Pathogenesis of Candida Auris: A Threat Emerging during Corona Pandemic

Abstract:

The genus Candida consists of several species, including the Auris species, a pathogen that quickly colonizes and spreads on hospital surfaces and causes invasive fungal infections even after regular disinfection. It is very potent as it is resistant to several antifungals like the Echinocandins and azoles, commonly used to treat invasive fungal infections. Due to this, there is a global threat to public health.

C.auris could also spread as a Nosocomial infection through contaminated arm-pit thermometers that will increase the spread and dissemination of C. Auris, to seek protection against which, these multi use devices used on several patients should be cleaned carefully.

In patients hospitalized with COVID-19, systemic fungal co-infections have been very common, which may increase the severity of the disease and be detrimental to the treatment process, and may also prove fatal.

COVID-19 infection suppresses the patients' immunity. The attenuated CD80 upregulation of monocytes can explain and abolish the release of IL6, TNF, IL1a, and IL1b against Candida species making the patient more susceptible to secondary co-infections.

The similarity between Covid and Candidiasis is that both emerge suddenly and spread astonishingly quickly, which cannot be easily comprehended by the traditional epidemiological analysis.

The dry biofilms formed in C. Auris protect the microbe from complete removal due to robust cleaning. It was also found that C. Auris particles were obtained from patients with chronic respiratory disease using genome sequencing and multilocus microsatellite genotyping.

In the timeline of April to July 2020, two-thirds of the COVID cases affected by candidemia admitted in the Intensive Care Unit in New Delhi were due to C. Auris, and the mortality rate was around 60%.

Key words: fungal infections, candida Auris, candidemia, immunocompromised, Corona

NARRATIVE REVIEW ARTICLE:

Introduction :

The first case of Candida Auris, a new and opportunistic nosocomial fungal pathogen, was initially found in Japan in 2009. Since then, the cases have been found in hospitals across five different continents. As the trends depict, it has been observed that a particular rise in the incidence of occurrence of Candida Auris has been seen during the COVID19 pandemic (1)

What generally makes treating C. Auris complicated is that it is a multi-drug resistant fungus that can cause invasive infection.

Objective: The study of the occurrence of novel Candida Auris during a covid pandemic and the risk factors, spread, and prevention involved.

History and Attributes:

First found in the year 2009, the retrospective analysis of the culture collections of C. Auris led to the identification of some of its isolates which were often misidentified as C. haemulonii, including a bloodstream isolate obtained in 1996. This was basically because, upon phylogenetic studies, C. Auris was closely related to C. haemulonii complex members. The criteria for identifying this complex's clades are geographical origin and their different infective behavior, like some isolates causing invasive infections, while some cause frequent outbreaks. A possible explanation for these differences is that C. Auris initially emerged from a common ancestor, then migrated to different geographical locations, and diversified genetically partly steered by antifungal prescribing practices. (2)

Thermotolerance and salinity tolerance are two unique features of C. Auris that distinguish it from its close relatives belonging to the C. haemulonii complex. Evolutionary stories explain this by suggesting that C.auris may have primitively existed as a plant saprophyte in specialized ecosystems and that climate change, specifically global warming, may have contributed to its ability to grow at higher temperatures leading to its evolution as a human pathogen proposing the aquatic environment as the natural habitat of C. Auris. (2)

On further exploration, several; clades of C. Auris were isolated from the untouched salt marsh area without human activity and from a beach. Therefore, the study succeeded in isolating C. Auris for the first time from the tropical coast, not from the usual hospital environmental setup, suggesting its association with the marine ecosystem. Funnily, some of these were multidrug-susceptible, while some were multidrug-resistant. These findings thus provided an environmental source for clinical isolates and that the common ancestor of C. Auris has likely adapted to higher temperatures recently.

The virulence factors associated with C. Auris infections are not completely understood yet. Genome comparisons have shown that C. Auris can adapt to different environments and possesses many pathogenic mechanisms which are in common with other Candida species. For infection, C.auris has pathways for cell wall modeling and acquiring nutrients along with the production of hydrolytic enzymes such as phospholipases and proteinases likely involved in the adherence of the fungus and the invasion of host cells while infecting. Along with this, they were found to carry out tissue invasion and immune destruction, and multidrug efflux. C. Auris genome also reads for several lytic enzymes like proteases, secreted lipases, and phospholipases. It also reads for several C. albicans factors like the orthologs of agglutinin that are needed for adhesion, biofilm formation, and virulence. The ALS3 and ALS4 sequence of C. Albicans are the adhesin genes identified in C. Auris. AlS3 is needed for the fungal hyphae to attach to the epithelial cells, endothelial cells, and the extracellular matrix proteins and thus lead to the endocytosis of the host cell. (3)

C Auris can form dry biofilms on several surfaces, thus making its own nosocomial transmission from several medical devices much more accessible. This is its survival mechanism to remain viable on such surfaces for months. This unique ability to form a biofilm, which belongs to C. auris, has enhanced its role as a persistent colonizer and increased its pathogenicity by protecting it from antifungal drugs. Additionally, several genes, particularly those encoding efflux pumps such as MDR and CDR homologs and enzymes that modify glucan with the crucial role in biofilm extracellular matrix formation, were raised during biofilm formation, and their inhibition increased fluconazole - susceptibility of biofilms.

Plasticity of both morphologic and metabolic types increase virulence in pathogens of both bacterial and fungal origin; this versatility allows the pathogenic organisms to adapt quickly to different environmental conditions.

Epidemiology in Relation with COVID-19:

The initial patient with respiratory colonization by C. Auris died within eight days in the intensive care unit even before the results of the culture could be obtained. The patients admitted next was diagnosed with C. Auris almost a month post being admitted for COVID. This then brought forth the need to screen patients admitted to the ICU for C. Auris. As a result, all patients except the first one infected with C. Auris received prophylaxis of long-term broad-spectrum antibiotics for bacterial infections before C. Auris colonization could be diagnosed. (2)

In COVID patients diagnosed with C. Auris candidemia almost 50% of people were diagnosed for covid after colonization. Except for the first patient, all the patients infected with C. Auris were simultaneously infected with other diseases.

Multiple strains of C. Auris were found to be resistant to azoles and some also to amphotericin B, but some were susceptible to echinocandins. In candidemia patients, a mortality rate of 50% was reported in a month after isolation of C. Auris. The sequencing of the entire genome of the isolated strains showed a proximal genetic relationship of the strains. (3)

The Auris species can be transmitted very easily in healthcare setups, similar to the transmission of pathogens resistant to multiple drugs, such as the members of the Enterobacteriaceae family resistant to carbapenem and those like Staphylococcus aureus resistant to methicillin. (4)

Although the equipment used by healthcare professionals for protection significantly reduces the transmission of pathogens by medical personnel, despite even the best infection control measures, a significant increase in the rate of staph infection has been recorded in patients with SARS during the outbreak. (5)

The COVID19 pandemic will likely affect underserved public health systems in developing countries that are not adequately prepared for this worst pandemic. ICU teams must confront the challenge of bed overcrowding and vulnerable infection prevention practices to prevent the spread of C. Auris under such conditions (6)

Risk factors:

The factors that increase the risk for raised incidence of candidiasis in patients with COVID19 involve invasive procedures such as intubation, which would predispose the lung tissue to the formation and proliferation of fungal colonies, especially in patients with a history of chronic lung disease. Other risk factors include prolonged corticosteroid therapy, the patient's improper immune disposition, and antimicrobial therapy.

When considering risk factors, in a study that compared coinfections in terminal patients with and without COVID19, the need for invasive ventilation was shown to be the most relevant factor in the development of coinfections with pathogens resistant to antifungals in severe cases of COVID19.

Risk factors for COVID19-related candidiasis include prolonged hospitalizations, mechanical ventilators, venous catheterization, surgery, and the use of broad-spectrum antibiotics. (7)

Similarly, COVID19 patients with candidemia are primarily found in the ICU and receiving immunosuppressants. For identifying risk factors, other studies demonstrated raised incidence of secondary candida infections resistant to echinocandins in an elderly patient hospitalized with COVID19. The antifungal treatment administered was ineffective and likely worsened the disease. The need for strict monitoring of resistance to antifungals was also observed to regulate the dynamic use of effective antifungal agents while managing the patients in the intensive care unit. (8)

Pathogenesis of Candidiasis in relation with COVID19:

Due to the coronavirus, the symptoms indicative of the infection include difficulties in breathing.

In seve,re cases, some typical symptoms are noted, on the occurrence of which immediate intervention in hospitals, including oxygenation and mechanical ventilation, is of utmost importance. In such cases, various other complications have been seen, including secondary infections acquired through hospitals with highly opportunistic pathogens, including yeast and fungal infections. Fungal co-infections have increased in COVID19 patients in intensive care units (ICU) affected by the current pandemic. (9)

The case incidence of the patients of COVID-19 that are critically ill-being affected by aspergillosis and yeast infections is 14.1% and 12.6%, respectively. This has been reported amongst several medical centers across Wales. (10)

One of the most significant concerns worldwide before the COVID pandemic hit us was how the microbes posed a threat to humanity as the bacteria and fungi developed antimicrobial resistance. To minimize the impact of this antimicrobial resistance, it has been advised to have adequate proper execution of measures to control infection. (11)

In patients with COVID, maximizing the prescription of antimicrobials is a complex process, especially in critical cases, as the characteristics of the images and parameters followed in the laboratories due to which there is confusion; thus, distinguishing between bacterial coinfection and effects of SARSCoV2 becomes difficult. The proper execution of measures to limit the spread of resistant pathogens in facilities such as COVID19 intensive care units could be complicated.

C. Auris can also form colonies on patients' skin that remain for a long time and contaminate the surrounding area, causing outbreaks in hospitals. (12)

Diagnosis and Identification:

The screening program for Carbapenemase Producing Organisms (CRO) identified a person recently hospitalized abroad who was housed in a single room under preventive contact arrangements tested positive for colonization of CRO. The authorities of the healthcare department demanded the patient undergo tests for colonization by C. Auris. In anticipation of the tests results, the laboratory under the microbiology department of the hospital identified a specimen of C. Auris in the isolate obtained from the patient. The case of C. Auris lead to the implementation of an extensive prevention plan for the infection in collaboration with the healthcare unit, which included isolation, cleaning, and disinfection of surroundings, education, hygienic precautions.

Reducing traffic in the operating room would be safer for the patients admitted to the hospital. The project included the need for adequately assessing, making observations directly during cases, proper data analysis presentation, proper literature research, and leadership training.

Treatment and difficulties:

Immunosuppressants inhibit all sorts of immune responses of the individual through appropriate mechanisms of immune mismanagement, thus increasing the susceptibility of patients to invasive fungal diseases. The current ways of treatment for those affected by severe COVID19 are immunomodulatory. These immunomodulators are anti-inflammatory

and thus essential to counteract the increased and unregulated release of cytokines that are pro-inflammatory in action. During the SARSCoV2 infection, these cause a cytokine storm, primarily in the lungs. Therefore, immunosuppressants are used to the treat severe cases of COVID19 in the intensive care unit. (13) The medications hence usually used are dexamethasone, methylprednisolone, hydrocortisone, etc.

In particular, corticosteroids have a qualitative immunosuppressant effect on immunity through the impairment of various effector immune cells, such as the monocytes, polymorphonuclear leukocytes, T lymphocytes, and macrophages, and are an essential immune risk factor acquired for pulmonary aspergillosis. (14)

Therefore, corticosteroids to treat end-stage COVID patients have contraindications like promoting secondary microbial infections in patients.

In the current COVID pandemic, the possible link between the use of corticosteroids based immunosuppressants and the prevalence of fungal infections in patients with end-stage COVID19 has been discussed. A study conducted in multiple COVID19 ICUs in Wales found that when corticosteroids are used in high dosages, they significantly raise the likelihood of COVID19 patients developing aspergillosis.

Even in Brazil, in a Chicago study of 111 COVID19 patients who received tocilizumab, scientists found a severe increase in candidemia in many seriously ill COVID19 patients who received high-dose corticosteroids. Also, the risk of fungal pneumonia in such cases can be identified by the presence of the antibody that inhibits the binding of IL6 to the membrane and soluble receptors. (15)

Contradicting, it was also observed, in a study report of 4,313 COVID19 patients in New York, corticosteroids usage did not seem to have a link with an increase in bacteremia or fungal disease compared to those who did not use corticosteroids when given in the first week of ingestion. This report thus advocates the administration of low doses of corticosteroids early itself. However, several other reports, also seem to have explained the high incidence of systemic fungal infections by administration of high doses of corticosteroids over a long period of time thus negating the benefits of these drugs. (16)

Conclusion:

Multiple types of hospital infections with poor scope of treatment due to C. auris have been identified. Thus, there is an immediate need of effective treatment guidelines and to

definitively identify C. auris infection in patients. Best disinfection and safety protocols are needed to prevent colonies of this opportunistic pathogen from forming in intensive care units and hospital wards. (17)

Increasing incidence of C. auris outbreaks in many countries on all inhabited continents makes C. auris the leading cause of invasive fungal infections in recent years. The outbreaks of this pathogenic fungus primarily in facilities that deal with care for elderly patients with debilitating comorbidities leading to high mortality rates making it a threat for healthcare. Incorrect detection through routine diagnostics along with rapid transmission and resistance to elimination by disinfection procedures carried out in surroundings. (18) The potential of C. auris to develop resistance to multiple classes of antifungal medications and their ability to survive in the healthcare sector escaping elimination makes C. auris the leading cause for invasive fungal infections in many healthcare facilities today.

Rapid and reliable identification methods and careful infection control measures can help contain the spread of C. auris and prevent and control outbreaks. Coinfection is possible in patients with COVID19 and while diagnosing it, clinicians cannot rule out co-infection with other respiratory pathogens, nor can they exclude COVID19 by detecting non-SARSCoV2 respiratory pathogens. (19)

Prevalence of coinfection by COVID19, risk of coinfection, distribution and influence of coinfection on the health of patients with COVID19. After receiving data on SARSCoV2 co-infection, antimicrobial agents may be recommended in suspected. The rapid transmission of C. auris in medical care despite rigorous infection control measures leads to outbreaks occurring amidst the COVID19 pandemic. Thus, rapid case detection and reporting is essential. The need for national and regional surveillance programmes is necessary to better understand the extent of C. auris infection and assess the clades, thus guiding the implementation of rigorous strategies in order to contain the spread of this pathogen. (20-28)

Reference:

1. Allaw, Fatima, Nada Kara Zahreddine, Ahmad Ibrahim, Joseph Tannous, Hussein Taleb, Abdul Rahman Bizri, Ghassan Dbaibo, and Souha S. Kanj. “First Candida Auris Outbreak during a COVID-19 Pandemic in a Tertiary-Care Center in Lebanon.”

Pathogens 10, no. 2 (February 3, 2021): 157. https://doi.org/10.3390/pathogens10020157.

2. Magnasco, Laura, Malgorzata Mikulska, Daniele Roberto Giacobbe, Lucia Taramasso, Antonio Vena, Chiara Dentone, Silvia Dettori, et al. "Spread of Carbapenem-Resistant Gram-Negatives and Candida Auris during the COVID-19 Pandemic in Critically Ill Patients: One Step Back in Antimicrobial Stewardship?" *Microorganisms* 9, no. 1 (January 3, 2021): 95. https://doi.org/10.3390/microorganisms9010095.
3. Ahmad, Suhail, and Wadha Alfouzan. "Candida Auris: Epidemiology, Diagnosis, Pathogenesis, Antifungal Susceptibility, and Infection Control Measures to Combat the Spread of Infections in Healthcare Facilities." *Microorganisms* 9, no. 4 (April 11, 2021): 807. https://doi.org/10.3390/microorganisms9040807.
4. Villanueva-Lozano, Hiram, Rogelio de J. Treviño-Rangel, Gloria M. González, María Teresa Ramírez-Elizondo, Reynaldo Lara-Medrano, Mary Cruz Aleman-Bocanegra, Claudia E. Guajardo-Lara, et al. "Outbreak of Candida Auris Infection in a COVID-19 Hospital in Mexico." *Clinical Microbiology and Infection* 27, no. 5 (May 2021): 813–16. https://doi.org/10.1016/j.cmi.2020.12.030.
5. Almeida, João N. de, Elaine C. Francisco, Ferry Hagen, Igor B. Brandão, Felicidade M. Pereira, Pedro H. Presta Dias, Magda M. de Miranda Costa, Regiane T. de Souza Jordão, Theun de Groot, and Arnaldo L. Colombo. "Emergence of Candida Auris in Brazil in a COVID-19 Intensive Care Unit." *Journal of Fungi* 7, no. 3 (March 17, 2021): 220. https://doi.org/10.3390/jof7030220.
6. Lai, Chih-Cheng, Cheng-Yi Wang, and Po-Ren Hsueh. "Co-Infections among Patients with COVID-19: The Need for Combination Therapy with Non-Anti-SARS-CoV-2 Agents?" *Journal of Microbiology, Immunology, and Infection* 53, no. 4 (August 2020): 505–12. https://doi.org/10.1016/j.jmii.2020.05.013.
7. Ezeokoli, Obinna T., Onele Gcilitshana, and Carolina H. Pohl. "Risk Factors for Fungal Co-Infections in Critically Ill COVID-19 Patients, with a Focus on Immunosuppressants." *Journal of Fungi* 7, no. 7 (July 9, 2021): 545. https://doi.org/10.3390/jof7070545.
8. Nobrega de Almeida, João, Igor B. Brandão, Elaine C. Francisco, Silvio Luis R. de Almeida, Patrícia de Oliveira Dias, Felicidade M. Pereira, Fábio Santos Ferreira, et al. "Axillary Digital Thermometers Uplifted a Multidrug- susceptible Candida Auris

Outbreak among COVID- 19 Patients in Brazil." *Mycoses*, June 7, 2021, 10.1111/myc.13320. https://doi.org/10.1111/myc.13320.

9. Arastehfar, Amir, Agostinho Carvalho, M. Hong Nguyen, Mohammad Taghi Hedayati, Mihai G. Netea, David S. Perlin, and Martin Hoenigl. "COVID-19-Associated Candidiasis (CAC): An Underestimated Complication in the Absence of Immunological Predispositions?" *Journal of Fungi* 6, no. 4 (October 8, 2020): 211. https://doi.org/10.3390/jof6040211.
10. Prestel, Christopher, Erica Anderson, Kaitlin Forsberg, Meghan Lyman, Marie A. de Perio, David Kuhar, Kendra Edwards, et al. "Candida Auris Outbreak in a COVID-19 Specialty Care Unit — Florida, July–August 2020." *Morbidity and Mortality Weekly Report* 70, no. 2 (January 15, 2021): 56–57. https://doi.org/10.15585/mmwr.mm7002e3.
11. Steele, Edward J., Reginald M. Gorczynski, Robyn A. Lindley, Gensuke Tokoro, Robert Temple, and N. Chandra Wickramasinghe. "Origin of New Emergent Coronavirus and Candida Fungal Diseases—Terrestrial or Cosmic?" *Advances in Genetics* 106 (2020): 75–100. https://doi.org/10.1016/bs.adgen.2020.04.002.
12. Arastehfar, Amir, Toni Gabaldón, Rocio Garcia-Rubio, Jeffrey D. Jenks, Martin Hoenigl, Helmut J. F. Salzer, Macit Ilkit, Cornelia Lass-Flörl, and David S. Perlin. "Drug-Resistant Fungi: An Emerging Challenge Threatening Our Limited Antifungal Armamentarium." *Antibiotics* 9, no. 12 (December 8, 2020): 877. https://doi.org/10.3390/antibiotics9120877.
13. Moser, Dominique, Katharina Biere, Bing Han, Marion Hoerl, Gustav Schelling, Alexander Choukér, and Tobias Woehrle. "COVID-19 Impairs Immune Response to Candida Albicans." *Frontiers in Immunology* 12 (February 26, 2021): 640644. https://doi.org/10.3389/fimmu.2021.640644.
14. Di Pilato, Vincenzo, Giulia Codda, Lorenzo Ball, Daniele Roberto Giacobbe, Edward Willison, Malgorzata Mikulska, Laura Magnasco, et al. "Molecular Epidemiological Investigation of a Nosocomial Cluster of C. Auris: Evidence of Recent Emergence in Italy and Ease of Transmission during the COVID-19 Pandemic." *Journal of Fungi* 7, no. 2 (February 15, 2021): 140. https://doi.org/10.3390/jof7020140.
15. Yadav, Anamika, Anubhav Singh, Yue Wang, Merlijn HI van Haren, Ashutosh Singh, Theun de Groot, Jacques F. Meis, Jianping Xu, and Anuradha Chowdhary. "Colonisation and Transmission Dynamics of Candida Auris among Chronic Respiratory Diseases Patients Hospitalised in a Chest Hospital, Delhi, India: A

Comparative Analysis of Whole Genome Sequencing and Microsatellite Typing." *Journal of Fungi* 7, no. 2 (January 26, 2021): 81. https://doi.org/10.3390/jof7020081.

16. Roh, Kyoung Ho, Yu Kyung Kim, Shin-Woo Kim, Eun-Rim Kang, Yong-Jin Yang, Sun-Kyung Jung, Sun-Hwa Lee, and Nackmoon Sung. "Coinfections with Respiratory Pathogens among COVID-19 Patients in Korea." *The Canadian Journal of Infectious Diseases & Medical Microbiology = Journal Canadien Des Maladies Infectieuses et de La Microbiologie Médicale* 2021 (May 12, 2021): 6651045. https://doi.org/10.1155/2021/6651045.
17. Samadder, Saikat. "Immunopathological Changes in SARS-CoV-2 Critical and Non-Critical Pneumonia Patients: A Systematic Review to Determine the Cause of Co-Infection." *Frontiers in Public Health* 8 (February 9, 2021): 544993. https://doi.org/10.3389/fpubh.2020.544993.
18. Jefferson, Elizabeth A. "Preventing a Candida Auris Outbreak at an Acute Care Hospital During the COVID-19 Pandemic." *American Journal of Infection Control* 49, no. 6 (June 2021): S11. https://doi.org/10.1016/j.ajic.2021.04.042.
19. Chowdhary, Anuradha, Bansidhar Tarai, Ashutosh Singh, and Amit Sharma. "Multidrug-Resistant Candida Auris Infections in Critically Ill Coronavirus Disease Patients, India, April–July 2020." *Emerging Infectious Diseases* 26, no. 11 (November 2020): 2694–96. https://doi.org/10.3201/eid2611.203504.
20. Alashqar, Mais B, Lulwah Alabdan, Mohammad Khan, Abdul Hakim Almakadma, and Sami Almustanyir. "A Case Report of a Candida Auris Infection in Saudi Arabia." *Cureus* 13, no. 5 (n.d.): e15240. https://doi.org/10.7759/cureus.15240.
21. Acharya, Sourya, Samarth Shukla, and Neema Acharya. "Gospels of a Pandemic- A Metaphysical Commentary on the Current COVID-19 Crisis." JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH 14, no. 6 (June 2020): OA01–2. https://doi.org/10.7860/JCDR/2020/44627.13774.
22. Arora, Devamsh, Muskan Sharma, Sourya Acharya, Samarth Shukla, and Neema Acharya. "India in 'Flattening the Curve' of COVID-19 Pandemic - Triumphs and Challenges Thereof." JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 43 (October 26, 2020): 3252–55. https://doi.org/10.14260/jemds/2020/713.
23. Bawiskar, Nipun, Amol Andhale, Vidyashree Hulkoti, Sourya Acharya, and Samarth Shukla. "Haematological Manifestations of Covid-19 and Emerging Immunohaematological Therapeutic Strategies." JOURNAL OF EVOLUTION OF

MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 46 (November 16, 2020): 3489–94. https://doi.org/10.14260/jemds/2020/763.

24. Burhani, Tasneem Sajjad, and Waqar M. Naqvi. “Telehealth - A Boon in the Time of COVID 19 Outbreak.” JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 29 (July 20, 2020): 2081–84. https://doi.org/10.14260/jemds/2020/454.
25. Butola, Lata Kanyal, Ranjit Ambad, Prakash Keshaorao Kute, Roshan Kumar Jha, and Amol Dattaroa Shinde. “The Pandemic of 21st Century - COVID-19.” JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 39 (September 28, 2020): 2913–18. https://doi.org/10.14260/jemds/2020/637.
26. Dasari, Venkatesh, and Kiran Dasari. “Nutraceuticals to Support Immunity: COVID-19 Pandemic- A Wake-up Call.” JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH 14, no. 7 (July 2020): OE05–9. https://doi.org/10.7860/JCDR/2020/44898.13843.
27. Dhok, Archana, Lata Kanyal Butola, Ashish Anjankar, Amol Datta Rao Shinde, Prakash Kesharao Kute, and Roshan Kumar Jha. “Role of Vitamins and Minerals in Improving Immunity during Covid-19 Pandemic - A Review.” JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 32 (August 10, 2020): 2296–2300. https://doi.org/10.14260/jemds/2020/497.
28. Gawai, Jaya Pranoykumar, Seema Singh, Vaishali Deoraoji Taksande, Tessy Sebastian, Pooja Kasturkar, and Ruchira Shrikant Ankar. “Critical Review on Impact of COVID 19 and Mental Health.” JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 30 (July 27, 2020): 2158–63. https://doi.org/10.14260/jemds/2020/470.