

Study on the *Agaricus bisporus* to enhance the Immunity against Covid-19

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Abstract-

On-going pandemic COVID-19 has raised a public health issue worldwide impacting number of people with a continuous increase in death rate. The causative agent of this disease is identified and named as SARS-CoV2 because of its genetic relatedness to SARS-CoV species that was responsible for the 2003 corona virus outbreak. The immense spread of the disease in a very small period demands urgent development of therapeutic and prophylactic interventions for the treatment of SARS-CoV2 infected patients till that Immunity is one of most important factor to fight against this Virus family. A plethora of research is being conducted globally on this novel corona virus strain to gain knowledge about its origin, evolutionary history, and what was the reason for Outbreak and how this chain broke at that time and concluded that people with good immunity fight easily against this Virus. The immune system protects our body against diseases and produces antibodies to kill pathogens. This review presents a brief overview of the immune system about its protection of the human body from COVID-19 virus; illustrates the process of the immune system, and its mechanism to fight virus. It is an effort to enhance immunity by using mushroom which can be one of the best immunity boosting agent among corona virus strains, which can hint towards the best natural Vitamin source as Immunity Booster for the prevention of this public threat.

Keywords: COVID-19, SARS-CoV2, Immunity Booster, Vaccine development

Abbreviations: PDB, protein data bank; RdRp, RNA-dependence RNA polymerase; HCoV, human corona virus.

Introduction-

Coronavirus disease 2019 (COVID-19), also known as COVID, is a Contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Corona viruses (CoVs) are single-stranded, positive-sense RNA viruses. The first known case of covid 19 infection was identified in Wuhan, China, on December 2019. The disease hasspread worldwide, leading to a pandemic [1].

Symptoms of Covid-19 are variable differ individually, but often include fever, cough, headache, fatigue, breathing difficulties and loss of smell and taste in most of the cases. At least a third of people who are infected do not develop noticeable symptoms but due to strong immunity many of them fight easily against Covid-19 without any severe complications. Around 14% develop severe symptoms (dyspnea,hypoxia) or more than 50% lung involvement on imaging. Older People are at a higher risk of developing severe symptoms but let's not forget that many Senior Citizens over age of 100+ recovered because of Strong Immune system. Corona virus is not the one to spread this year one of their family Member SARS has already reported over worldwide during the year 2002 and many died due to no treatment availability but chain broke because of good immune system most of them recovered well. From there scientists collected data that healthy diet plays a crucial role to fight against this Covid-19, to break this chain till every individual get vaccinated. Healthy Diet include Protein, Minerals, Vitamins etc.

The diet given to the Covid Patient was Preferably Eggs, Rice and one vitamin enriched fruit like Oranges. Our study says that Mushroom is one of the Source of Vitamins and it could be healthy diet to increase Immunity among Individuals.

Research Gap-

This review paper will be demonstrating how Mushroom will act as a Natural Immunity Booster against Corona virus strains.

What is Corona virus?

Coronaviruses (Fig. 1) are a large family of viruses that cause upper respiratory tract and intestinal illness. The name “coronavirus” comes from crown-like spikes that covers all over the surface of the viruses in this family. *Coronam* is Latin for “crown.”

Most coronaviruses affect humans and animals, such as bats and pigs. Seven coronaviruses have spread to humans.(Fig. 2)

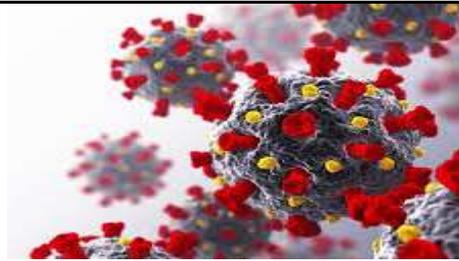


Figure 1-3D view of Covid-19 surface

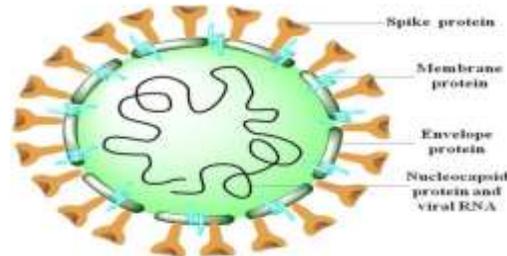


Figure2-.Covid-19 Inner View

Corona virus Evolution-

Scientists first identified a human infected with Corona virus in 1965. It caused a common cold. Later, researchers found a group of similar human and animal viruses and named it after its crown-like appearance.

Seven corona viruses can infect humans. The type of virus that causes SARS emerged in Southern China in 2002 and spread to 28 other countries. More than 8,000 people were infected by July 2003, and 774 had died in China. A small outbreak in 2004 involved only four cases of the same infection. This corona virus causes fever, headache, and respiratory problems such as cough and shortness of breath when the condition becomes fatal.

MERS started in Saudi Arabia in 2012. Almost all of the 2,500 cases have been in people who live in or travel to the Middle East. This corona virus is less contagious than its SARS cousin but much more deadly, killing many people. It has the same respiratory symptoms but is also known to cause kidney failure [2].

Coronavirus Types-

Scientists have divided coronaviruses into \$ sub groups- alpha, beta, gamma, and delta [10]. Seven of these viruses are found to infect people that are 229E (alpha), NL63 (alpha), OC43 (beta), HKU1 (beta), MERS-CoV [a beta virus that causes Middle East respiratory syndrome (MERS)], SARS-CoV [a beta virus that causes severe acute respiratory syndrome (SARS)], SARS-CoV-2, which causes COVID-19[4][11].

How variants Spread?

When a virus is widely circulating in a population causing many infections, the likelihood of the virus mutation increases. The more opportunities a virus has to spread itself, the more it replicates and the more opportunities it has to undergo changes. Most viral mutations have very less impact on the virus to cause infection, but depending on where the changes are located in the virus's genetic material, they affect a virus's properties, such as transmissions [3].

Where Did the Coronavirus Come From actually?

Experts say SARS-CoV-2 originated in bats. That's also how the coronaviruses behind MERS and SARS got started.SARS-CoV-2 has come in contact with humans at one of Wuhan's open-air "wet markets." They are where customers buy fresh meat and fish, including animals that are killed on the spot.Some wet markets sell wild banned species like cobras, wild boars, and raccoon dogs. Crowded conditions can allow viruses from different animals to swap genes. Sometimes the virus changes so much that it can start to infect and spread among people [20].The Wuhan market did not used to sell bats at the time of the outbreak. That's why early suspicion comes on pangolins, sold illegally in markets in China [16]. Some coronavirus strains that infect pangolins are similar to SARS-CoV-2.As SARS-CoV-2 spread both inside and outside China, it infected people who had no direct contact with animals. That meant the virus is transmitted from one human to another categorizing it as a communicable disease (Fig. 3). It had spread in U.S. and around globe, people are unwittingly catching and passing on the Coronavirus [5]. This growing worldwide disease transmission is now a pandemic.

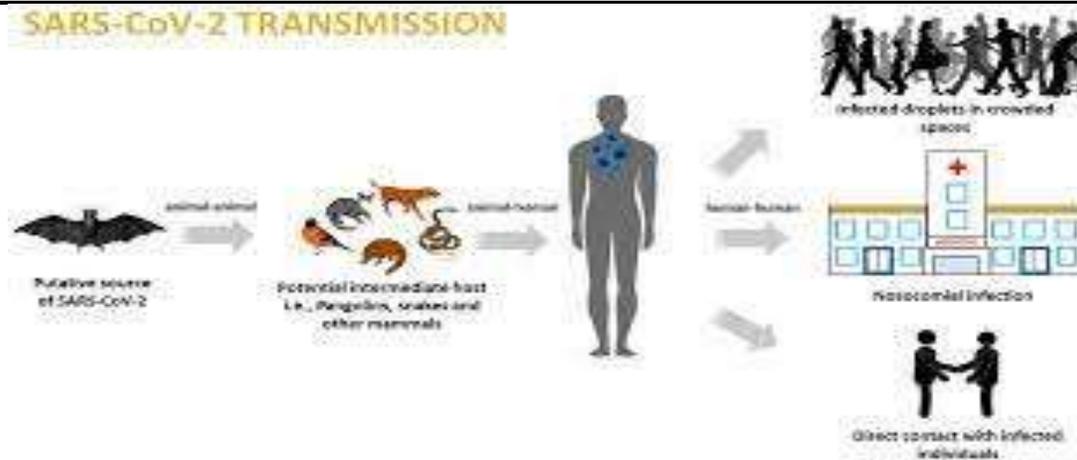


Figure 3-Coronavirus spread from Bat to Humans

Symptoms of coronavirus-

The Most common Symptoms of coronavirus are Fever, Dry cough as well Fatigue. Other symptoms include loss of taste or smell, nasal congestion, conjunctivitis, Sore throat, headache, muscles pain, Skin rashes, Nausea or vomiting, Diarrhea, Dizziness. Symptoms of severe COVID-19 disease include shortness of Breath, Persisting pain in Chest, loss of appetite, Confusion, higher temperature[21]. Other common symptoms known are irritation, confusion in mind, Consciousness, Anxiety, Depression, sleep disorders, more severe and rare neurological complications such as strokes, brain inflammation and nerve damage(Fig. 4)[7].

To prevent infection and to slow transmission of COVID-19, do following: Wash your hands regularly with soap and water/clean with alcohol-based hand sanitizer [22]. Maintain at least 1 meter distance from people coughing or sneezing. Avoid face touch.

Stay home if you feel unwell [23]. Refrain from smoking and activities like alcohol consumption that weaken the lungs and liver. Practice physical distancing by avoiding unnecessary travels and staying away from groups of people. Have a proper diet and makes immunity strong [12].

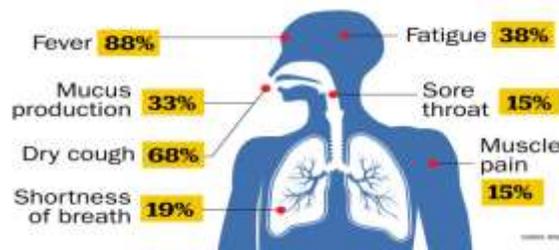


Figure 4-Covid-19 Symptoms

What is involved with the testing?

Polymerase Chain Reaction remain as the primary COVID-19 diagnostic testing method in the US and is done in same way as of in 2003.

To collect a sample for this test, a healthcare provider will likely perform one of the following: swab nose or the back of throat, aspirate fluid from lower respiratory tract, take a saliva or stool sample [25]. After sample collection, nucleic acid is extracted from the virus sample and then amplified parts of its genome by Reverse transcription PCR technique. This gives the researchers a larger sample for viral comparison. Two genes can be found within the SARS-CoV-2 genome [18].

Test results are seen to be positive if both Genes are found there, if only 1 gene is found and negative if neither Gene is seen. The new approved POC testings allowed for samples to be collected and tested at that location, resulting in quicker times. Cepheid POC Devices produce test results within 45 minutes [8].

Mechanism of immune system in the human body against COVID-19

As long as the immune system is functioning normally, infections such as COVID-19 cannot be severe. The three types of immunity we have are innate immunity (rapid response), adaptive immunity (slow response), and passive immunity. However, when the body encounters germs or viruses for the first time, the immune system cannot work properly, and illness can occur depending on the defense mechanism of the immune system. When the cells of the immune system become well known to the pathogen, they complete their jobs by recirculating between central and peripheral lymphoid organs and migrating it and from sites of injury via blood. Blood carries these immune cells from one site to another, flows throughout the body, and acts as a pipeline for the immune system. The cells again enter into the bloodstream to be transported to the tissues throughout the body after exiting the nodes via outgoing lymphatic vessels.

After being affected by virus, immune cells responses to mediate antibody. The B cells are assisted by T cells to differentiate into plasma cells, which then produce specific antibodies to a viral antigen. A neutralizing nature of antibody is efficient in fully blocking the virus from entering into host cells to limit the infection and plays a very intense protective role at the later stage of infection and also prevent infection relapping. A cellular immune response can be observed inside the infected cells, which is mediated by T-lymphocytes. The overall adaptive immune response is directed by helper T cells, and cytotoxic T cells which plays a vital role in the clearance and cleaning of virus-infected cells.

Information from SARS-CoV and MERS-CoV allow the Exploration of knowledge to understand how SARS-CoV-2 escapes the host's immune response, because data on SARS-CoV-2 remain limited till Now.

In the First phase, doctors attempt to boost immune response, and in the second phase they attempt to suppress it. Vitamins should be used immediately after the Coughing begin, they are highly lung protective.

How Mushroom can be a Natural Immunity Booster?

Mushrooms are the only source of vitamin D and one of the few non fortified food sources. Vitamin D helps in building and maintaining strong Bones by helping body to absorb calcium. Vitamin D is available via diet, supplements and sunlight, referred to as the "sunshine vitamin." The list of health benefits medicinal mushrooms provide is lengthy (think: brain booster, hormone helper, antioxidant powerhouse). But each mushroom has unique properties and provides its own distinct health advantages.

All mushrooms contain some vitamin D, but mushrooms have the unique ability to increase vitamin D amounts due to UV-light or sunlight exposure (Fig. 5). Similar to humans, mushrooms naturally produce vitamin D following exposure to sunlight or a sunlamp, mushroom's sterol – ergosterol – converts to vitamin D when exposed to sunlight.

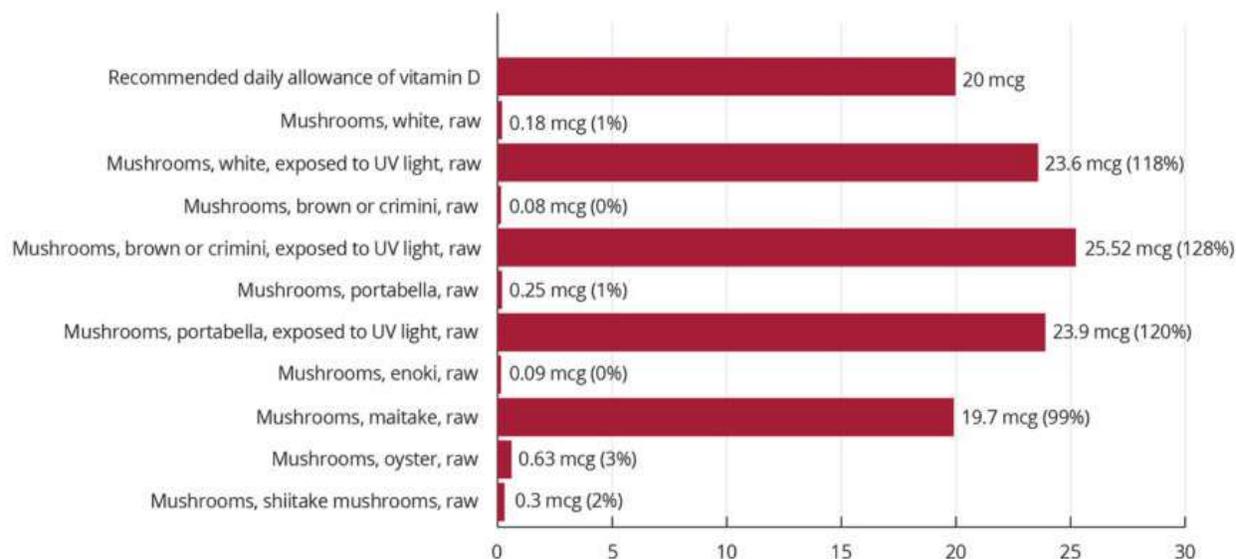


Figure 5-Mushrooms producing more Vitamin D on exposure to Sunlight

Agaricusbisporus- It is also known as Button mushroom (Fig. 6). Vitamin D2 is essential for a human body and mushrooms are proved to be one of the best sources of it. The highest ergosterol content was found in button mushrooms. The conversion of Ergosterol to Vitamin D2 was about 4 times higher when the gills were exposed to UV-A irradiation than when the outer caps were exposed to the same.



Figure 6- Benefits of *Agaricusbisporus*

Reishi:- Reishi (Fig. 7) is known as nature's Xanax. This fungus is one of the Popular Medicinal mushroom. Reishi may be able to do it all, aids in weight loss, keeps the immune system in check, and may even fiercely fight cancer cells. What makes this mushroom unique, is its calming properties due to the compound triterpene present in Reishi mushroom in fair amount. These mood-boosting compounds alleviate anxiety, ease depression, and encourage better sleep, as seen in mice. Triterpene's positive Effect on Nervous system does not stop there. It can also promote healing and sharpen focus.



Figure 7-Benefits of Reishi Mushroom

Lion's Mane:- Lion's mane (Fig. 8) is used for some natural mental clarity. This feathery "pom-pom" lion's mane mushroom is packed with Many antioxidants and also strengthens the immune system like any medicinal mushroom. But lion's mane is rare in the fact that it stimulates the production of the bioprotein nerve growth factor and myelin (an insulation around nerve fibers). Both NFG and Myelin are very crucial for brain health. An imbalance in them can contribute to neurological diseases such as Alzheimer's disease and multiple sclerosis. Thus making lion's mane some serious brain food. This miraculous mushroom has also been shown to improve cognition in a small human study, memory in mice, increases concentration, and alleviate anxiety and irritability.



Figure 8- Benefits of Lion's mane

Chaga:-Chaga mushrooms(Fig. 9) are an antioxidant powerhouse, making them an excellent contender for fighting free radicals and inflammation. This dark black mushroom combats oxidative stress (which is linked to skin aging),and may prevent or slow down the growth of cancer, and has been found to lower amount of low-density lipoprotein (LDL), the “bad” cholesterol. Most of the studies on Chaga are done on human cells and mice, but the signs point out to this mushroom being good for you — inside and out.



Figure 9-Benefits of Chaga Mushroom

Shiitake:- These Mushroom are good for the heart. Shiitakes (Fig. 10) have been shown to lower LDL in mice, and they contain compounds that inhibit the absorption and production of cholesterol in the liver. These nifty mushrooms also contain phytonutrients, which aid in preventing plaque buildup and, as shown in a rat, maintain healthy blood pressure and circulation.



Figure 10-Benefits of shiitake Mushroom

Turkey Tail:- Turkey tail(Fig. 11)mushroom contains a compound called polysaccharide-K (PSK) that stimulates immune system to work effectively. PSK is so effective that it is an approved anticancer prescription drug in Japan. Turkey tail has been known to improve the survival rate of people with keratin cancers, fight leukemia cells, and improve the immune system of people receiving chemotherapy.



Figure 11-Benefits of Turkey Tail

Cordyceps:- It is known for being very stimulating for the Energy . Cordyceps (Fig.12) can help the body to utilize oxygen efficiently and enhance bloodflow and is helpful for athletes or those who actually do regularly work out. This mushroom has been known to not only improve exercise and athletic performance, but also speed up post-workout muscle recovery [33].



Figure 12-Benefits of Cordyceps

Stages of corona virus infection

Phase 1: Cell invasion and viral replication in nose

Both SARS-CoV-2 and SARS-CoV gain entry in the body through a receptor called ACE2. Most commonly known for their role in controlling blood pressure and electrolytes, these receptors are also present in lungs, back of throat, gut, heart muscle, and kidneys. In 2004, researchers in the Netherlands reported that ACE2 receptor cells were not present on the surface layer of cells in the nose and were, not an important site for the SARS-CoV replication for the virus. In SARS, there is rarely any upper respiratory tract symptoms, and viral units are hardly present outside the lungs. This fact then took the focus away from continuing to look for ACE2 receptors in the nose.

Recently, a team of researchers has found the ACE2 receptors on goblet (secretory) cells in and on ciliated (hairy) cells in the nose. Now, scientists have found ACE2 receptors in the mouth and on the tongue, potentially indicating a hand-to-mouth route of transmission. Researchers had also found a plentiful supply of a protease called TMPRSS2, which chemically splits off top of the coronavirus spike to allow the SARS-CoV-2 RNA to enter into the nasal cells. Once it gets inside the cell, the virus's genetic material directs the cell to manufacture millions of new copies of itself.

As a result of it, SARS-CoV-2 can bind 10 times more tightly to insert its RNA into the cell, explains why COVID-19 spreads so rapidly.

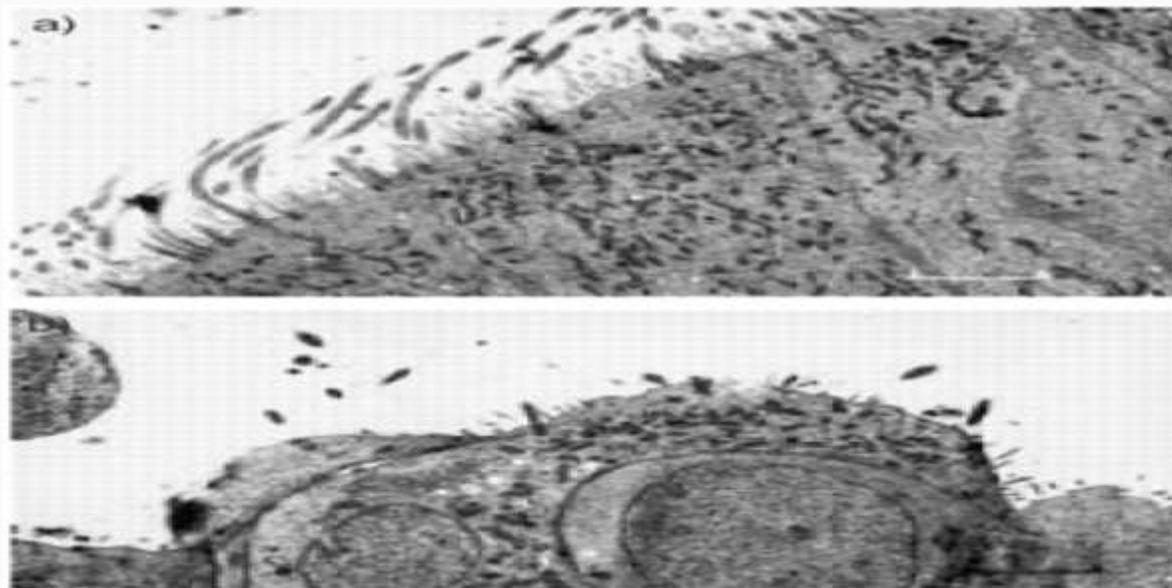


Figure13 : Transmission electron micrograph of nasal epithelium before and after coronavirus inoculation. a) Transmission electron micrograph day 0. This shows a normal tissue with an intact well-ciliated surface and minimal disruption; b) Transmission electron micrograph day 3. This shows an abnormal tissue with severely disrupted cell surface. Marked loss of cilia is seen. Internal scale bars = 2.9 μm

Phase 2: Reproduction in the lungs and Immune system gets attentive

The study in Germany had showed that the viral copying occurs in the upper respiratory tract. Seven out of nine participants listed a cough among their initial symptoms of infection. Difference in the falling numbers of the viral units in Upper respiratory Tract, numbers in the Sputum rose for almost all of the participants. In two individuals with some signs of lung infection, the virus in sputum peaked at day from 10-11. It was present in the sputum up to day 28 in a single person. Among all participants, there was an average of 7 million units in 1 ml (about 35 million units per teaspoon). This amount is about 1,000 times more than that present in

people with SARS. In the lungs, the ACE2 receptor sits on the top of lung cells called pneumocytes. They have an important role in producing a surfactant - a compound that coats the air sacs (alveoli), thus helping maintain enough surface tension to keep the sacs open for the exchange of oxygen and carbon dioxide. As soon as the body recognizes a foreign protein, it mounts the first immune response. One part of the body's immune response - the lymphocytes, begin to produce the first defense IgM-type of antibodies and then the longer term specific neutralizing antibodies (the IgG type).

Phase 3: Pneumonia

Few people infected with COVID-19 have suffered disease and go for hospitalization because of short of breath. Of these individuals, 75% have evidence of bilateral pneumonia. Pneumonia in COVID-19 occurs when parts of the lungs consolidate and collapse. Reduced surfactant in the alveoli from the viral destruction of pneumocytes makes it difficult for the lungs to keep the alveoli open for exchange of oxygen and carbon dioxide.

As part of the immune system response, the white blood cells, such as neutrophils and macrophages, rush into the alveoli. Meanwhile, blood vessels around the air sacs becomes leaky in response to inflammatory chemicals that white blood cells release. This fluid puts pressure on the alveoli from outside and, in combination with lack of surfactant, causes them to collapse. As a result, breathing becomes difficult, and the surface area in the lungs where oxygen transfer usually takes place becomes reduced, leading to breathlessness.

Phase 4: Acute respiratory distress syndrome, the cytokine storm and multiple organ failure may occur

The most common time for onset of critical disease is 10 days, and it can come on suddenly in a small proportion of population of people with mild or moderate disease. Severe acute respiratory distress syndrome (ARDS) is the inflammation stage which gives way to fibrosis stage. Fibrin clots form in the alveoli and fibrin-platelet microthrombi (small blood clots) pepper the small blood vessels in the lungs that are responsible for gas exchange within the alveoli. There is hope that drugs already licensed for anticlotting action in strokes could be helpful for treating this stage. Cytokines are chemical mediators that white blood cells such as macrophages release, and they then engulf infected cells. These cytokines - which have names such as IL1, IL6, and TNF α - have actions which include dilating the vessel walls and making them more permeable.

Immune Response

Adaptive Immune Responses

Immune response of T cells-MERS-CoV and SARS-CoV are β -coronaviruses that can cause deadly lower respiratory tract contaminations and extra-pulmonary manifestations. T cells, CD4+ T cells, and CD8+ T cells especially assume a critical antiviral job by adjusting the defense against pathogens and the danger of creating autoimmunity or overpowering inflammation. CD4+ T cells advance the creation of virus-specific antibodies by actuating T-dependent B cells. Be that, CD8+ T cells are cytotoxic cells and can murder viral tainted cells. CD8+ T cells represent about 80% of all-out infiltrative fiery cells in the pneumonic interstitium in SARS-CoV-infected patients and assume an essential job in clearing CoVs in tainted cells and prompting safe injury. What's more, by contrasting T-cell-deficient BALB/c mice (transduced by ad5-hdp4) with controls and B-cell deficient mice, a few specialists verified that T cells could get by in the contaminated lungs and devastate the tainted cells. The significant job of T cells as oppose to B cells in the control of the development of MERS-CoV disease. A cross-reactive T cell reaction prompts a diminishing in MERS-CoV. However, CD4+ T cells are increasingly defenseless to MERS-CoV contamination. The consumption of CD8+ T cells doesn't influence and postpone viral replication at the hour of contamination with SARS-CoV. Depletion of CD4+ T cells is related to a diminished aspiratory enrollment of lymphocytes and killing immunizer and cytokine creation, bringing about a solid immune mediated interstitial pneumonitis and deferred freedom of SARS-CoV from lungs. Additionally, T cells produce proinflammatory cytokines through the NF-kB flagging pathway. The IL-17 cytokines select monocytes and neutrophils to act on the site of disease with irritation and actuate other downstream cytokine and chemokine falls, for example, IL-1, LL-6, IL-8, IL-21, TNF- β , and MCP-1.

Humoral immune responses

The B cell subsets with phenotypes normal for credulous, non-isotype-switched, memory cells, and antibody-secreting cells collect in CoVs. The antigen incitement of MERS-CoV disease was explained by utilizing the particular 9-mer peptide "CYSSLILDY", which situated at position 437 to 445 inside the area of the S glycoprotein. The arrangement has the most noteworthy B cell antigenicity plot and can frame the best number of connections with MHCI alleles in an electronic simulation. Reports show that the humoral invulnerability is basic to control diligent period of CoV contamination. More antibodies confined from patients who have to endure MERS-CoV contamination have been portrayed, including MCA1, CDC-C2, CSC-C5, CDC-A2, CDC-A10, MERS-GD27, and MERS-GD33 [34].

Strategies to overcome impact of covid 19 with the use of immunity boosters

Ayurveda

The traditional Chinese medicines and Ayurveda since the Vedic period provides with the remedies to lessen the severity of the illnesses caused by microorganisms. It is considered as the world's oldest medical network, which is believed to treat wide array of infections without causing any side effects. It is also well equipped with diverse treatment modules for multifaceted noxious diseases. The ayurvedic specialists and health care professionals have been aware of subsistence of wide range of microorganisms as well as infections that are caused by them. The Ayurveda and Siddha practices originally arose in India and are still extensively practiced for curing plethora of infections. By identification and isolation of bioactive phytochemicals and compounds, their effectual characterization in the medicinal plants might help to combat such deadly infectious diseases. The repurposing of the ancient medicinal plants, provide a new approach for defeating the viral infections and their transmission. At present time of global pandemic, it is vital to stumble on solutions for the long sprint and to prevent further transmission of such a fatal disease. Currently, there are vaccinations developed for the treatment of COVID-19, but still the employment of traditional medicines, which were used in previous epidemic out-break are taken into consideration. Also Chinese herbal medicine (CHM) is one of the greatest herbal medicine modules and it is also an imperative component of traditional Chinese medicines (TCM). These have been suggested to alleviate contagions in the form of warm water extracts for almost 2000 years from about 10,000 herbal medicines since the ancient times.

Plant based therapeutics

Recently, in India, it was suggested by the Ministry of AYUSH to drink Kadha as a booster of immunity and lowering the tenderness and fatigue caused during COVID-19 catastrophe. A Kadha is an extract prepared from less juicy or dry ingredients like spices and herbs by crushing them and dissolving in hot water. The Ministry of AYUSH with its conventional acquaintance has shown an extensive custom of maintenance of nation's health and its participation has augmented manifolds in this COVID-19 pandemic crisis. All ayurvedic healthcare professionals had generally recommend classical ayurveda medicine, however AYUSH-64 a novel formulation prepared by CCRAS provides resistance against malaria and other types of fevers. The decoction of sunthi (*ZingiberofficinaleRoscoe.*), lavanga (*Syzygiumaromaticum*) and maricha (*Piper nigrum*) are recommended to the healthy as well as COVID-19 infected person, as it provides support to the humoral and cell mediated responses and also lowers the air way hyper-responsiveness and nasal congestion. Various ayurvedic products and fatty acids in the form of ghee and oils are implicated in the up-regulation of resistance. The resistance enhanced in a pleiotropic manner and the bioactive compounds participate in various procedures of adaptive as well as innate immune responses. Similarly, the bioactive compound in *Curcuma longa Linn.* i.e. curcumin, is identified to block the cytokine releases, specifically interleukin-1, interleukin-6, pro-inflammatory cytokines and tumor necrosis factor- α and is directed to be consumed with milk. Inhibition of cytokine discharge is one of the prime clinical development associated with experimental modules of flu and other infectious diseases and have also been compared to COVID-19 where similar cytokines storm play an imperative role in transience. Moreover, AYUSH ministry has recommended certain preventive and medicinal plants for prevention and prophylactic of COVID-19 including warm extracts of *Tinosporacordifolia* (advised for chronic fever), *Andrograhispaniculata* (advised for fever and cold), *Cydoniaoblonga*, *Zizyphus jujube* and *Cordiamyxa* (enhancing antioxidant, immune-modulatory, anti-allergic, smooth muscle relaxant, anti-influenza activity) and *Arsenicum album 30* (found effective against SARS-CoV-2, immune-modulator).

Terpenoids

In a recent report by the structure of terpenoid constituents and COVID-19 protease were elucidated from the different databases such as PubChem and Protein Data Bank (PDB). Followed by this, the sophisticated technique of molecular docking was used by employing MVD (molegro virtual docker) software. Nine different terpenes were analyzed for their inhibitory effects. These included thymoquinone extracted from *Nigella sativa*. Molecular dynamic simulations have also shown that thymoquinone can interact with the attachment of the SARS-CoV-2 to HSPA5 substrate-binding domain b (SBDb) to stress cells and thus reduces the possibility of infection. Nevertheless, it is potentially the time to switch thymoquinone from experiments to clinical trials for Covid-19 pandemic. Salvinorin A derived from *Salvia divinorum*, Bilobalide and Ginkgolide A extracted from *Ginkgo biloba*, citral from *Backhousiacitriodora*, menthol from *Mentha*, Noscapine extracted from the family Papaveraceae, Forscolin from *Plectranthusbarbatus* and Beta Selinene from *Apiumgraveolens*. The fallout of this experiment illustrated strapping interactions of the terpenoids in the two enzymatically secluded regions. The fastening of varied amino acids as they were present in the secluded regions of the active site in all 9 compounds was observed and played a significant function in enzymatic catalysis. It was later revealed in the study that terpenoids were able to successfully suppress the virus protease enzyme activity.

Flavanoids

They are present naturally in plants including quercetin, naringin, hesperetin and catechin and they have been analyzed for its activity against plethora of animal viruses such as HSV-1, respiratory syncytial virus etc. The anti-viral activity of flavonoids was reported earlier, to be against severe acute respiratory syndrome coronavirus (SARS-CoV) (Yi et al. 2004). The major mechanism by which they suppress the viral infection is by inhibition of cellular receptor kinases including MAPKs, the serine/threonine-specific protein kinase (Akt) and the phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3-K) and as consequences interferes with cellular signal transduction cascades.

Glycyrrhizin is the chief constituent of *Glycyrrhizaglabra* root and is rich in flavonoids, β -sitosterol, hydroxyl coumarins and glycyrrhetic acid. Observation of imperative anti-SARS-CoV activity is shown by Glycyrrhizin. The anti-SARS-CoV activity of Glycyrrhizin was further confirmed by various studies. More recently, the in-silico experimentation revealed that Glycyrrhizin has similar behaviour against COVID-19 disease and acts as a potential inhibitor to the virus[31].

Role of diet in Corona virus infection

Recently, a discussion had begun on the global management strategy against COVID-19 based on the hypothesis that individual's macro- and micronutrient status combined with antiviral drugs and herbs can be an ally against the infection. The hypothesis is that people's nutritional and oxidative scavenging capacity may be able to provide fundamental data to predict severe and acute pulmonary distress following SARS-Cov2 infection. Consequently, the scientific community had addressed the role of balanced diets, nutritional supplements, and micronutrients, including folk herbal formulations, in reducing hospitalization and the severity of pulmonary impact in COVID-19 by preventing the most serious forms of CoV infection. This led to an animated debate on the potential effectiveness of some vitamins, micronutrients, and traditional Chinese medicines in preventing COVID-19. While current research is still far to assess the suggestions and issues raised by the authors in this short communication, it is undoubtedly true that determining an individual's current metabolic status, including macro- and micronutrients, is an essential factor in defining any individuals' deficiencies, which will need to be addressed urgently through a proper diet, specifically personalized nutritional supplementation, and lifestyle changes.

The scientific community has recently addressed the role of balanced diets, nutrients from raw food and natural food products, and micronutrients, including folk herbal formulations such as Chinese medicine, in reducing hospitalization and the severity of pulmonary impact in COVID-19 by preventing the most serious and exacerbated forms of the infection. The common idea underlying this approach is that COVID-19 has an extraordinary complex spectrum of clinical processes. These includes the individual's ability to limit the severity of the infection's development through immunity, genetics, lifestyle, and environment. Therefore, people's nutritional and oxidative scavenging capacity provides fundamental data to predict severe and acute pulmonary distress following SARS-Cov2 infection. Despite some concerns about the possible toxicity of many xenobiotic compounds retrieved from plant extracts on the market, natural products in the diet may reduce COVID-19 exacerbation following the viral infections. Undoubtedly, COVID-19 remains a complex pathology where there is a significant association with some metabolic disorders, particularly with obesity-related hypertension, usually associated with the elderly and the infection's course. The challenge is to improve the diet and encourage lifestyle to reduce the impact of disease. A recent comment by Young and Zampella addressed twomojor areas of concern, including the discussion of the potential antiviral properties of some herbal products, such as *Withaniasomnifera L.* and some natural derived extracts. The ability of withanolides from *Withaniasomnifera L.* (or ashwagandha), particularly withanoside 5, exhibits very high molecular docking properties and binding affinity against SARS-CoV2 components and makes a promising use of some folk medicines to fight against the clinical consequences of the COVID-19 outbreak [35].

Mucormycosis

Mucormycosis (Fig.13)is type of a fungal infection. It's relatively rare, but very serious. Formally known as zygomycosis, this infection tends to occur most often if you have weakened immunity from an illness or poor health condition. It is important to get treatment. If it is left untreated, mucormycosis can be fatal.

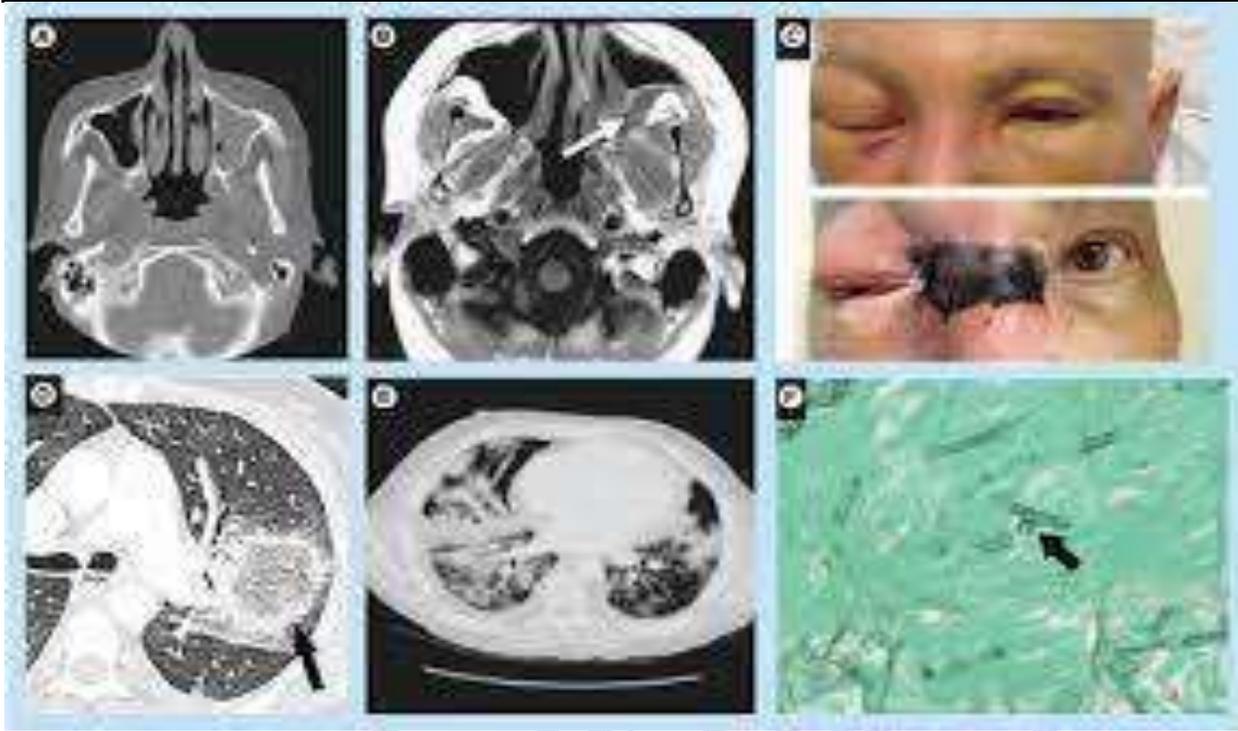


Figure 14-Epidemiology and treatment of Mucormycosis

Symptoms

Mucormycosis presents itself as either a respiratory infection or a skin infection. Symptoms of a related sinus or respiratory infection may include cough, fever, headache, nasal congestion and sinus pain. With a skin infection, mucormycosis can develop within any part of the body. It may initially occur at one site of skin trauma, but it can quickly spread to another area. Must ensure to look out for symptoms such as blackened skin tissue, blisters, fever, redness, swelling, tenderness and ulcers.

Causes

Mucormycosis is caused by exposure to mucormycete mold. These organisms generally occur in leaves, piles of compost, soil and rotting wood. We can contract mucormycosis by breathing in affected mold spores in the air. This is referred to as sinus (pulmonary) exposure. In turn, one may develop the infection in his central nervous system (rarer), eyes, face, lungs, sinuses. The fungus can also infect the skin via a cut or burn (cutaneous exposure). In such cases, the wound or burn ends up becoming the region of infection. While these types of molds can naturally occur in the environment, not everyone exposed to it will get the fungal infection. You may be at an increased risk of contracting this type of infection if you have a weak immune system. Conditions that may increase your risk of infection includes burns, cuts and scrapes, cancer, recent organ transplant, HIV or AIDS, diabetes (especially if it's not being treated properly), surgery.

Diagnosis

People having mucormycosis even don't know that they have this problem. An individual may get diagnosed with the condition upon going to the doctor for a lung, sinus, or skin infection. One should see the doctor for any type of suspected infection. Mucormycosis is diagnosed by looking at sample of tissues in lab. Collection of sample of nasal discharge if you have a suspected sinus infection.

Prevention

Mucormycosis isn't contagious, so a person can't get it from an infected person. Self-care is prevention. If one has a weakened immune system, it's important to keep himself safe outdoors. Wearing a mask and bandaging until they heal properly, will help

prevent fungal infections. One may also consider taking extra precautions during the summer and autumn months, as of an increased amount of the fungal spores in the environment.

Treatment

The first step is receiving intravenous (IV) antifungal cure like Surgical debridement involves cutting away all of the infected tissues. Removing infected tissues is to prevent the infection from spreading further. If you respond well to IV therapy and tissue removal, your doctor will more likely remove your IV and give you oral medications to take. Common antifungal medications include amphotericin B, posaconazole and isavuconazole [32].

Healthy food works as best immunity boosters against COVID-19

According to the WHO, healthy foods and hydration are vital for health. Individuals consuming a well-balanced diet are healthier with a strong immune system and have a very less risk of chronic illness, infectious diseases. Vitamins and minerals are equally vital. Vitamin B is insoluble in water and protects body from infection. Vitamin C protects from many flu-like symptoms. Insufficient vitamin D and vitamin E may lead to severity in coronavirus infection, Vitamin D can be found in sunlight and Mushrooms, and vitamin E can be found in, oil, seeds, and some fruits. Insufficient iron and excess iron can lead to a risk. Foods rich in protein should be at the top of priority list because it has immune properties (immunoglobulin production) and potential antiviral activity. Therefore, in a regular meal, individuals should eat fruits, vegetables, legumes, nuts, whole grains, and foods from animal sources. Around 8–10 cups of water should be drunk daily. Malnutrition is dangerous for patients with COVID-19 and thus proper nutrition must be provided. Fruit juice, tea, and coffee can also be consumed in limited quantities. Too much caffeine, sweetened fruit juices, fruit juice concentrates, syrups, fizzy drinks, and still drinks should be avoided. Unsaturated fats, white meats, and fishes should be consumed. Saturated fat, red meat, more than 5 g of salt per day, and industry processed food should be avoided. Along with diet, physical exercise regularly is important to boost the immune system and should have proper sleep, till every individual gets vaccinated and after vaccination also we have to take care a lot on our immune system.

Conclusions-

This review is on boosting the immune system is a potential resource for the enhancement of patients with COVID-19. Our paper conclude Mushroom can be a good source of immunity to fight against Coronavirus. Further research could focus on other natural immunity boosters over COVID-19. If the possible challenges can be overcome, this can be a great achievement. Finally, nutrition (eg, dietary recommendations) to boost the immune system should be explored and recommended because moreover vaccination, medicine natural immunity is most important to fight against COVID-19 or other severe health issues.

References-

- [1]Wikipedia, April 2020, COVID-19.<https://en.wikipedia.org/wiki/COVID-19>
- [2]Hansa D. Bhargava, MD, April 2020, Coronavirus History.
- [3]WHO, March 2021, The effects of virus varieties on COVID-19 vaccines
- [4] WebMD, Variants of Coronavirus.<https://www.webmd.com/lung/coronavirus-strains#1>
- [5]Navpreet Kaur, Rimaljot Singh, Zahid Dar, Rakesh Kumar Bijarnia, NeelimaDhingra, and Tanzeer Kaur, August 2020, Genetic comparison among various coronavirus strains for the identification of potential vaccine targets of SARS-CoV-2, 89: 104490.
- [6]Jacob Koshy, April 2020, Coronavirus | How does the immune system respond to a coronavirus attack? .article31319716.ece,
- [7]WHO, October 2020, Coronavirus disease (COVID-19).
- [8]Leilani Fraley, RN, MSN, July 2020, What to Know About COVID-19 Diagnosis.

[9]WHO,Coronavirus.https://www.who.int/health-topics/coronavirus#tab=tab_1

[10]National Center for Immunization and Respiratory Diseases (NCIRD), February 2020,Division of Viral Diseases , Human Coronavirus types.

[11]Medical News Today, September 2020, what are the different types of coronavirus?

[12] Mayo Clinic, June 2021,Coronavirus disease 2019 (COVID-19).

[13] TIMESOFINDIA.COM, May 2021, Coronavirus: White fungus cases on rise; Signs, symptoms and who is at risk.

[14]Mohammad Asaduzzaman Chowdhury, Nayem Hossain, Mohammad Abul Kashem, Md. Abdus Shahid, Ashraful Alam, November 2020, Immune response in COVID-19: A review. Volume 13, Issue 11, 1619-1629

[15]Prompetchara Eakachai, Ketloy Chutitorn, Palaga Tanapat, March 2020, Immune responses in COVID-19 and potential vaccines: lessons learned from SARS and MERS epidemic Asian Pac J Allergy Immunol, 1-9. doi: 10.12932/AP-200220-0772.

[16] Q. Li, X. Guan, P. Wu, *et al.* March 2020, Early transmission dynamics in Wuhan, China, of novel coronavirus infected pneumonia N Engl J Med, 382(13):1199-1207. doi:10.1056/NEJMoa2001316

[17]Wikipedia, Immune System, https://en.wikipedia.org/wiki/Immune_system

[18]Cologne, April 2020, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-.How does the immune system work?

[19] Wu Z, McGoogan JM, 2020, Characteristics and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of Report of 72314 cases from the Chinese Center for Disease Control and prevention. JAMA .2020;323(13):1239-1242. doi:10.1001/jama.2020.2648

[20] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, *et al.*, January 2020, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China Lancet, 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.

[21]Samuel Scott Perdue, Britannica, Immune system physiology

[22]Wikibooks, February 2021, Human Physiology/The Immune System.

[23]Khan Academy, The immune system review

[24] Jay Hilotin, March 2020, 3 Types of Immunities: Your best defence vs coronavirus. Gulfnews/World

[25]Felsenstein Susanna, A. Herbert Jenny, S. McNamara Paul, M. Hedrich Christian, April 2020 COVID-19: immunology and treatment options Clin Immunol, 215 (2020), doi: 10.1016/j.clim.2020.108448

[26]The Mushroom Council, Vitamin D. <https://www.mushroomcouncil.com/vitamin-d/>

[27]Natalie Olsen, R.D., L.D., ACSM EP-C, Tiffany La Forge, April 3, 2020 , 6 Mushrooms That Act as Turbo Shots for Your Immune System

[28]Nimesh Singh, Bharat Suthar, Abhay Mehta, Neeti Nema and Archna Pandey, 2020, Corona Virus: An Immunological Perspective Review, DOI: 10.23937/2378-3672/1410050

[29]Ahmed Zainul Abideen, FazeedaBinti Mohamad, MohdRohaizat Hassan ,October 2020,Mitigation strategies to fight the COVID-19 pandemic—present, future and beyond, 2586-940X

[30]Balaji Krishnakumar, Sravendra Rana, June 2020,COVID 19 in INDIA: Strategies to combat from combination threat of life and livelihood. doi.org/10.1016/j.jmii.2020.03.024 ,389-391

[31]Kanika Khanna, Sukhmeen Kaur Kohli, Ravdeep Kaur, Abhay Bhardwaj, Vinay Bhardwaj, Puja Ohri, Anket Sharma, Ajaz Ahmad, Renu Bhardwaj, and Parvaiz Ahmad, 2020 October 3,Herbal immune-boosters: Substantial warriors of pandemic Covid-19 battle, doi: 10.1016/j.phymed.2020.153361

[32]KristeenCherney, Mucormycosis, Healthline

[33]Tiffany La Forge, 6 Mushrooms That Act as Turbo-Shots for Your Immune System, Healthline

[34]Nimesh Singh, Bharat Suthar, Abhay Mehta, NeetiNema and Archna Pandey, May 22, 2020, Corona Virus: An immunological perspective review, International journal of immunology and immunotherapy, 10.23937/2378-3672/1410050

[35]Amin Gasmi, Salvatore Chirumbolo, Massimiliano Peana, Sadaf Noor, Alain Menzel, Maryam Dadar & Geir Bjørklund, February 2021, The Role of Diet and Supplementation of Natural Products in COVID-19 Prevention,https://doi.org/10.1007/s12011-021-02623-3

