p. 422–6. Available from: <http://dx.doi.org/10.15585/mmwr.mm6914e4>; access on 24/04/2020
 34. Guo Y-R, Cao Q-D, Hong Z-S, Tan Y-Y, Chen S-D, Jin H-J, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. *Mil Med Res*. 2020 Mar 13;7(1):11.
 35. Simon AK, Katharina Simon A, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age [Internet]. Vol. 282, *Proceedings of the Royal Society B: Biological Sciences*. 2015. p. 20143085. Available from: <http://dx.doi.org/10.1098/rspb.2014.3085>; access on 24/04/2020
 36. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020 Apr;8(4):420–2.
 37. Hon KLE, Leung CW, Cheng WTF, Chan PKS, Chu WCW, Kwan YW, et al. Clinical presentations and outcome of severe acute respiratory syndrome in children [Internet]. Vol. 361, *The Lancet*. 2003. p. 1701–3. Available from: [http://dx.doi.org/10.1016/s0140-6736\(03\)13364-8](http://dx.doi.org/10.1016/s0140-6736(03)13364-8); access on 24/04/2020
 38. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020 Mar 28;395(10229):1033–4.

39. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis [Internet]. Vol. 0, Clinical Chemistry and Laboratory Medicine (CCLM). 2020. Available from: <http://dx.doi.org/10.1515/cclm-2020-0369>; access on 24/04/2020
40. Lee P-I, Hu Y-L, Chen P-Y, Huang Y-C, Hsueh P-R. Are children less susceptible to COVID-19? J Microbiol Immunol Infect [Internet]. 2020 Feb 25; Available from: <http://dx.doi.org/10.1016/j.jmii.2020.02.011>; access on 24/04/2020
41. Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang Z-J. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China [Internet]. Vol. 323, JAMA. 2020. p. 1313. Available from: <http://dx.doi.org/10.1001/jama.2020.2131>; access on 24/04/2020
42. Harries A, Takarinda KC. Faculty Opinions recommendation of Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention [Internet]. Faculty Opinions – Post-Publication Peer Review of the Biomedical Literature. 2020. Available from: <http://dx.doi.org/10.3410/f.737420993.793572382>; access on 24/04/2020
43. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. JAMA [Internet]. 2020 Mar 17; Available from: <http://dx.doi.org/10.1001/jama.2020.4344>; access on 24/04/2020
44. Tagarro A, Epalza C, Santos M, Sanz-Santa Eufemia FJ, Otheo E, Moraleda C, et al. Screening and Severity of Coronavirus Disease 2019 (COVID-19) in Children in Madrid, Spain. JAMA Pediatr [Internet]. 2020 Apr 8; Available from: <http://dx.doi.org/10.1001/jamapediatrics.2020.1346>; access on 24/04/2020
45. Kalaiselvi R, Brundha MP. Prevalence of hysterectomy in the South Indian population [Internet]. Vol. 9, Research Journal of Pharmacy and Technology. 2016. p. 1941. Available from: <http://dx.doi.org/10.5958/0974-360x.2016.00398.x>; access on 24/04/2020
46. Priyanka Shenoy B, Brundha MP. Awareness of Polycystic ovarian disease among females of age group 18-30 years. 2016 Aug 1;8(8):813–6.
47. Dilbaz B. COVID-19 Infection and Pregnancy: What Do the Societies Recommend? [Internet]. Vol. 30, Journal of Clinical Obstetrics & Gynecology. 2020. p. 29–34. Available from: <http://dx.doi.org/10.5336/jcog.2020-75346>; access on 24/04/2020
48. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China [Internet]. Vol. 63, Science China Life Sciences. 2020. p. 706–11. Available from: <http://dx.doi.org/10.1007/s11427-020-1661-4>; access on 24/04/2020
49. Stock J. Data Gaps and the Policy Response to the Novel Coronavirus [Internet]. 2020. Available from: <http://dx.doi.org/10.3386/w26902>; access on 24/04/2020
50. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed Asymptomatic Carrier Transmission of COVID-19 [Internet]. Vol. 323, JAMA. 2020. p. 1406. Available from: <http://dx.doi.org/10.1001/jama.2020.2565>; access on 24/04/2020
51. Du R-H, Liang L-R, Yang C-Q, Wang W, Cao T-Z, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study [Internet]. Vol. 55, European Respiratory Journal. 2020. p. 2000524. Available from: <http://dx.doi.org/10.1183/13993003.00524-2020>; access on 24/04/2020
52. Ng EKO, Ng P-C, Ellis Hon KL, Frankie Cheng WT, Hung ECW, Allen Chan KC, et al. Serial Analysis of the Plasma Concentration of SARS Coronavirus RNA in Pediatric Patients with Severe Acute Respiratory Syndrome [Internet]. Vol. 49, Clinical Chemistry. 2003. p. 2085–8. Available from: <http://dx.doi.org/10.1373/clinchem.2003.024588>; access on 24/04/2020
53. Peiris JSM, Chu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLM, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study [Internet]. Vol. 361, The Lancet. 2003. p. 1767–72. Available from: [http://dx.doi.org/10.1016/s0140-6736\(03\)13412-5](http://dx.doi.org/10.1016/s0140-6736(03)13412-5); access on 24/04/2020
54. Swetha S, Brundha MP. Analysis of knowledge about the hospital warning symbols among the postgraduate dental students-A comparative study [Internet]. Vol. 10, Research Journal of Pharmacy and Technology. 2017. p. 975. Available from: <http://dx.doi.org/10.5958/0974-360x.2017.00177.9>; access on 24/04/2020
55. Prentice E, Jerome WG, Yoshimori T, Mizushima N, Denison MR. Coronavirus replication complex formation utilizes components of cellular autophagy. J Biol Chem. 2004 Mar 12;279(11):10136–41.
56. Stockman LJ, Reed C, Kallen AJ, Finelli L, Anderson LJ. Respiratory Syncytial Virus and Staphylococcus Aureus Coinfection in Children Hospitalized with Pneumonia [Internet]. The Pediatric Infectious Disease Journal. 2010. p. 1. Available from: <http://dx.doi.org/10.1097/inf.0b013e3181eb7315>; access on 24/04/2020
57. Chan DFY, Li AM, Chu WCW, Chan MHM, Wong EMC, Liu EKH, et al. Hepatic steatosis in obese Chinese children [Internet]. Vol. 28, International Journal of Obesity. 2004. p. 1257–63. Available from: <http://dx.doi.org/10.1038/sj.ijo.0802734>; access on 24/04/2020
58. He R, Leeson A, Ballantine M, Andonov A, Baker L, Dobie F, et al. Characterization of protein-protein interactions between the nucleocapsid protein and membrane protein of the SARS coronavirus. Virus Res. 2004 Oct;105(2):121–5.
59. Bonanno GA, Ho SMY, Chan JCK, Kwong RSY, Cheung CKY, Wong CPY, et al. Psychological resilience and dysfunction among hospitalized survivors of the SARS epidemic in Hong Kong: A latent class approach [Internet]. Vol. 27, Health Psychology. 2008. p. 659–67. Available from: <http://dx.doi.org/10.1037/0278-6133.27.5.659>; access on 24/04/2020
60. Prashaanthi N, Brundha MP. A Comparative Study between Poptlet Notes and Conventional Notes for Learning Pathology [Internet]. Vol. 11, Research Journal of Pharmacy and Technology. 2018. p. 175. Available from: <http://dx.doi.org/10.5958/0974-360x.2018.00032.x>; access on 24/04/2020
61. Muthukumar Balaji S, Brundha MP. Awareness of About Breast Cancer among Dental Surgeons. 2016 [cited 2020 Jun 4]; Available from: <https://www.semanticscholar.org/paper/Awareness-of-About-Breast-Cancer-among-Dental-Balaji-Brundha/63f44173d90b35bffa33eed0aeb52ac547ef1567>
62. Esposito S, Bosis S, Pelucchi C, Tremolati E, Sabatini C, Semino M, et al. Influenza vaccination among healthcare workers in a multidisciplinary University hospital in Italy [Internet]. Vol. 8, BMC Public Health. 2008. Available from: <http://dx.doi.org/10.1186/1471-2458-8-422>; access on 24/04/2020
63. Coates BM, Staricha KL, Ravindran N, Koch CM, Cheng Y, Davis JM, et al. Inhibition of the NOD-Like Receptor Protein 3 Inflammasome Is Protective in Juvenile Influenza A Virus Infection [Internet]. Vol. 8, Frontiers in Immunology. 2017. Available from: <http://dx.doi.org/10.3389/fimmu.2017.00782>; access on 24/04/2020

64. Scher HI, Fizazi K, Saad F, Taplin M-E, Sternberg CN, Miller K, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med*. 2012 Sep 27;367(13):1187–97.
65. Tregoning JS, Schwarze J. Respiratory viral infections in infants: causes, clinical symptoms, virology, and immunology. *Clin Microbiol Rev*. 2010 Jan;23(1):74–98.
66. Shreya S, Brundha MP. Alteration of Haemoglobin Value in Relation to Age, Sex and Dental Diseases-A Retrospective Correlation Study [Internet]. Vol. 10, *Research Journal of Pharmacy and Technology*. 2017. p. 1363. Available from: <http://dx.doi.org/10.5958/0974-360x.2017.00241.4>; access on 24/04/2020