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A Relationship between Sleep Cycle and Immunity against COVID-19 Infection

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Abstract

The outbreak of coronavirus in 2019 has devastated the world and led to a global pandemic. The infectious disease COVID-19 which is caused by severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) emerged from a zoonotic reservoir. The data suggest that the recent outbreak has similar genetic emergence to those of SARS and MERS. The patients are assisted with major breathing problems and the rapid transmission results in the apocalypse for humans. To arrest the viral infection, immunity is the preliminary key of the individual for defending against the pathogen. The production of T cells plays a crucial role in the immune system response to the virus. Therefore, sleep and the circadian system strives for an impact on immune functions. It has further reinforced the major and specific role of sleep that takes part in boosting the immune system. In this review, we provide an emphasis on pathogenicity, adaptive immunity in the terms of enhancing the system and also the role of the sleep cycle in context to the COVID-19 infection.

Keywords: COVID-19; Immunity; Cytokines; Sleep cycle

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Introduction

Viral infections generally affect the upper or the lower respiratory tract. Study has shown respiratory infections can be classified by the causative virus, eg. Influenza, they are generally classified clinically according to symptoms which can cause respiratory syndrome like the common cold, bronchiolitis, croup, pneumonia. Although specific pathogens commonly cause characteristic clinical manifestations which could cause different symptoms like rhinovirus typically causes the common cold, Respiratory Syncytial Virus [RSV] typically causes bronchiolitis. The severity of viral respiratory illness varies widely; recently a viral disease is spreading around the globe causing a global pandemic which comes from the family of Coronaviridae [1].

At the end of 2002, an unfamiliar agent was found in the province of southern China, Guangdong. The infectious disease was named as a Severe Acute Respiratory Syndrome (SARS) as it was severe and transmissible from human to human. The illness mainly has flu-like symptoms, which began with high fevers, dry cough and shortness of breath which gradually proceed to pneumonia within 3-4 days. It was the first pandemic of the 21st century which occurred in South-East Asia, North America and Europe. The accelerated spread of the SARS-CoV that causes SARS has led to 28 countries reporting cases. The mortality rate greatly varied with age, it was high in elderly people and relatively affected a few children[2]. After a decade, in June 2012 another highly pathogenic virus emerged in the Middle Eastern countries [3], named Middle East Respiratory Syndrome (MERS) caused by MERS-CoV where a man died due to pneumonia and renal failure in Saudi Arabia. The virus was isolated from his sputum [4]. This virus was directly transmitted from dromedary camels to humans but causes little to no disease in the animals [5]. The virus continued to develop and flow to other countries because of the transit of infected persons [4]. The authorities of Saudi reported 1386 total cases of which 587 died as of April 18, 2018. MERS remains a major public concern due to a high mortality rate and lack of vaccine [6]. In late 2019, the world witnessed another outbreak, emerge in the Central city of China, Wuhan. The disease was designated as Corona Virus Infectious Disease (COVID-19) caused by the novel coronavirus which was denoted as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) [7]. Deliberately the virus has spread over the world which imposed major public health. Soon it was declared to be a pandemic by WHO[8]. The seventh

coronavirus is the SARS-CoV-2 which is known to infect humans. Including MERS-CoV and SARS which causes severe disease, on the other hand, HKU1, NL63, OC43 and 229E are likely correlated with mild symptoms[9]. Coronaviruses are globally found in humans as well as in animals. The virus is classified in the family Coronaviridae and the order Nidovirales. They can be grouped into four genera, including α-/β-/γ-/δ-Coronavirus. The α and β can infect only mammals, while the γ and δ primarily infect birds [8]. So far, the diversity of coronavirus has been detected in bats. In the case of genome, SARS-CoV-2 shows similarities to other beta coronaviruses that are found in bats. About 96.2% SARS-CoV-2 is identical to a bat CoV RaTG13, also 79.5% to SARS-CoV [8]. There are two notable features of SARS-CoV-2 First is based on the structure and biochemical experiments, it was found that SARS-CoV-2 upgrade itself to the human receptor ACE2 for its binding. Secondly, the presence of, functional polybasic cleavage site at the S1-S2 boundary through the infusion of 12 nucleotides, which also led to the predicted addition of three O-linked glycans around the site [9]. SARS-CoV-2 infection occurs through the transmission of virus-containing droplets and aerosols from an infected individual. The invasion of the droplets gives rise to the disease which can occur with fever, non-productive cough, and in severe cases, it leads to acute respiratory syndrome and even kidney failure. Sometimes the infection can be disastrous. On the other hand, about 80% of the patients experience asymptomatic or mild symptoms [10]. Several researches are presently inspecting the possible response of the immune system during this infection. In most of the scenarios it has shown that the patient develops an abandoned immune response, which is caused by hyper activation of macrophages and monocytes. As a result, the total number of lymphocytes decreases and thereby neutrophils, IL-6 increases. Above all for cell-mediated immunity, the virus-specific T-cells and for humoral immunity, B-lymphocyte plays a key role in the adaptive immune response for all viral infections. Truly, the Helper T lymphocyte can devote to the aggravation of the inflammatory response by activating the Th1/Th17 while the production of specific antibodies is provided by B-lymphocytes for SARS-CoV-2 which is aimed to neutralize the virus. It is recognized that the first line of defence during viral infection is provided by the prior production of immunological memory (IgM) and high affinity immunoglobulins (IgG) for long term immunity. Consequently, the IgM detection in the serum level tells a recent exposure to the virus, and the exposure that occurred several days before is suggested by the detection of IgG in the serum [10]. Moreover, many evidences showed that for the recognition and killing of infected cells which is invaded in the lungs of infected individual-specific T-cell responses against SARS-Cov-2 is important [11]. T-cell is a type of white blood immune cell involved in bringing an adaptive immune response. The two types of T-cells, CD8+ and CD4+ T-cells play a vital role in neutralizing the foreign virus. CD8+ T-cell can directly kill the infected cells and also recruit other immune cells by cytokine signalling. On the other hand, CD4+ T-cell can recruit B-cells [12]. The main target of vaccines and therapies is the viral spike glycoprotein which is especially responded by CD4+. In most of the cases, the activated T-cell help in the recovery by mounting an immune attack on the infected cells and providing an immunological memory. Evidence suggests that a high degree of T-cell activation in response to SARS-CoV-2 infection can make the immune system robust which can be mounted either during COVID-19 [13]. Many findings showed that sleep has the potential to enhance the efficiency of T cell responses. The greatest solution to boost our immunity and tackle the novel coronavirus is sleep which at the same time can help to strengthen our immune system. It is a physiological process that has regulatory properties. Several studies have demonstrated that total sleep deprivation modifies various components of the immune system such as the CD4+, CD8+ and NK cells. It has been suggested that both sleep and immune system are connected through a bidirectional communication [14]. The endocrine milieu during sleep supports the interaction of APC and T-cells, which enhance the production of IL-12, the balance of Th1/Th2 cytokine, the increase in Th cell proliferation and also the facilitation of naïve T-cells to migrate towards lymph nodes [12]. Slow wave sleep and the circadian system act together to generate a pro-inflammatory hormonal milieu. The change in hormone supports the early steps to generate an adaptive immune response in the lymph node. Therefore, sleep enhances the Th1 response which boosts the production of B cells and strengthens the bond between the natural killer cells and infected cells which results in the elimination of infectious agents (**Figure 1**).

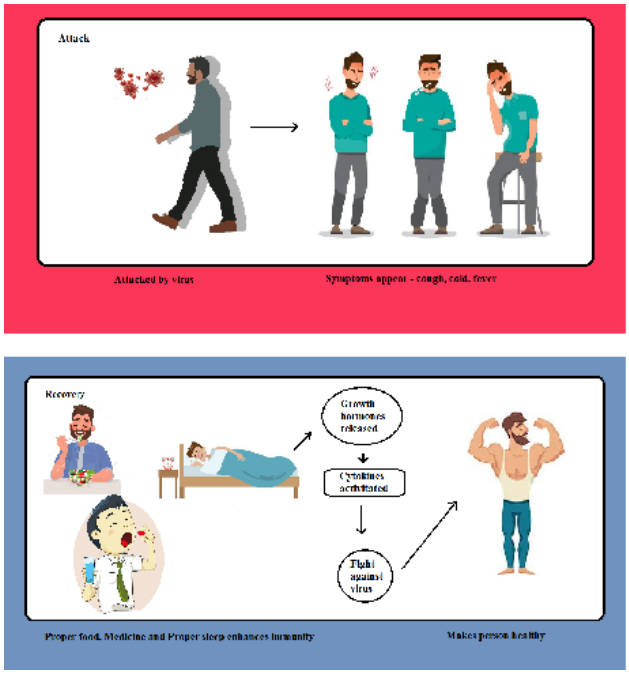

Figure 1: Graphical representation.

Pathogenesis of SARS-CoV-2

The genome is 29,903 bp for SARS-CoV-2 (ssRNA) coronavirus which was submitted to NCBI on 17 January, 2020 from Wuhan, China. Study showed that the virus causing COVID-19 disease is a SARS-like coronavirus that was previously reported in bats, Wuhan [15].

The SARS-CoV-2 virus is composed of four different proteins (envelope, spike protein, membrane and nucleoside) and an RNA strand. The virus is enveloped in shape and is covered with spikes (S) protein which is important for CoV [16]. The S protein helps the receptor to bind and membrane fusion. It is crucial for determination of the tropism of the host and capacity of the transmission of the virus. The S protein is further functionally divided into S1 and S2 domains. S1 domain is responsible for the binding of the receptor and for cell membrane fusion S2 domain is responsible [15]. Angiotensin-Converting Enzyme 2 (ACE2) was known as a cell receptor for SARS-CoV which is similar to SARS-CoV-2 [15]. According to the research SARS-CoV-2 uses ACE2 as an entry receptor [17]. It binds with hACE2 with approximately 10 to 20 fold of affinity higher than S protein of SARS-CoV. It indicates SARS-CoV-2 also shares the same life cycle with SARS-CoV [18].

The spikes (S) of SARS-CoV-2 bind to receptors of human ACE2 through its receptor binding domain (RBD) which is proteolytically activated from human proteases. But according to the study, unlike SARS-CoV, the entry of SARS-CoV-2 cell is pre-activated by pro-protein convertase furin, which reduces its dependency on cell proteases which is targeted, which is further required for entry. The RBD hidden in the spike is potential to allow SARS-CoV-2 which maintains the efficient cell entry by evading immune surveillance. As the virion is bonded with ACE2 protein, another TMPRSS2 protein helps the virion to open the spike protein while cleaving the membrane which allows the virion to enter in the cell (**Figure 2**). The virion then releases the RNA strand which is then translated into protein and gives rise to more RNA strands. Now when the cell is in the developing stage, one strand of the virion enters the Golgi bodies and evolves new virions which burst out from the cell where membrane and envelope proteins are present. In this way one virion particle has the ability to give rise to several hundred new virions which are equally capable of infecting new cells [19].

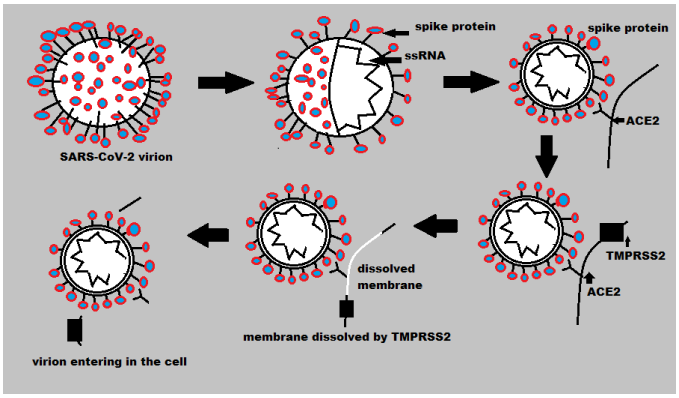

Figure 2: Entry mechanism of SARS-CoV-2 inside the cell with the help of TMPRSS2 protein by binding the spike protein with ACE2 present in the cell.

According to reports, the transmission of SARS-CoV-2 from human-to-human is possible when the individuals are in the stage incubation or when the individuals are showing symptoms, while some individuals are contagious but remain asymptomatic and are still capable of transmitting the virus [20]. Transmission occurs when the respiratory droplets of exhaled virus released from an infected individual are inhaled (within 1 meter). The virus is also capable of remaining airborne for a prolonged period. Transmission can also occur from infected surfaces, such as skin-to-skin, and through coming in contact with infected inanimate objects then mediating it through the nose, mouth and eyes [21]. SARS-CoV-2 is reported that it can survive for several hours on sterile sponges and contaminated metal surfaces [22]. The latex surgical gloves, if not handled carefully or disposed after handling an infected individual, increases the opportunity for transmission. The virus is carried by the dust when inhaled and could transport into tracheobronchial regions and deep alveolar regions, and increases the infection chances [23].

Symptoms and Diagnosis

Usually, after the SARS-CoV-2 infects a person, the COVID-19 symptoms start to appear after an incubation period which is of 2-14 days, with an average period which is of 5-6 days. Generally, the COVID-19 onset is marked by symptoms like dry cough, fever, muscle pain and fatigue, some other symptoms also accompany these symptoms like lymphopenia, headache, and dyspnoea. Some uncommon symptoms also include production of sputum and hemoptysis [24]. According to the reports patients infected with COVID-19 also showed symptoms of diarrhea or nausea. After the infection begins, patients may start to face difficulties in breathing, which could also result in Acute Respiratory Distress Syndrome (ARDS) by the day 8-9. The patient may start to experience some abdominal distress, pain and pneumonia, as the patient's condition worsens and is also accompanied with failures of other functions depending on their health status and immune system [25].

In Most cases, patient's age ranges from 30-79 years of age. The individuals with coexisting medical conditions, such as diabetes, hypertension and cardiovascular diseases are more prone to get infected with SARS-CoV-2 [23]. A large case study indicated that the patients with coexisting medical conditions have less chance of survival as the case-fatality rate is elevated among those patients. Although in most of the patients infected with SARS-CoV-2 pneumonia is present, few cases also complained of pleuritic chest pain [25].

According to the study, as the patient's symptoms get severe, patients are classified as mild, severe, and critical types. Mild patients had non-pneumonia or mild pneumonia. Some can be asymptomatic also. Severe patients had dyspnea, blood oxygen saturation less than 93%, respiratory frequency less than 30/min. critical patients had several conditions such as, respiratory failure, multiple organ failures [26] (Table 1).

Clinical types	Symptoms
Mild	Non-pneumonia or mild pneumonia, asymptomatic.
Severe	Dyspnea with blood saturation oxygen level less than 93%, respiratory frequency less than 30/min.
Critical	Respiratory failures, multiple organs functions failures.

Table 1: Symptoms of various clinical types.

The SARS-CoV-2 pathogenesis leads to pneumonia and acute respiratory disorders like symptoms which seems to be complex and is held responsible for initiation of an excessive particular immune reaction in the hosts. Most patients infected with COVID-19 have similar symptoms, such as fever and influenza like features. However, some patients start to develop ARDS rapidly and multiple organ failure, depending on the individual patient's immune system and coexisting medical conditions [27]. Reports of clinical examination reveal a reduced number of peripheral lymphocyte count and lymphocytopenia d to reduction of CD4T and CD8T cells. ACE2 is responsible for regulating blood pressure, and an attack of SARS-CoV-2 on ACE2 receptors present in endothelial cells results in coagulation, hypotension, cardiac injury, kidney dysfunction and many more secondary infections [20].

Immunity against Viral Infection

The viable antiviral reactions of the host immunity, including the generation of different proinflammatory cytokines, the activation of T cells, CD4 and CD8+ T cells, are basic for controlling the viral replication, restricting the spread of infection, inflammation and cleaning the contaminated cells [28]. As the strongest and specialized antigen-presenting immunity.

The viable antiviral reactions of the host immunity, including the generation of different proinflammatory cytokines, the activation of T cells, CD4 and CD8+ T cells, are basic for controlling the viral replication, restricting the spread of infection, inflammation and cleaning the contaminated cells [1,28]. As the strongest and specialized antigen-presenting cells, dendritic cells play a necessary role in linking up innate and adaptive immunity by stimulating the activation of T-lymphocytes and B-lymphocytes. The mature dendritic cells can adequately activate T cells in the central link of association, regulation and maintenance of immune responses, whereas the immature dendritic cells have the ability of strong migration. In such a way, once the maturation process of dendritic cells is blocked, it precisely affects the initiation of next adaptive immune response [29, 30]. Adaptive immune response starts when memory T lymphocytes perceive viral antigens introduced by dendritic cells. Dendritic cells are organized underneath the respiratory tract, including the airway epithelial tissue, lung parenchyma, and the alveolar spaces of the lungs [31], where they continually screen for invading pathogens by their dendrites that are stretched out to airway lumen through the tight junctions of epithelial cells. Considering the infection with influenza virus, the conventional dendritic cells (cDCs) migrate from lungs to lymph nodes, where the cDCs present antigen derived from the virus to T lymphocytes [32,33]. The viral protein is degraded into immune peptides by the self-infected dendritic cells. The immune peptides are transported to the endoplasmic reticulum from the cytosol and they bind with Major Histocompatibility Complex (MHC) class I molecules. For the recognition by virus specific CD8+ cytotoxic T cells (CTL), MHC class I is transferred to the cell membrane. Nonetheless, the endosomes in which viral proteins degrade are associated with the MHC class II molecule. Therefore, for the recognition by CD4+ T helper (Th) cells, these complexes are presented on the cell membrane. This process may prompt B cell proliferation and development to antibody producing plasma cells [34]. The known MERS-CoV and SARS-CoV that can cause lethal lower respiratory tract infection and extra pulmonary manifestations [35,36]. T cells, CD4+ T cells, and CD8+ T cells especially play an important antiviral role by adjusting the clash against pathogens and the hazard of creating autoimmunity or inflammation [37]. Similarly, in any viral infection or influenza viral infection, T cells and B cells play a significant role in adaptive immunity in which T cells are known as CD4+ T and CD8+ T cells. Moreover, CD8+ T cells separate into cytotoxic T lymphocytes (CTLs), which produce cytokine and effector molecules which restrict viral replication and kill infected cells. Besides, type I IFNs, IFN-γ, IL-2, and IL-12 also help CD8+ T cells to differentiate into CTLs [38,39]. Therefore, T cells are crucial for the restriction of viral infection. Upon infection with the virus, CD8+ T cells are activated by dendritic cells which migrate from lungs to the T cell region of the lymph nodes, leading to proliferate and differentiate T cells into CTLs [40]. Simultaneously targeting the virus-infected cells, cytotoxic granules are produced by CTLs that contain molecules like perforin and granzymes (e.g., GrA and GrB). The target cells bind with perforin which results in the formation of pores on the cell membrane to bolster passive diffusion of granzymes and thus induce apoptosis. It has also been noticed that virus replication is restricted by GrA through cleavage of viral and host cell proteins that are involved in protein synthesis [41,42]. Also, CTLs have the capacity to promote apoptosis by expressing cytokines, such as TNF, FASL, and TRAIL, which mobilize death receptors in virus-infected cells [43]. Post-infection dendritic cells and virus-specific CTLs disperse in blood, lymphoid organs, and the site of infection [44]. These memory CTL cells are quick in response to secondary virus infection, and the activation and differentiation process derived during first infection affects their efficiency during a secondary infection [45]. Another important type of immune cell is CD4+ T cell that is involved in adaptive immunity against viral infection. CD4+ T cells characterize into Th1 cells in response to viral infection, confer to their stimulators, including co-stimulatory molecules, antigen and cytokines secreted by dendritic cells, epithelial cells, and inflammatory cells [46]. Antiviral cytokine, such as IFN-γ, TNF, and IL-2 are expressed by Th1 effector CD4+ T cells, and also activate alveolar macrophages [47,48]. The clearance of viral infection is initiated by IL-2 and IFN-γ produced by Th1 cells which regulate CD8+ T-cell differentiation [49,50]. Moreover, CD4+ T cells are also able to comprehend into Th2, Th17, regulatory T cells, follicular helper T cells, and even as killer cells [51]. IL-4 and IL-3 are produced by the binding of Th2 cells to virus derived MHC class-II associated peptides by antigen presenting cells which promote B cell responses mostly. In addition, it has been noticed that Th17 and regulatory T cells are associated in regulating cellular immunity against viral infection [52]. B cells serve a definite, pioneer centre-derived memory population that serve as an extensive therapeutic target for the advancement of humoral immunity and interruption of autoimmunity [53]. Considering the data from recent studies, it has suggested that SARS-CoV-2 infection can lead to immune deregulation through affecting the subsets of T cells. The former review implies that the total count

of lymphocytes and the subset of T cells are reduced in patients with SARS CoV infection [37,54]. The momentous alleviation of T cells is noticed in COVID-19 and more definite in severe cases. Comparing the patients, it has marked that the level of helper T cells, regulatory T cells, and suppressor T cells are remarkably below the normal level in severe patients than that of the non-severe ones. It was already mentioned that the T cells are crucial for the maintenance of the immune system with suppressing the activation, proliferation, and proinflammatory function of most lymphocytes including CD+4 T cells, CD+8 T cells, NK cells, and B cells [55,56]. Additionally, the percentage of naive T helper cells strengthen while the percentage of T memory helper cells and likewise CD8+ cytotoxic suppressor T cells decreases in severe COVID-19 [57,58]. The symmetry between the primary T cells which have not encountered virus before and memory T cells is fundamental for deliberating the capable immune response [59]. The reduction of Natural killer cells and B cells are also seen in COVID-19 in addition to the T cells.

Impact of Sleep Cycle in Immunity

We, humans, are diurnal creatures. We spend about one-third of our life being asleep. Sleep is significantly needed by all higher life forms which include us and absence of sleep has physiological consequences which could be serious [60]. Most adults take a consolidated 7-8 hours sleep during the night. The main reasons we sleep at night are partly because the environment is quiet and falling asleep is quite easy when the temperature of the core is falling low which is during evening and night as compared to falling asleep when the core temperature is high or is rising that is during morning and afternoon is difficult [61,62]. To sleep at other times is possible, as evident by the lifestyle that night workers adapt but, even if the environment is quiet, daytime sleep is more fragmented and shorter. A good sleep removes the feelings of fatigue [63]. The amount of sleep consists of different sleep stages. It is termed as sleep architecture which refers to structural organization of sleep [60]. There are mainly two types of sleep Rapid eye movement sleep (REM) and Non-Rapid eye movement sleep (NREM). NREM is further divided into 4 stages: stage 1, 2, 3 and 4. Each has a unique characteristic representing relative depths including variation in brain waves pattern, muscle tone, eye movement [64]. Over the course of the sleep cycle, NREM and REM sleep alternate cyclically. A sleep normally begins with a small period of NREM stage 1 which is progressed towards stage 2, followed by stage 3 and 4 then to REM. However, cycles between stages of NREM and REM changes throughout the night [61,65]. The NREM sleep constitutes 75%-80% of total time spent in sleep, and REM sleep constitutes the remaining 20-25%. The four sleep stages of NREM sleep's most important feature is the slow-wave sleep which is being considered to be the deepest stage of sleep. It is the stage 4 of NREM sleep. Following the period of stage 4 of NREM sleep the stages reverse to reach REM sleep. The interchange of cycles between NREM and REM takes place during the whole sleep-wake cycle for the whole remaining night [63,66].

Sleep plays a significant role in our health. While more sleep will not necessarily prevent us from getting sick, sleep deprivation could cause adverse effects on our immune system, which could leave us susceptible even to mere infections or flu. Without sufficient amounts of uninterrupted sleep, our body does not make enough cytokines, which is a kind of protein that targets infections and inflammation, effectively creates an immune response. The response by the immune system is generally regulated by three keen physiological processes such as wakefulness, NREM or slow sleep and REM sleep. The tendency to sleep is associated with the IL-1 levels in the brain, which is being highest at sleep onset, accompanied with cytokines such as IL-2, IL-6, IL-8, IL-15 and IL-18 as study shows this cytokines increase NREM sleep or slow sleep while some pro-inflammatory cytokines manage body's physiologic temperature and inclination [67]. Many case study and founding studies show sleep deprivation such as insomnia, alcoholism and stress shifts the cytokine from type to type 2 leading towards type 2 functions, which naturally takes place during the period of aging. Moderate drinkers and people with less sleep deprivation have high levels of tumour necrosis factor cytokine (TNF-α) IL-1, IL-12 and IL-6. T-helper cells (CD3+, CD4+), T-cytotoxic cells (CD8+) activity is reduced in insomniacs and decreased natural killer cells are observed along with elevated levels of inflammatory cytokines [68,69]. Sleep naturally supports the initiation of an adaptive immune response, studies revealed that a proper sleep cycle enhances the influence of cytokines and promotes the interaction of the Antigen Presenting Cell (APC) with T helper cells, such as IL-12 [70]. The invading antigen is recognized and processed by APC which forwards fragments of antigen to Th cells, while the two kinds of cells form an immunological synapse. A Th1 response is induced by associated release of IL-12 from APC which then supports the function of cytotoxic T cells which is antigen specific further initiating the antibodies production by B cells [12]. Cytokines such as TNF-α plays a significant role in Sleep, specifically Slow-Wave Sleep (SWS) which helps in release of growth hormones and reduction of stress hormones, which supports the early stages of adaptive immune response in the lymph nodes [71,72] (**Figure 3**). As the reports shows, the antiviral reactions between host immunity and the virus, which also includes the generation of different pro-inflammatory cytokines, the activation of T cells (CD4+, CD8+) are important to control the viral replication by restricting the infection to further spread. The proper sleep enhances and helps in elevating the levels of cytokines in our body [73].

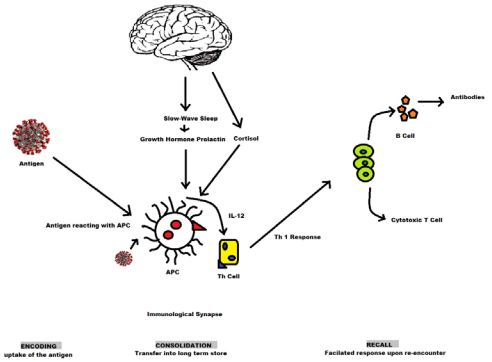

Figure 3: Slow-wave sleep giving rise to growth hormones, which enhances the interleukins to give rise to the antibodies against the antigen by recognizing it with the help of APC.

Basically, against viral infections our body reacts with an adaptive immune system which is supported by sleep. Similarly to the infection caused by SARS-CoV-2, adaptive immunity comes forward. When the viral antigen is introduced in the lungs by the respiratory tract, it is presented to dendritic cells which starts a series of processes from which the adaptive immune system can recognize the viral antigen and form memory T lymphocytes [74,75]. For the recognizing the viral particle CD4+ T helper cells are presented to cell membranes, further promoting the process of B cell proliferation and development of the antibody producing plasma cells takes place [76]. More importantly, the T cells, CD4+ and CD8+ cells show an antiviral characteristic by adjusting itself. Further the CD8+ T cells separate into cytotoxic T Lymphocytes (CTLs), which gives the production of cytokine. Cytokine restricts the replication of viruses and kills the infected cells [77,78]. The cytokine is released, when a proper sleep-wake cycle takes place and deprivation of sleep can cause fewer cytokines, which can cause the immune system to weaken, making us more prone to viral infection such as SARS-CoV-2 [12].

Results and Discussion

As, due to the COVID-19 pandemic all around the world, all health-care workers and hospital staff are working 24/7. They are working as the first line of defence against the pandemic. Due to their efforts of working 24/7, they are sleep deprived, which leaves them vulnerable to COVID-19 infection. Similarly, individuals with the age group above 50 are also sleep deprived due to their aging factors, which makes them more prone to the infection of SARS-CoV-2.

Conclusion

Sleep deprivation could cause many physiological consequences as well as psychological consequences which can affect the decision making ability of health care staff as well. The lockdown and quarantine methods are established by governments of many nations for their citizens, so the citizens can get enough sleep and eat enough nutrients, which can help them to create a strong immune system for themselves while restricting the transmission of virus to minimum. Sleep helps the patient's immune system to react with medicines better to fight against COVID-19. Proper Sleep cycle also enhances the immune system by releasing cytokines and other growth hormones, which could fight off infection caused by not only SARS-CoV-2, but also against any other pathogens.

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