General Article

Human immune response: A review study in the background of COVID-19 pandemic

Jayanta Talukdar[1*], Pallabi Nath[2]

[1]Lecturer, Department of Forensic Medicine, North Eastern Institute of Ayurveda and Homeopathy, Shillong, INDIA.
[2]Assistant Professor, Department of Political Science, Puthimari College, Kamrup, Assam, INDIA.
Email: jtalukdar84@gmail.com

Abstract

Background: Immunity is the state of being able to resist a particular infection or toxin by the host. Pathogens when gain entry to the body, the body produces an immune response against it in an attempt to eliminate it. Depending on the nature of the pathogen and health status of the host, immune response is varied and may succeed or failed to eliminate the pathogen. Human immune responses are of three types innate immunity, acquired immunity and passive immunity. When the Covid 19 pandemic has devastated the whole world and no proven effective drug has still not been found, the human immune response against it, is the area where the health researchers are now mainly emphasizing. Understanding of immune response against the virus is also instrumental in vaccine development. In the present study, attempt has been made to understand human immune system as a whole and against Covid-19.

Key words: Immunity, Covid-19, Pandemic etc.

[*]**Address for Correspondence:**
Dr Jayanta Talukdar, Lecturer, Department of Medicine, NEIAH, Shillong, INDIA.
Email: jtalukdar84@gmail.com

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INTRODUCTION

The Covid-19 pandemic that has put the mankind in an unprecedented crisis and is caused by severe acute respiratory syndrome coronavirus-2(SARS-CoV-2),first detected in December 2019 in Wuhan, China.[i] Afterward the disease has spread every corner of the world ,currently second wave of the disease has hit different countries hard, Specially India causing devastating situation with increased mortality as well as infectivity rate[ii] Though the vaccine has been developed against the virus, considering the continuous mutation which is the characteristic of the virus,things yet very far from settlement. The new agent belongs to a large family of coronaviruses known since decades to mankind. These viruses are zoonotic pathogens, at times infect humans with further spread via human to human transmission. The family has a notorious historical background being responsible for major outbreaks in the past including severe acute respiratory syndrome (SARS-CoV) in 2002 and Middle East respiratory syndrome (MERS-CoV) in 2012.[iii] Better understanding of immunopathogenesis of covid 19 is must to formulate any treatment or preventive protocol against it. In this piece of work,authors has made an attempt to discuss the various aspects of human immune response to SARS CoV-2 along with the viral reaction against it.

Objectives-

1. To understand the human immune system in general
2. To understand the mechanism of SARC Cov-2 pathogenesis
3. To understand how human immune response acts against the virus

METHODOLOGY

Data are collected from secondary sources using different internet based search engine including scopus, Web of science, Pubmed, Web of John Hopskin University etc and various Text book. Then data are reviewed and analysed.

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Human Immune system- The immune system confer body the ability to resist almost all types of organism or toxins that tend to damage the tissues. Our immune system can be divided into three categories. They are mainly innate immunity(rapid response),acquired immunity(slow response) and passive immunity.[iv] The inborn innate immunity results from general process, rather than from the process directed against specific pathogen. Such innate immune system involves one of the first line of immune response. The innate immune system comprises of organs including the skin,mucous membrane which acts as a barrier against invasion by pathogen. It also includes group of cells such as tissue macrophages, neutrophils, natural killer cell etc. Innate immune response are non specific, and can attack any foreign pathogen, tumour cells and even infected cell.[v-vi] Adaptive immunity on the other hand which is mostly concerned with detailed and more specific action against invading microbes, toxins. It is much controlled and highly specified form of immunity . This acquired immunity is again two types namely Cell mediated and Humoral immunity. Cell mediated immune response involves the activation of cells that could lead to destruction and elimination of the foreign body. The T lymphocytes are responsible for the cell based immune responses. For their action against any antigen, T-lymphocytes need antigen presentation by antigen presenting cell. The presentation involves action of proteins that culminates in formation of histocompatibility complex with the antigenic material. Accordingly, the presentation of histocompatibility complex class I (MHC I) leads to activation of Cytotoxic T cells.These cells are significant in cell based immune responses. In essence, upon viral infection, the viral proteins are presented on the MHC I which in turn activates the cytotoxic T cells there by mounting a response against the virus. Humoral immune response is associated with B lymphocytes activation and subsequent release of specially produced antibodies. In terms of antigen presentation, the proteins of the invading agent are presented on MHC II thus leading to activation and subsequent proliferation of B-cells. The B cells continue to produce antibodies otherwise known as Immunoglobulins and facilitation of Antigen-antibody complex formation. This complex formation is paramount to elimination of the invading agent as the antibodies are specific towards the consequent antigen. At the center of all these activations in the adaptive immunity are the Helper T-cells. They are referred to as architects of all immune responses. The B-cells also develop into specialized Memory B-cells having the tendency to store the memory of the antigen which initially caused the immune response and subsequent production of the specified Antibodies .*Passive immunity* is again two types and they are natural immunity which we receive from our mother and artificial immunity that we receive from medicine in form of antibody.[viiviiiix]

OVERVIEW OF CORONA VIRUS: Coronaviruses are a group of highly diverse, enveloped, single-stranded RNA viruses in the family of Coronaviridae having crown like appearance. First discovered in the 1960s, they can be further classified into four main genera: *Alpha*.beta,gamma and delta corona viruses.[x] Currently, there are seven strains of corona viruses that are known to infect humans, including the recently identified novel strain SARS-CoV-2. Other strains that infect human are HCoV-229E, HCoV-OC43, HCoV-NL63, HCoVHKU1, SARS-CoV(beta corona viruses that causes Severe Acute Respiratory Syndrome or SARS in 2002-2003), and MERS-CoV(beta corona virus that causes Middle East Respiratory Syndrome or MERS in 2012). SARS-CoV-2 belongs to the genus of Betacoronavirus, and based on evolutionary analysis,it is found that they are most similar to the SARS-like coronavirus from the Chinese horseshoe bat, with a nucleic acid homology of 84%. SARS-CoV-2 also has 78% similarity with SARS-CoV and 50% with MERS-CoV, at the nucleic acid level.[xi]

IMMUNE RESPONSE TO THE VIRUS: The host immune response which may varied from person to person are always associated with invasion of SARS-CoV-2. The spike glycoprotein (S protein) on the viral envelop binds to its receptor, angiotensin-converting enzyme 2 (ACE2), on the surface of human cells. ACE2 receptors are abundantly present on the surface type 2 pneumocyte of lung alveoli.[xii] On one side, the virus has a concave surface with a ridge. It makes a larger binding interface to make more contacts with receptor and that is the reason of higher affinity of SARS-CoV-2 S protein binding to ACE2 which is 10 to 20 times higher than that of the SARS S protein, suggesting that SARS-CoV-2 might transmit more readily from person to person.[xiii] It is transmitted through respiratory droplets from coughing and sneezing. It enters our nasal system by inhaling and starts replicating. The spike protein present on the surface of COVID-19 gets pinched inside the host cell binding to the ACE2 receptor. Here, the protease furin present in the host cell plays a vital role for the virus to enter by cleaving the S protein which was absent in SARS-CoV.[xiv] Innate immunity is the first line of defence against virus invasion. Viral infection of mammals activates intracellular pattern recognition receptors that sense pathogen associated molecular patterns, such as double-stranded RNA or uncapped mRNA. The recognition of pathogen associated molecular patterns results in subsequent cytolytic immune responses, mainly through the type I interferons (IFN) and natural killer cells.[xv] Acquired immunity also plays an important part in viral clearance via activated cytotoxic T cells that destroy

virus-infected cells and antibody-producing B cells that target virus specific antigens. Patients with COVID-19, especially those with severe pneumonia, are reported to have substantially lower lymphocyte counts and higher plasma concentrations of a number of inflammatory cytokines such as IL-6 and tumor necrosis factor (TNF) Studies reported that CD4+ T cells, CD8+ T cells, and natural killer cells were reduced in severely ill or patients who died. compared with those with mild disease symptoms. Notably, the proinflammatory subsets of T cells, including IL-17-producing CCR4+ CCR6+ CD4+ (T-helper 17 or Th17) cells and perforin and granulysin-expressing cytotoxic T cells were increased, which could be partly responsible for the severe immune injury in the lungs of this patient. [xvi]The anti-viral immune response is crucial to eliminate the invading virus, but a robust and persistent anti-viral immune response might also cause massive production of inflammatory cytokines and damage to host tissues. The overproduction of cytokines caused by aberrant immune activation is known as a cytokine storm. In fact, in the late stages of coronavirus disease, including SARS, MERS, and COVID-19, cytokine storms are a major cause of disease progression and eventual death. Notably, patients admitted to the intensive care unit (ICU) had higher plasma concentrations of IL-2, IL-7, IL-10, granulocyte-colony stimulating factor, IFNγ-induced protein-10 (IP-10), macrophage chemoattractant protein-1, macrophage inflammatory protein 1α, and TNF compared to those not admitted to the ICU. Two other studies also showed that plasma IL-6 concentrations were above the normal range in patients with severe symptoms of COVID-19 compared with healthy individuals and those with milder symptom. Increased proimflammatory response leads to immune mediated injury to the lung parenchyma, causing disruption of gaseous exchange across alveolar wall. The characteristics of cytokine storm, including hypercytokinaemia, unremitting fever, cytopenias, hyperferritinaemia, and multi-organ damage, are commonly seen in seriously ill patients with COVID-19. It is suggested that alveolar macrophages expressing ACE2 are the primary target cells for SARS-CoV-2 infection. These activated macrophages may play an important part in cytokine storm during COVID-19. Thus, early identification and appropriate treatment of this hyperinflammatory status is important for reducing the mortality of patients with COVID-19. [xviixviiixix]

ESCAPE STRATEGY ADOPTED BY VIRUS FROM IMMUNE RESPONSE: During the millions of years they have coexisted with their hosts, viruses have learned how to manipulate host immune control mechanisms. In brief, most mechanisms rely on the inhibition of innate immune responses especially interferon recognition and signaling. Interferon is the first key antivirus response of the host. *For* adaptive immune evasion, antigen presentation via MHC class I and MHC class II was downregulated when the macrophages or dendritic cells were infected with MERS-CoV, which would markedly diminish T cells activation. Antigenic variability in viruses also help them to escape from the host immune response. Evidences shows that coronaviruses are also adapted to escape immune detection and down regulate human immune responses. The longer incubation period is probably due to their immune evasion properties, efficiently escaping host immune detection at the early stage of infection.[xxxxi]

DISCUSSION

Based on limited understanding of pathogenesis of Covid -19 different treatment module are being tried but till now no clinically confirmed antiviral drug has been introduced for SARS-CoV-2 infection. However fortunate development is vaccine which has been showing lots of hope. We should have mass vaccination drive so that to cover maximum populations.On the other hand boosting of immune system is definitely the most critical step stop an infection in its track, before it has established a foothold in the body. Healthy foods as well as hydration are vital for efficient immunity. People consuming a well balanced diet are healthier with a strong immune system and have less risk of chronic illness, infectious diseases. The importance of vitamins and minerals are proven . Vitamin C protects us from flu like symptom. Lack of vitamin D and E can make us more prone to infection of viral disease. Zinc is necessary for maintaining our immune system. Food rich in protein should be on the top priority. Along with diet, physical activity is another factor. People should be active and do physical exercise regularly to boost the immune system and should have proper sleep. Ministry of AYUSH has prescribed some natural way to improve immunity. These can be more vital and useful alternative preventive measure against covid 19. Then again the cytokine storm is an major area of concern in treating covid 19 patient. As we have evidences that excessive cytokine secretion is responsible for lung injury, different immunomodulators are being tried.

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