

# Treatment of COVID-19 Effects on Reproductive health and Fertility with Traditional Medicinal Plants-A Review

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## ABSTRACT

Omicron a new variant or mutant of Covid-19 have emerged from Africa and is reported worldwide. Two waves of COVID-19 have already been passed across the world and many stressed conditions of third wave can be observed also, however different kinds of vaccines developed for different kinds of variants. Vaccines develop immunity in the body of humans against coronavirus disease 2019. The SARS-CoV-2 virus the infective agent of COVID-19 caused presymptomatic or non-symptomatic illness, contagious infections, spreading primarily through respiratory droplets. During this pandemic of COVID-19 main topic to study is that how this virus affects males and females reproductive abilities and whether pregnant women with COVID-19 are at increased risk of fatality. Availability of health and clinical services might affect reproductive health, pregnancies, birth rate and assisted reproductive technology services around the world. Thus coronavirus could also impact pregnancies and birth rate in 2020, with many people avoiding getting pregnant. It seems that one should be alert to the possible impact of COVID-19 on the reproductive system. The number of pregnancies has been also increased due to lockdown or other reasons, however, pregnant women have afraid of increased risk for severe illness from COVID-19 compared to non-pregnant ladies and other adverse outcomes, such as preterm birth. Hormonal levels including sex hormones, in both males and females, have been affected also due to stress, anxiety and other reasons. Termination of ART and fertility services also caused increased infertility. Only medicinal plants and nutraceuticals are the hope to check the transmission and boost immunity to combat Covid-19.

**Key-words:** COVID-19, Infertility, Nutraceuticals, Reproductive health, SARS-CoV-2

## INTRODUCTION

The family of Coronaviruses causes illness in individuals. COVID-19 disease caused by a new strain of coronavirus, Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2, SARS-CoV, and MERS-CoV are three recent examples of SARS-CoV-2. Coronavirus disease 2019 is an infectious acute respiratory disease, which is caused by a novel coronavirus. Pandemics of COVID-19 cause deep problems to the general day to day lives of

people and become a serious medical concern to the global economy. This pandemic has affected millions of people live, by sickness or another reason during the pandemic COVID-19. Since many countries are trying to lock their population by enforcing strict quarantine to control the spread of this highly communicable disease. Many countries around the world implemented containment measures to reduce disease transmission and various precautions and safety measures that can control the spread of COVID-19. Some actions have been taken by governments includes testing and tracing, bans on large gatherings, nonessential business and school and university closures, international and domestic mobility restrictions and physical isolation, and total lockdowns of regions and countries or distant parts of the country. By SAH (stay-at-home) control consumption

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levels of alcohol amongst young adults with hazardous drinking that is associated with drinking events. On 31 December 2019 World Health Organization reported about the cases of pneumonia in Wuhan City, Hubei Province, China, of unknown microbial aetiology. Ozili and Arun <sup>[1]</sup> reported the statistics data of the spread of the coronavirus in major regional areas such as the European region, Region of the Americas, Eastern Mediterranean, Western Pacific Region, South East Asia and African Region.

Initially, it was noticed that the COVID-19 pandemic would be localized in China only. Later it spread across the world through the movement of infected and non-infected individuals. Economically it was painful when people were asked to stay at home. The severity of this pain was felt in various sectors of the economy like travel bans affecting the aviation industry, sporting event cancellations affecting the sports industry, mass gathering prohibition affecting the event organizers and entertainment industries <sup>[2,3]</sup>. This coronavirus had been detected in samples taken from those individuals, who were indulged in event and entertainment industries. On January 30, 2020, WHO first declared a public health emergency, after rapid spreading of this epidemic around the world, on 11 March 2020, it was declared a pandemic. People outside our household, make sure to take precautions to prevent the spread of COVID-19: Always wear a mask, when go outside the home. Maintain at least 6 feet (about 2 arm lengths) distance. Avoid crowds and poorly ventilated indoor spaces <sup>[4]</sup>.

Out of hundreds of coronaviruses, most viruses circulate among pigs, camels, bats and cats. Sometimes these viruses jump to humans from animals and can cause disease. Three of them can cause more serious even fatal diseases. SARS corona virus (SARS-CoV) emerged in November 2002 and caused severe acute respiratory syndrome (SARS) and this virus disappeared by 2004. The Middle East respiratory syndrome (MERS) is caused by the MERS coronavirus (MERS CoV). MERS was identified in September 2012 which is transmitted from an animal reservoir in camels and continues to cause sporadic and localized outbreaks. The third novel coronavirus that emerged in this century is called SARS-CoV-2, it causes coronavirus disease 2019 (COVID-19), which emerged from China in December 2019. Through previous research based on SARS and MERS, scientists investigate for rapid development of COVID-19 diagnostics,

therapeutics and vaccines. In these investigations, more research is required to understand how the virus infects cells and causes disease, and what precautions can prevent to stop the spread of disease <sup>[5,6]</sup>.

**Affect at Global Level-** The whole world is facing a worldwide pandemic and according to the UN it is the greatest test since Second World War. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections caused by the novel coronavirus. In this respiratory infection symptom severity ranges from a mild common cold-like illness to severe viral pneumonia leading to an acute respiratory syndrome, which is potentially fatal. Although some patients may be asymptomatic some characteristic symptoms include fever, cough and dyspnoea etc. Some complications of this severe disease include multi-organ failure, septic shock and venous thromboembolism.

Since the start of the pandemic, the U.S. recorded the highest seven-day average of new COVID-19 cases on October 25<sup>th</sup> 2020. The U.S. recorded more than 83,000 new cases of COVID-19, the highest daily counts breaking all the records set. While in 2021 the US accounted for the world's highest number of cases and deaths at 34,174,752 and 611,611, respectively, according to the CSSE. According to the John Hopkins dashboard the U.S. was facing a dangerous third wave that is threatening to be worse. The country had reported more than 8.6 million cases of COVID-19 and more than 225,200 deaths. COVID-19 hospitals were also rise in number across the nation. Even on June 21, 2021, Michigan's ICU bed capacity reached up to 99% full, according to the data of the Michigan state department.

As the virus spread almost everywhere in the country that brings the global economic crisis, but according to expert advice wearing masks can save many lives. In a published study (Friday in the journal *Nature Medicine*, University of Washington's Institute for Health Metrics and Evaluation) the researchers predict that if more than 95% of people in the U.S. wear masks, it could be sufficient to ameliorate the worst effects of the epidemic <sup>[4,7]</sup>.

Their models predict that such universal mask-wearing can save an additional 129,574 life between Sept 22 and the end of February 2021.



Firstly, the spread of the virus encouraged social distancing which led to the shutdown of financial markets, corporate offices, businesses and events. Secondly, the exponential rate at which the virus was spreading and the heightened uncertainty about how bad the situation could get. During this period the impact

of social distancing policies affects economic activities and stock market indices. Some observations were seen during the lockdown period like restrictive measures, monetary policy measures, fiscal policy measures and public health measures (Table 1) [8].

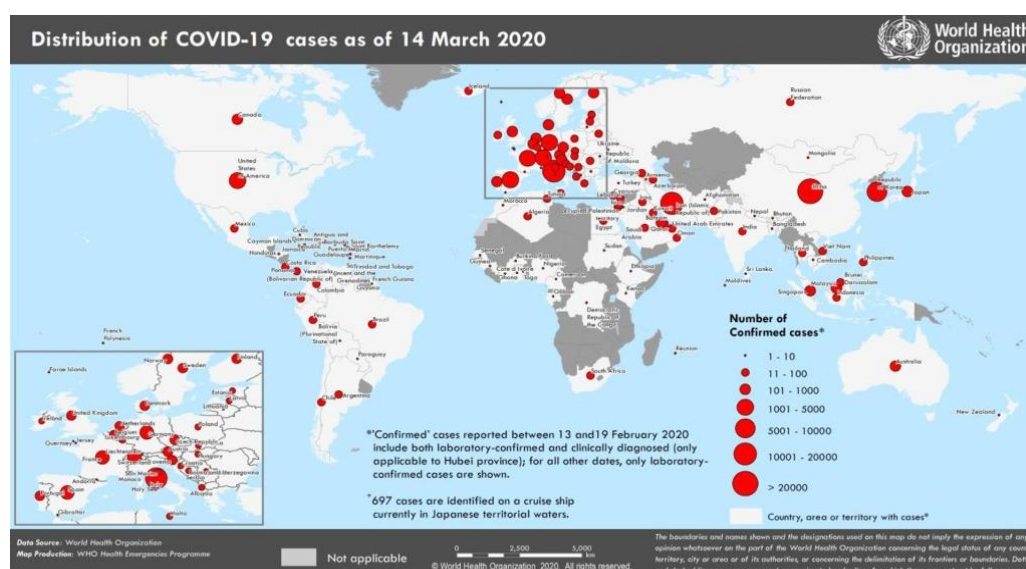
**Table 1:** WHO Coronavirus Disease (COVID-19) Dashboard: Situation by Country, Territory and Area (Data last updated: June 26, 2021, 05:18 GMT) (Source: World corona meter-WHO)

Name Cases	cumulative total Cases	newly reported in last 24 hours	Deaths cumulative total	Deaths newly reported in the last 24 hours	Transmission Classification
Global	181190692	+23,089	3925285	+551	
United States of America	34,482,672		619,152		Community transmission
India	30,183,143	+674	394,524		Clusters of cases
Brazil	18,322,760		511,272		Community transmission
Russian Federation	5,409,088		132,064		Clusters of cases
France	5,766,315		110,939		Community transmission
Spain	3,782,463		80,779		Community transmission
United Kingdom	4,699,868		128,066		Community transmission
Italy	4,256,451		127,418		Clusters of cases
Argentina	4,374,587		91,979		Community

The findings reveal that the increasing number of lockdown days, monetary policy decisions and international travel restrictions severely affected the level of economic activities. In contrast, the imposed restriction on internal movement and higher fiscal policy spending had a positive impact on the level of economic activities, although the increasing number of confirmed coronavirus cases did not have a significant effect on the level of economic activities [9,10].

Since COVID-19 was declared a pandemic by WHO global spread of COVID-19 may rise into colder months due to

other infections. Scientists are doing their tired fewer efforts at the global level to develop therapies for the infection. Vaccine trials are heading into different phases. Since the origin of Coronavirus disease 2019, quite 15 million cases are reported, causing over 250,000 cases in over 170 countries. In 2019 a gradual decline in births in the US was recorded compared to the last 35 years, it could lead to a "demographic time bomb". In 2020 some people choose not to get pregnant or are unable due to the halt on some fertility treatments thus coronavirus could also impact birth rates. [7,11,12].



**Fig. 1:** Areas with reported confirmed cases of COVID-19, 10 March 2020

(Source: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200310-sitrep-50-covid-19.pdf>)

In the UK, SARS-CoV-2 infected pregnant admitted patients to the hospital were 4.9 per 1000 maternities. Most of them were in the second or third trimester. Out of these infected women, 41% were aged 35 years or older, 56% were from other ethnic minority groups and others were overweight [13].

COVID-19 pandemic will increase mortality due to the virus; it is also likely to have an impact on other health care services. As COVID-19 affects the respiratory system, and people with COVID-19 present some symptoms at the beginning of the illness including dry cough, fatigue, fever, breathing difficulties and muscle pain and these symptoms may develop into pneumonia, loss of taste and smell, diarrhoea and lymphopenia [14]. In COVID-19 time the ability of the virus affect males and females' reproductive abilities and also pregnant women with COVID-19 are at increased risk of fatality. Persistent fever remains due to high temperature and triggering a secondary autoimmune response which leads to an inflammation of one or both testicles (autoimmune orchitis) are also involved in the COVID-19 mechanism [15,16].

By mid-January, India had seen a sustained reduction in daily cases, to about 16,000 every day from a peak of around 98,000 daily. The gap between the peak of the first wave, around mid-September 2020, and the onset of the second wave, was about five months. In India, the second wave of COVID-19 began around the middle of February 2021. According to the reports of there, whole families being infected and test positivity ratios more

than 50%, were first vigorously denied by the state but confirmed soon after. In early April daily cases, the first cross numbers were seen at the peak of the first wave (a bit shy of 98,000 cases). In the first three weeks of April 2021, almost 1,000 bodies were disposed of with COVID-19 protocols in Bhopal (India). According to another report, on one day alone, Kanpur reported five times as many funerals as normal, amounting to almost 400 extra funerals. The second Covid-19 wave had been more deadly, with over 1.4 lakh deaths happening in the last 7 weeks alone. The daily count of cases in India peaked on May 6. That day, more than 4.14 lakh cases were discovered. There has been a steady decline in the detection of new cases after that. Since the trend in death numbers usually has a two-week lag, it might be the time that the death count begins to decline as well [17].

Shocking as these mismatches are, they are not without international precedent. A study from Zambia, which involved random testing of the deceased found ten times as many COVID-19 deaths as recorded. Another study from Damascus, Syria found that a tiny 1.25% of possible COVID-19 deaths had been recorded. According to data from the third national survey, across India, just 3% of infections were detected through testing in 2020. There are also major variations in apparent death rates between urban and rural areas. India's national serosurveys are consistent with a story of 'missing' rural deaths. The period between the second



and third national serosurveys (roughly from September to the end of 2020), saw a very substantial rural spread. Even as the pandemic slowed in the cities and the country's total case-load declined, rural prevalence jumped to 19% from 5.2%. Nationwide, total infections tripled during this period, but recorded deaths only doubled. India already has the world's third-largest death count. Only the United States, which has recorded over 5.84 lakh deaths, and Brazil, which has seen 4.48 lakh deaths, has a higher death count. India now accounts for 16% of the global confirmed cases, and 9% of global deaths [18].

### Impact of Covid-19 on Human Reproductive Health-

Cold and dry environments are more effective for the survival and spread of droplet-mediated viral diseases while warm and humid environments are less effective for viral transmission. Although, the role of temperature and humidity in the transmission of COVID-19 has not been established yet. It is proved that viruses could infect testis directly [14,19,20].

The male reproductive system has an immunosuppressive environment in the blood-testis barrier which protects seminal viruses from immune observation. With this information, we should know how to protect ourselves and our families against flu by getting a flu vaccine. Also, pregnant ladies might be at an increased risk for severe illness from COVID-19 compared to non-pregnant ladies and other adverse outcomes, such as preterm birth. Although SARSCoV-2

to the end of 2020), saw a very substantial rural spread. mainly attacks respiratory systems, manifestations of multiple organs have been detected. A significant concern was raised about whether COVID-19 may affect female and male reproductive functions. Several findings imposed more restrictions on social relationships between individuals even if inside the family, adding more physiologic load. In this context, there is a crucial need to identify the biological and behavioural reproductive risk factors associated with COVID-19 disease [21-23].

The contribution of individuals to different social and economic activities depends on the maintenance of a good quality of life and health. The ongoing COVID-19 pandemic raised at the end of December 2019 has drastically affected different aspects of human wellbeing. The pandemic not only affected the health of individuals but also negatively affected mental health and social interaction. This review illustrates a) scientific findings related to the impact of the COVID-19 pandemic on the reproductive process, considering gender, hormonal balance, gonad functions, pregnancy, and ART, b) the sociosexual dimension of COVID-19 disease and precautions that should be taken to avoid infection via sexual transmission or vertical transmission, which may alleviate the fear associated with continuing normal social relationships and economic.



**Fig. 2:** Effect of COVID -19 on individual life

The above data shows supporting an increased risk of severe illness from the virus COVID- 19. Adults with COVID-19 having obesity, overweight, or smoking habits are at risk. According to available data, we can say at this time, adults of any age might be at an increased risk for a severe illness caused by COVID-19 with the following

conditions: asthma, cystic fibrosis, high blood pressure, neurologic conditions like dementia, liver disease, pregnancy, pulmonary fibrosis, thalassemia and diabetes mellitus. Children are at a heightened risk of exploitation, violence and abuse when schools and daycare centres are closed, movement restricted and



economies going through the global recession [24].



(By Curtsey: Reports published in News Papers and other media)

**Fig. 3:** India should brace for third COVID -19 wave

The above data shows supporting an increased risk of severe illness from the virus COVID- 19. Adults with COVID-19 having obesity, overweight, or smoking habits are at risk. According to available data, we can say at this time, adults of any age might be at an increased risk for a severe illness caused by COVID-19 with the following conditions: asthma, cystic fibrosis, high blood pressure, neurologic conditions like dementia, liver disease, pregnancy, pulmonary fibrosis, thalassemia and diabetes mellitus. Children are at a heightened risk of exploitation, violence and abuse when schools and daycare centres are closed, movement restricted and economies going through the global recession [24].

Several endocrine glands are responsible for the production of many hormones, which send important 'messages' through our bloodstream. These messages inform our body to regulate processes like breathing, water balance, blood pressure and more metabolic activities. Cortisol (stress hormone) is the most significant hormone because it controls our stress response. When the body is stressed, cortisol levels can rise even up to high levels which are dangerous and leads to increased risk of infections. Studies of patients who are confirmed with COVID-19 infection shows significantly increased cortisol levels as compared to the normal reference range [25,26]. Pandemics also cause deep problems to the general day to day lives of people. Research reveals that COVID-19 transmits from human to human, through direct contact and small droplets

arrived from the infected people.

As per the history of COVID-19, in June 2020, around seven million people have had confirmed COVID-19 cases and around four hundred thousand people have died around the world, and every day the numbers keep rising. People infected with COVID-19 also could get the infection by many other viruses such as mumps virus, hepatitis viruses B/C, herpes simplex virus, human papillomavirus, Coxsackie virus, influenza, HIV (human immunodeficiency virus) and SARS-CoV-1 (severe acute respiratory syndrome coronavirus 1). SARS-CoV-1 could also infect the male genital system and impair fertility. It seems that due to persistent fever secondary autoimmune response leads the patient into inflammation of one or both testicles (orchitis). Psychiatric disorders have been observed during the COVID-19 public health crisis, experts are concerned that psychiatric comorbidity may increase virus-related mortality and predispose patients to poorer outcomes [14,27-29].

### **Assisted Reproductive Technology to manage Reproductive Health care of males-**

Fertility services deal with patients with other healthcare services including counselling, blood tests, clinical consultations, transvaginal ultrasounds and ART techniques to the procedures like testing genetic defects/abnormalities, hysteroscopy, laparoscopy and any others. The testis degeneration is attributed to an increase in testicular



temperature that is an indirect effect of the Viruses could destroy testicular parenchyma and develops orchitis in 20-30% of cases, as they have high tropism for the testes. Xu *et al.*<sup>[14]</sup> reported that SARS-CoV-1 create leukocyte infiltration in the testis that could affect the function of Leydig cells, damage the blood-testis barrier, and also destroy the seminiferous epithelium. A study was done by Ma *et al.*<sup>[25]</sup> on 81 years aged SARS-CoV-2 infected men and 100 year aged healthy men. In that study, 81-year aged men with COVID-19 shows a significantly increased luteinizing hormone (LH) level but decreased testosterone/LH and follicle-stimulating hormone/ (FSH) levels ratios suggest potential hypogonadism. One can conclude that artificial reproductive techniques such as IUI (intrauterine insemination), IVF injectable protocols, egg collection and embryo transfer and follow up the patient until getting positive pregnancy test then for the whole duration of pregnancy (40 weeks) ultimately this will put infertile couples at more risk of infection and infection transmission.<sup>[18,22]</sup> The current novel COVID-19 pandemic is revealing intense differences between men and women in disease outcomes global. The sex and gender disparities found in COVID-19 emphasize the impact of sex and gender and treatment according to sex and gender. Biological and behavioural factors contribute to differences between men and women in these comorbidities<sup>[30,31]</sup>.

All findings suggest that COVID-19 could be an impact on men's reproductive health-inducing spermatogenic and

inflammatory milieu.

fertility failure. Conclusive research seems that it is rash to make definitive conclusions at present, this should alert to the possible impact of COVID-19 on the male reproductive system<sup>[16,22]</sup>. It can be concluded that COVID-19 has created unprecedented consequences for adolescents, young adults and old age peoples in the contemporary world might be due suspended of teaching, sports, entertainment services in malls, theatres and clubs in the towns or cities and locked down, and there is not much certainty surrounding the pandemic, particularly regarding when it will be over. Due to many reasons like psychological, physical and mental stress on the individual's body physiology might be caused changes in the levels of biochemical and hormones affects the adults of reproductive age change their potential ability of fertilization resulted in effects on pregnancies and birth rate at global level during COVID-19<sup>[32,33]</sup>.

Following precautions, measures have been taken at the individual as well as the country level to check and combat pandemic COVID-19. For safety Stay At Home (SAH) is the main precautionary measure. The safest way at home with the people who live with us or virtually with friends and family. Although vaccination is the most effective preventive measure of COVID-19, however, there are several reasons like a financial problem due to lockdown, availability of doses, social and personal opinion and myths that have been involved in the fully vaccination and success of vaccination<sup>[34]</sup>.



(By Curtsey: Reports published in News Papers and other media)

**Fig. 4:** Effect of COVID -19 on individual life

At all times nature will have the signs to treat new diseases and only human intelligence needs to identify these signs and investigate the new drugs

phytochemically and clinically. Since, several plants have been explored for antiviral, antibacterial, antifungal, anti-inflammatory and other therapeutics around the world.



During pandemic time Ayurvedic, Homeopathic and Yoga treatment of Covid-19 effects [35]. In India Kwath, which is the extract/mixture of traditional herbal remedies like Giloy or Guduchi- *Tinospora cordifolia* (means 'Amrita', which means the root of immortality), Basil or Tulsi- *Ocimum sanctum* (Queen of herbs), Turmeric or Haldi- *Curcuma longa*, Ashwagandha- *Withania somnifera*, Ginger root, Licorice, Dalchini-Cinnamon, Amla- *Phyllanthus emblica*/ emblic/Indian gooseberry/amalaki,

systems were reemerged for precautions and effective Papaya- *Carica papaya*, Aloe and doing Yoga exercise were recommended by Ministry of Health/AYUSH and at another social and digital media level to prevent effects and boost immunity in patients. Some of these plants like *Curcuma longa*, *Withania somnifera*, *Phyllanthus emblica*, and *Carica papaya* affect the fertility potential both in men and women [36].



(By Curtsey: Reports published in News Papers and other media and journals)

**Fig. 4:** Traditional immunity boosters

## CONCLUSIONS

A strong inter-relationship between people and plants according to needs had been established since time immemorial. Plant species have always been a fundamental source for the discovery of drugs. Herbs, vegetables and yoga have been used to boost immunity and inflammations caused by Covid-19 infections. They have chemical diversity, metabolites, phytochemicals which plays a significant role in new drug development. People had used traditional herbal medicinal plants to fight against pandemics in the past years since scientifically many plants have been reported antiviral properties and enhanced immunity. Gloy, Cinnaminson, Ocimum, Lemon, Aloe and several other plants species have been used by people in the form of syrup, capsule, pills, Kawata or other forms. Now in these days, the dependency of human beings on medicinal plants might have increased several folds around the world, since plants products do not cause adverse or side effects, as compared to synthetic compounds, suggests that plants are the alternate source to prevent COVID-19. Recently during the COVID-19 pandemic, people are using traditional medicinal plants and claiming that herbal

treatment effectively prevents or cure COVID-19 effects. However, further scientific approval is required from concerned authorities like FDA. The authorities should test the validity of these medicinal plants and spread the knowledge through awareness programs.

## CONTRIBUTION OF AUTHORS

**Research concept-** Dr. PC Mali and Dr. Samiya Khan

**Research design-** Dr. PC Mali and Dr. Samiya Khan

**Supervision-** Dr. PC Mali

**Materials-** Dr. PC Mali and Dr. Samiya Khan

**Data collection-** Dr. PC Mali and Dr. Samiya Khan

**Data analysis and Interpretation-** Dr. PC Mali

**Literature search-** Dr. PC Mali and Dr. Samiya Khan

**Writing article-** Dr. PC Mali and Dr. Samiya Khan

**Critical review-** Dr. PC Mali and Dr. Samiya Khan

**Article editing-** Dr. Samiya Khan

**Final approval-** Dr. PC Mali

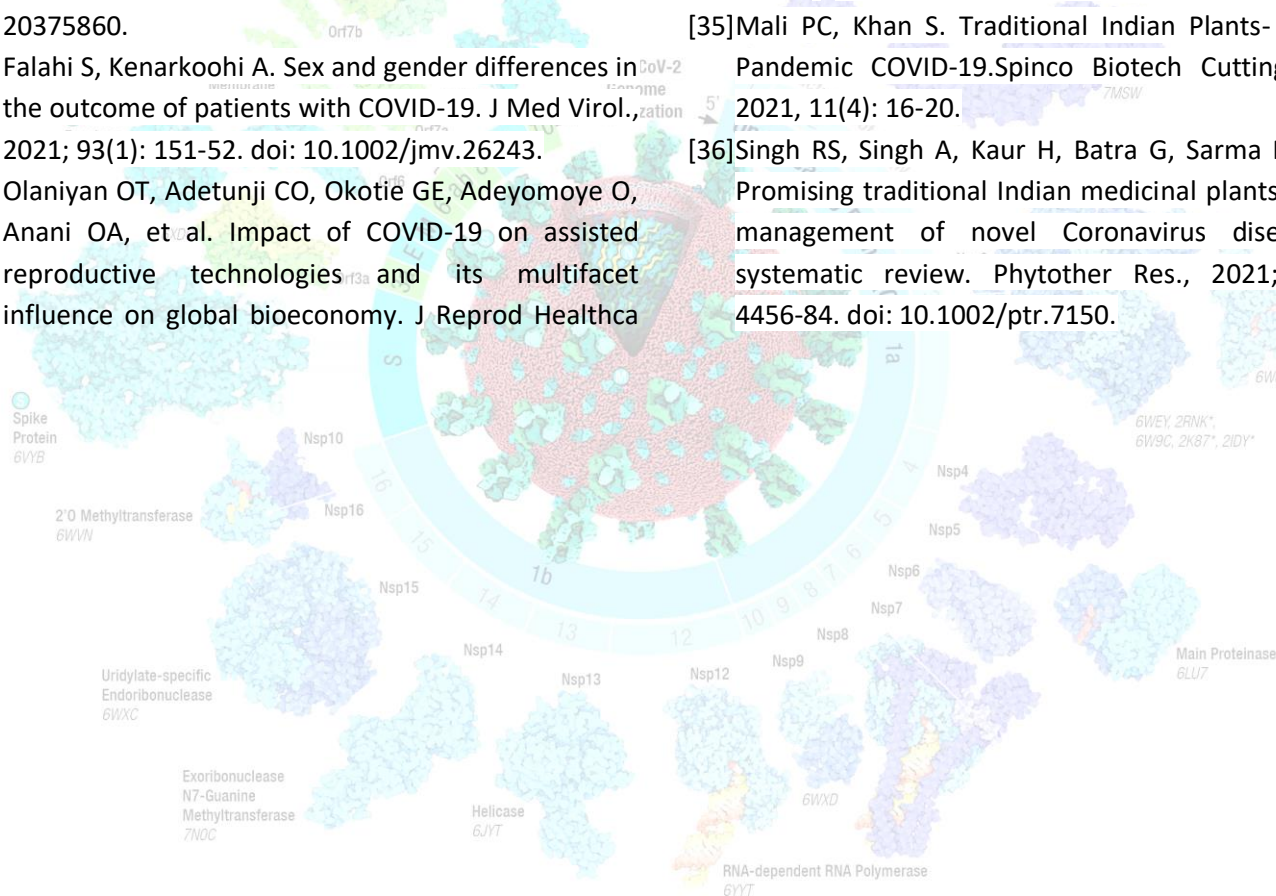
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