Immunosenescence and ACE2 protein expression: Association with SARS-CoV-2 in older adults

Gustavo Acosta Altamirano1, Carlos E Miguel Rodríguez1, María del Rocio Reyes-Montes3, Esperanza Duarte-Escalante3, Rocío Acosta-Reyes2, Carlos U Torres-Estrella1 and Omar E Valencia-Ledezma1*

1Research Unit, Regional Hospital of High Specialty of Ixtapaluca, Federal Highway Mexico-Puebla Km. 34.5, Town of Zoquiapan, Ixtapaluca 56530, Mexico
2Medical Towers, La Joya Hospital, San Miguel de Allende Guanajuato Mexico
3Mycology Unit, Faculty of Medicine, Department of Microbiology and Parasitology, National Autonomous University of Mexico, Mexico City 04510, Mexico

Abstract

At the end of 2019, in Wuhan, China, an outbreak of cases of respiratory tract infection emerged and its progressive infection mainly affects adults, generating many cases of pneumonia. A type of coronavirus named SARS-CoV-2, with genomic similarity to SARS-CoV and MERS-CoV, was identified as the etiological agent. The evolution of this pandemic has made it possible to verify the similarity in the pathophysiological mechanisms between these three viruses, identifying the Angiotensin-Converting protein-Enzyme 2 (ACE2) as the primary receptor for SARS-CoV-2. This age group is more prone to developing extrapulmonary complications from SARS-CoV-2 since the clinical and pathological findings suggest a particular relationship between greater expression of ACE2 and the comorbidities of chronic degenerative diseases and the greater expression of ACE2 at the level of the respiratory tract. It has also revealed the mechanisms by which the virus evades the innate immune response and the Th1-type adaptive response. The objective of this work was to analyze immunosenescence and its relationship with SARS-CoV-2 infection, through the review of the most recent articles (2021-2022), which describes the senescent state of the elderly. In addition, it intends to highlight the probable causes for which the most vulnerable population group (adults over 60 years of age) is more prone to presenting complications during the infection.

Introduction

On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic due to the rapid spread of a new coronavirus whose origin dates back to 2019 in Wuhan, China and causes COVID-19 disease [1]. This pathogen shares 79% genomic similarity with SARS–CoV and 51% with MERS-CoV, for which it was subsequently officially named severe acute respiratory syndrome coronavirus 2 (SARS–CoV–2) by the WHO [2]. SARS–CoV–2 has shown a greater transmission capacity than SARS–CoV, causing the COVID-19 disease, characterized by the presence of fever, cough and fatigue as the main signs and symptoms. The evolution of this pandemic has made it possible to understand the behavior and pathophysiological mechanisms of the virus and identify the people most vulnerable to infection and risk factors that can trigger the development of severe illness from COVID-19. Risk factors include from the genetic level to age-related factors, a study carried out through a meta-analysis of the human genome, showed a correlation between a group of genes on chromosome 3 and susceptibility to SARS–CoV–2 infection. These genes, in turn, were shown to correlate with genes encoding the ABO blood group system, suggesting that certain blood groups, particularly type A, are more susceptible to SARS–CoV–2 infection [3]. Further
study showed that these risk genes are probably inherited by Neanderthals and are found in greater abundance in South Asian and European populations [4]. Comorbidities are an essential factor in the development of COVID-19 disease because, in some way, it compromises the patient’s health status, due to all inflammatory processes, the risk of clinical complications increases. At the beginning of the pandemic, the population aged 60 years or older, with the presence of some comorbidities such as type 2 diabetes, Systemic Arterial Hypertension (SAH), Chronic Obstructive Pulmonary Disease (COPD) and asthma, with incomplete medical treatment, had a higher risk of infection and complications [5]. According to reports, mild to moderate disease occurs in 30 to 80% of populations, in 70,000 cases of COVID-19, the mild disease was presented in 81% with mild pneumonia or without it, moderate in 14% presented pneumonia with hypoxemia and severe disease was presented in 5% with respiratory failure requiring mechanical ventilation, shock or multi-organ failure [6,7]. However, the immunological ability of each individual is also affected by age. This phenomenon known as immunosenescence impairs the body’s ability to deal with infectious agents, thus compromising the immune response [8]. The objective of this work was to analyze immunosenescence and its relationship with SARS-CoV-2 infection, through the review of the most recent articles (2021-2022), which describes the senescent state of the elderly. In addition, it intends to highlight the probable causes for which the most vulnerable population group (adults over 60 years of age) is more prone to presenting complications during the infection.

Pathophysiology of COVID-19

The general structure of the virus: To understand the pathogenic mechanisms of the virus, we must address its general structure. The virus capsid is made up of four main structural proteins: Spike (S), Membrane (M), Envelope (E) and proteins of the Nucleocapsid (N) (Figure 1). Inside this capsid, is the virus genome. The CoV genome is conformed of a positive-sense, single-stranded RNA, 29.9 kb in size [9]. Within the genome are the sequences that encode the structural proteins, 16 non-structural proteins (NSP1–16) involved in the replication of the viral genome and, finally, 11 accessory proteins encoded by different open reading frames (ORFs): ORF3a, ORF3b, ORF3c, ORF3d, ORF6, ORF7a, ORF7b, ORF8, ORF9b, ORF9c and ORF10 [6]. One of the functions of accessory proteins is to antagonize the host’s interferon type 1 (IFN-1) response, regulating the cellular apoptosis response [10].

Homotrimers of the S proteins form the spikes on the viral surface and are responsible for binding to host receptors [11]. The Mpro or 3CLpro protein is the viral protease. It is responsible for cleaving the polyproteins of the virus, resulting in non-structural proteins [12]. Protein E has transmembrane domains, so it can function as a viroporin, embedding itself in host cell membranes and promoting virus assembly and release [13]. The N protein is vital for the packaging of the viral genome. It has two domains, both of which can bind to the RNA genome of the virus through different mechanisms [9]. The Membrane protein (M) crosses the host cell membrane and can attach to the other structural proteins. For example, binding to the N protein stabilizes the N–RNA complex within the virion, promoting viral assembly [14].

Mechanism of infection

The infection mechanism of SARS-CoV-2 is very similar to that of SARS-CoV since they have angiotensin-converting enzyme 2 (ACE2) as a receptor ligand [15,16]. SARS–CoV–2 infection is triggered by the binding of the RBD domain of the S1 subunit to the host receptor ACE2 (Figure 2). These receptors have an expression in the nose, mouth, heart, lungs, liver and...
kidney [17,18]. It is pertinent to mention that our work team has observed the presence of these receptors on the back of the hand (data not shown). ACE2 is expressed primarily in a small subset of lung cells called type II pneumocytes [18]. Other studies have shown the presence of ACE2 in epithelial cells of the upper respiratory tract, macrophages and dendritic cells, with this we infer that contagious infections are favored in the elderly population [19]. These findings could explain some mechanisms by which this virus alters the patient’s innate immune response.

Once SARS-CoV-2 binds to its receptor, the host’s transmembrane protease serine 2 (TMPRSS2) binds the S protein, favoring virus entry [20]. Thus, the virus enters the cell, and viral replication takes place. To initiate an antiviral response, cells of the innate immune response recognize viral invasion through pathogen-associated molecular patterns (PAMPs). For an RNA virus like the coronavirus, genomic RNA is recognized by endosomal RNA receptors, TLR3 and TLR7 and cytosolic RNA sensor, RIG-/MDA5. The previous leads to the activation of an intracellular signaling cascade of the NF-κB and IRF3 types. In the nucleus, these transcription factors induce the expression of interferon type 1 (IFN-1) [19], which acts as the first line of defense against viral infection at the site of entry; thus, this IFN-1-like response should be able to suppress viral replication and spread at an early stage.

On the other hand, SARS-CoV can interfere with IFN-1 production, and this mechanism is closely related to the severity of the disease [19]. It has been shown that different SARS-CoV-2 proteins can antagonize the host IFN-1 response in different ways; for example, SARS-CoV-2 ORF3b is a potent IFN-1 inhibitor [20,21]. The prior is associated with the ORF3b C-terminal domain length and its ability to inhibit IRF3 translocation to the nucleus [21]. Also, the ORF6 protein inhibits it by blocking STAT translocation to the nucleus [20,22] and the ORF7a inhibits IFN-1 signaling by polyubiquitinating, thus enhancing its ability to antagonize IFN-1 [20,23]. Other proteins capable of antagonizing the IFN-1 response are ORF8 and the structural proteins M and N (Figure 3) [20].

The patient’s innate immune response is crucial for recovery. However, the adaptive immune response is more relevant in reducing vulnerability to reinfection and the body’s ability to combat intracellular microorganisms [24-26]. Evidence indicates that the Th1-type response is key to successfully controlling SARS-CoV, MERS-CoV and probably SARS-CoV-2 [12]. This response is also efficient against infections by intracellular pathogens (viruses and bacteria). Targeting a Th1 response is favored by dendritic cells and interleukin-12 (IL-12)-producing phagocytes [27]. It has been reported that patients admitted to intensive care units (ICU) showed a hyperactive immune response characterized by elevated levels of granulocyte colony-stimulating factor (GCSF), inducible protein 10 (IP10), monocyte chemotactic protein 1 (MCP1), macrophage inflammatory protein 1-alpha (MIP1α) and tumor necrosis factor-alpha (TNFα), collectively referred to as a cytokine storm [28]. This cytokine storm is proportional to the severity of the disease. However, SARS-
CoV-2 infection also elicits a Th2-type immune response that induces the secretion of IL-4 and IL-10, cytokines that suppress inflammation [1] but favor antibody production.

Currently, other factors that alter the innate immune response and facilitate the infection and replication of the virus are being investigated. Some of these factors are environmental temperature and vitamin D3 deficiency, as they affect high-affinity nuclear receptors such as the Vitamin D Receptor (VDR) [29]. These receptors, when stimulated, favor cellular stress in response to an infection by microorganisms. In this way, the high infection rate in countries with a greater latitude could be related to individuals’ physical proximity in cold climates. However, more studies are still needed to validate these hypotheses [30]. In addition, experimental and meta-analysis studies have shown an association between serum vitamin D levels and the severity of COVID-19. It is also stated that the amount of CD4+ and CD8+ T cells is reduced when there is a lack of vitamin D. In addition, it has been proven that T lymphocytes increase with vitamin D supplementation. In turn, the increase in the PD-L1 expression is inhibited, thus eliminating the suppressive effect of PD-L1 on CD4+ and CD8+ T lymphocytes, and lymphopenia is prevented, reducing severity and mortality [31,32].

**Immunosenescence: A decreased progression of the immune system**

It has been shown that more than half of the deaths related to COVID-19 were individuals over 60 years of age, with an average age of 72.5 years. A study of 100 cases of COVID-19 deaths in China showed that elderly patients with chronic diseases, cardiovascular diseases and diabetes accounted for most COVID-19-related deaths [33]. Although an increase in life expectancy is anticipated worldwide in the coming years (WHO), it is not necessarily associated with a better quality of life for older adults. The aging process triggers pathophysiological dysfunctions in different tissues, organs and systems, including the immune system. Changes in the immune response associated with aging result in decreased effectiveness of the humoral and cellular immune responses. These changes in the immune system are collectively termed “immunosenescence” and are characterized by decreased innate and adaptive immune responses and latent production of pro-inflammatory cytokines [34]. It has been described that when the death of aged T cells occurs, the thymus replenishes its reserve with virgin T cells, which does not occur in individuals aged 60 to 70 years, where thymic production is reduced by 90% compared to newly borns.

**Inflammation**

Chronic inflammation is closely related to immunosenescence and the development of some comorbidities; although the mechanisms have not been fully elucidated, some factors favor this pro-inflammatory state. It is known that the decrease in cell repair mechanisms is affected with age, which causes damage at the genome and proteome level; for example, accelerated shortening of telomeres in the leukocyte population has been related to the development of coronary heart disease [35].

Likewise, the latent production of pro-inflammatory cytokines during aging is called inflammatory aging. This concept refers to a low-grade pro-inflammatory phenotype associated with aging progression, along with an increase in serum proinflammatory cytokines such as IL-6, IL-1α, TNF-α, IL-1 and C-reactive protein [36–38]. This pro-inflammatory state that causes damage to healthy tissue due to the latent production of pro-inflammatory cytokines results from the inability of the immune system to eliminate pathogens, as well as infected, neoplastic, and senescent cells [35,39]. In addition, the increase in pro-inflammatory cytokines such as TNF and/or IL-6 has been related to the development of Alzheimer’s and cardiovascular diseases [40–42]. On the other hand, the increase in pro-inflammatory cytokines due to the deregulation of monocyte populations and functions is also influenced by age [43].

On the other hand, it has been shown that external agents, such as some pathogens, can affect the inflammatory state of the host; for example, the specific response of T cells, generated pre-infections by cytomegalovirus (CMV) in older people, cause deregulation of the process inflammatory, promoting greater severity in patients with SARS-CoV-2 infection [44].

**Cellular senescence**

Cellular senescence consists of multiple phenotypic changes in long-lived (old) cells, including short telomeres, cessation of proliferation, size increase and acquisition of increased activity of lysosomal acid beta-galactosidase called Senescence-Associated (SA)–βGal that serves as a biomarker of senescent cells regardless of their tissue or organ of origin. The most important characteristic of senescent cells is the acquisition of the Senescence-Associated Secretory Phenotype (SASP), which allows them to secrete significant amounts of pro-inflammatory cytokines (including IL-6, TNF-α, IL-1β, IL-8 and others) [45,46]. Immunosenescence is further characterized by decreased immune responses such as infected, neoplastic, and senescent cells [35,39]. In addition, the increase in pro-inflammatory cytokines such as TNF and/or IL-6 has been related to the development of Alzheimer’s and cardiovascular diseases [40–42]. On the other hand, the increase in pro-inflammatory cytokines due to the deregulation of monocyte populations and functions is also influenced by age [43].

On the other hand, it has been shown that external agents, such as some pathogens, can affect the inflammatory state of the host; for example, the specific response of T cells, generated pre-infections by cytomegalovirus (CMV) in older people, cause deregulation of the process inflammatory, promoting greater severity in patients with SARS-CoV-2 infection [44].

**Immunosenescence: A decreased progression of the immune system**

It has been shown that more than half of the deaths related to COVID-19 were individuals over 60 years of age, with an average age of 72.5 years. A study of 100 cases of COVID-19 deaths in China showed that elderly patients with chronic diseases, cardiovascular diseases and diabetes accounted for most COVID-19-related deaths [33]. Although an increase in life expectancy is anticipated worldwide in the coming years (WHO), it is not necessarily associated with a better quality of life for older adults. The aging process triggers pathophysiological dysfunctions in different tissues, organs and systems, including the immune system. Changes in the

**Inflammation**

Chronic inflammation is closely related to immunosenescence and the development of some comorbidities; although the mechanisms have not been fully elucidated, some factors favor this pro-inflammatory state. It is known that the decrease in cell repair mechanisms is affected with age, which causes damage at the genome and proteome level; for example, accelerated shortening of telomeres in the leukocyte population has been related to the development of coronary heart disease [35].

Likewise, the latent production of pro-inflammatory cytokines during aging is called inflammatory aging. This concept refers to a low-grade pro-inflammatory phenotype associated with aging progression, along with an increase in serum proinflammatory cytokines such as IL-6, IL-1α, TNF-α, IL-1 and C-reactive protein [36–38]. This pro-inflammatory state that causes damage to healthy tissue due to the latent production of pro-inflammatory cytokines results from the inability of the immune system to eliminate pathogens, as well as infected, neoplastic, and senescent cells [35,39]. In addition, the increase in pro-inflammatory cytokines such as TNF and/or IL-6 has been related to the development of Alzheimer’s and cardiovascular diseases [40–42]. On the other hand, the increase in pro-inflammatory cytokines due to the deregulation of monocyte populations and functions is also influenced by age [43].

On the other hand, it has been shown that external agents, such as some pathogens, can affect the inflammatory state of the host; for example, the specific response of T cells, generated pre-infections by cytomegalovirus (CMV) in older people, cause deregulation of the process inflammatory, promoting greater severity in patients with SARS-CoV-2 infection [44].

**Cellular senescence**

Cellular senescence consists of multiple phenotypic changes in long-lived (old) cells, including short telomeres, cessation of proliferation, size increase and acquisition of increased activity of lysosomal acid beta-galactosidase called Senescence-Associated (SA)–βGal that serves as a biomarker of senescent cells regardless of their tissue or organ of origin. The most important characteristic of senescent cells is the acquisition of the Senescence-Associated Secretory Phenotype (SASP), which allows them to secrete significant amounts of pro-inflammatory cytokines (including IL-6, TNF-α, IL-1β, IL-8 and others) [45,46]. Immunosenescence is further characterized by decreased immune responses such
as antigen presentation and naive T-cell priming, increased myeloid lineage differentiation, altered type 1 interferon (IFN) responses, decreased cytotoxic function of CD8+ T cells and decreased phagocytic function for many innate response cells [46]. In addition, senescent cells change their intracellular homeostasis, including telomere shortening and oxidative stress, which induce the activation of signaling pathways such as NF-κB. The latter favors the production of cytokines, chemokines, growth factors and bioactive lipids [47,48], assuming that senescent cells change their profile to a cytokine–secreting phenotype (senescence–associated secretory phenotype, SASP) [49,50].

The cell death process that occurs daily due to physical and chemical stress, as well as the accumulation of metabolic and catabolic products that are not efficiently eliminated through phagocytosis by cells of the innate immune system, accumulate and induce the activation of cell recognition receptors patterns (pattern recognition receptors, PRRs) [51]. Additionally, infectious processes during aging can exacerbate the pro-inflammatory condition due to the accumulation of pathogen-associated molecular patterns (PAMPs) and the release of damage-associated molecular patterns (DAMPs), which trigger the inflammatory process through their interaction with PRRs. Signaling through PRRs results in the activation of the transcription factor NF-κB, which is the primary activator and inducer of the SASP phenotype [52]. DAMPs can signal through the Nod-3 receptor (Nod-like receptor 3, NLRP3), inducing inflammasome activation and secretion of pro-inflammatory cytokines such as IL-1β and IL-18 [53].

Inflammatory aging also induces the degeneration of autophagy processes through which cell content is recycled, generating nutrients and energy to maintain cell homeostasis, thus contributing to the elimination of cell debris (senescent cells) and metabolic products, preventing their recognition by PRRs, as well as the development and progression of the inflammatory process [54,55]. In this context, deficiencies in autophagy induce protein aggregation and the accumulation of dysfunctional or damaged mitochondria that cause alterations in oxidative respiration, triggering the production of reactive oxygen species (ROS). Oxidative stress induces the inflammasome pathway through activation of the NLRP3 receptor [56-58], which activates the pro-inflammatory caspase pathway, caspase-1, to cleavage inactive cytokine precursors such as IL-1β and IL-18 [54,59,60].

Additionally, oxidative stress induces the release of Cpg–rich mitochondrial DNA with the ability to activate the inflammatory response through its interaction with Toll–Like Receptors (TLRs) and Nod-Like Receptors (NLRs) and the subsequent production of pro-inflammatory cytokines [61,62]. Furthermore, impaired proteasome function also occurs during aging, contributing to the accumulation of misfolded protein aggregates that also induce pro-inflammatory pathways' activation [63]. The intestinal microbiota during aging plays a fundamental role in the activation of the inflammatory response, due to the large number of molecules that they secrete and that are capable of activating the inflammatory response of the host, among these is the LPS, which constitutes a constant stimulation for the immune system in the cells of the intestine, due to changes in composition and diversity and develops a predominantly Th-1 type inflammatory response characterized by a reduced number of associated intestinal bacteria to an anti-inflammatory response. In addition, intestinal permeability increases during aging, which favors bacterial translocation and inflammation [64–66].

Evidence associated with vaccination shows an imbalance in pro- and anti-inflammatory mechanisms, lower production and diversification of T lymphocytes, altered immunosurveillance and synthesis of antibodies before immunization with SARS-CoV-2 and a decrease in immunological memory. Nutrition in geriatric individuals is essential to combat sarcopenia and bone fragility. Some food components that contribute to immunocompetence are proteins, vitamin D, n-3 fatty acids, antioxidant vitamins (vitamins C and E), zinc, selenium and iron, which are relevant for the senior population [67].

**Immunosenescence and SARS-CoV-2**

Immunosenescence is a process associated with the deterioration of the immune system caused by aging. This process has become relevant in recent years because it has been reported that COVID-19 disproportionately affects older adults. The CDC has also reported that people ages 65 to 74 are 90 times more likely to die from COVID–19 than people ages 18 to 29 [68].

Recent research mentions that aging is related to the immune system’s ability to maintain the organism in homeostasis with the individual’s intestinal microbiota. In addition, it is inferred that there is no single pattern that can define the immunological profile of the population over 60 years of age since there are multiple factors that alter the immune response, such as environmental exposure, nutritional status, and psychological status as humans age [66]. The phenomenon of senescence implies apoptosis when cells reach the end of their replicative potential or are exposed to various stressors, such as infection. Senescent cells accumulate in the tissues of older individuals and contribute to the development of age-related disorders. However, it was only in 2011 that it was determined that eliminating senescent cells could delay the appearance of diseases associated with aging. This discovery confirmed senescence as a hallmark of aging [69]. Immunosenescence originates as the inability of the innate and adaptive immune responses to act efficiently [70].

Older adults present deterioration of multiple functions such as the neutrophils’ phagocytic capacity, the synthesis of reactive oxygen intermediates, the efficiency of intracellular destruction, secretion of cytokines and chemokines, antibacterial defenses, wound infiltration and repair, and antigen presentation [71,72]. On the other hand, a mortality study in patients with a molecular diagnosis of COVID–19 at the Regional Hospital of High Specialty of Ixtapaluca showed that of 646 hospitalized adults, 426 were under 60 years of age, and 220 were 60 years of age or older. The authors pointed out
that diabetes and hypertension were two of the most frequent comorbidities in Mexican patients. More febrile symptoms were also found in older adults, emphasizing that cellular senescence may be a condition for presenting more complex symptoms of hypertension during SARS–CoV–2 infection. It was also shown that mortality was significantly higher in the older adult group [73]. Similarly, a statistical analysis performed in the USA showed a higher prevalence for adolescents and young people than for older adults [74]. However, another study on the prevalence of COVID–19 in children, adolescents, and adults conducted through a database of the COVID–19 Monitoring Program in school children in Brazil, reported 3.5%, 3.6%, and 6.0% in children, adolescents and adults, respectively [75]. The previous confirmed that population diversity has a direct correlation with the Figures reported cases of COVID–19 [76].

**Lymphopenia**

In the process of immunosenescence, there is lymphopenia marked by decreased function of regulatory T cells, which increases susceptibility to autoimmune and inflammatory responses [77]. On the other hand, the condition and reduced ability of senescent macrophages to phagocytize apoptotic cells promote a proinflammatory state. During COVID–19, there is a significant reduction in peripheral lymphocytes, mainly CD4 and CD8 T cells and is associated with an increased risk of developing a secondary bacterial infection and viral sepsis. The exact mechanism leading to lymphopenia is unknown; however, it has been proposed that SARS–CoV–2 could directly infect T cells [78]. Older adults have a less efficient response to eliminate the viral load, which generates a cytokine storm with inadequate immune response and immunological memory, as well as a direct attack by SARS–CoV–2 on other organs. Systemic immune pathogenesis caused by cytokine storm and microcirculatory dysfunctions leads to viral sepsis due to lymphocyte depletion and dysfunction, therefore an adaptive immune response cannot be initiated early and effectively. This uncontrolled infection leads to increased macrophage infiltration and further damage to the lung [79]. The increased susceptibility to viral lower respiratory tract infections is primarily related to defective innate immunity [80].

Currently, only limited information is available on the innate response of the host infected with SARS–CoV–2, some studies show the involvement of innate immunity in the defense against COVID–19. Among these is a study of 99 cases in Wuhan, where an increase in total neutrophils (38%), a decrease in total lymphocytes (35%), an increase in serum IL–6 (52%) and an increase in C–reactive protein (84%) [81]. Another study conducted in the same city confirmed the same results in 41 patients, showing an increase in neutrophils and a decrease in lymphocytes, which correlated with the severity of the disease and death of the patients [82,83]. On the other hand, among the main risk factors for acute respiratory distress syndrome (ARDS) are diabetes, obesity, poorly controlled systemic arterial hypertension (SAH), low levels of T lymphocytes (CD3 and CD4), levels elevated aspartate aminotransferase, - albumin, creatinine, glucose, low–density lipoproteins, serum ferritin, lactate dehydrogenase and D–dimer [84,85].

**Vaccines in immunosenescence**

The vulnerability of older adults to COVID–19 prioritizes vaccination in this age group. Immunization studies in older adults against influenza have shown that immunosenescence decreases its efficacy since an efficacy of 30% – 40% has been shown in older adults, who are the most vulnerable population. However, in the case of vaccination against SARS–CoV–2, in older adults, the results of clinical trials have been promising. In adults 70 years and older, a dose of the Pfizer/BioNTech vaccine was 57% to 61% effective in preventing COVID–19 and a dose of the AstraZeneca/Oxford University vaccine was 60% effective to 73%%. Administration of a second dose increased the efficacy of the Pfizer vaccine by 85% – 90% [86]. On the other hand, it is essential to consider epigenetics to predict the variability in vaccination efficacy in different regions. In addition, a second factor to consider is the individual’s nutritional status, since it is essential to generate a protective, effective and long–lasting immune response in the host [87]. On the other hand, a study shows that the expression of ACE2 receptors in the nasal epithelium depends on age, and is important since it is the first point of contact between SARS–CoV–2 and the host. In children, it has been shown that there is a lower expression of ACE2 than in older adults, which explains the high frequency of COVID–19 in older adults. These factors may affect the severity of illness and late recovery from pneumonia caused by SARS–CoV–2 infection in older adults [88,89]. Since March 2020, older adults around the world have shown disproportionate effects caused by SARS–CoV–2, reflected in high mortality rates, compared to young adults and children, so it is recommended to vaccinate the world population and prevent the generation of new viral variants [90].

**Conclusion**

The present work suggests that decreased cellular–type immune response presented by individuals over 65 years of age and the presence of comorbidities such as uncontrolled type 2 diabetes or SAH favor the development of complications such as ARDS, sepsis, multi–organ dysfunction and subsequent death of the patient. Aging and the state of immunosenescence, accompanied by the effect of inflammation, affect the immune response against viruses in older adults. The imbalance in the pro– and anti–inflammatory mechanisms, the reduced production and diversification of T lymphocytes and the lowered synthesis of antibodies against immunization are pointed out. Likewise, the overexpression of ACE2 receptors in older adults and decreased generation of antibodies to the vaccines are highlighted. The preserved and diminished Th2–type response in patients older than 65 years will allow their recovery, especially by producing IgM, IgG and IgA isotype antibodies, which can limit fatal outcomes. It is necessary to evaluate the immune response in elderly patients in saliva or in nasopharyngeal swabs at intervals to determine the immune status and thus have senescence data. Additionally, other factors can improve the response immunity of this age group, including warm climate, exposure to UV rays and adequate nutrition with vitamin D intake [91]. To reduce infections
in immunized older adults with greater susceptibility to infections, the correct use of nasal and mouth masks [92], frequent hand washing and healthy social distancing will help protect the elderly.

I’ve Commons Attribution 4.0 International License (http://creativecommons.org/ licence/4.0/), which permits unrestricted use, distribute- tion, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

Statement of human and animal rights

This is a review article and none of the authors have performed studies with human or animal participants for it.

Disclaimer

The opinions expressed in this document are those of the
original author(s) and the source, provide a link to the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References


Citation: Altamirano GA, Miguel Rodríguez CE, Reyes-Montes MDR, Duarte-Escalante E, Valencia-Ledeza OE, et al. (2022) Immunosenescence and ACE2 protein expression: Association with SARS-CoV-2 in older adults. Open J Asthma 6(1): 008-017.DOI: https://dx.doi.org/10.17352/oja.000018
Citation: Altamirano GA, Miguel Rodríguez CE, Reyes-Montes MDR, Duarte-Escalante E, Valencia-Ledeza OE, et al. (2022) Immunosenescence and ACE2 protein expression: Association with SARS-CoV-2 in older adults. Open J Asthma 6(1): 008-017.DOI: https://dx.doi.org/10.17352/oja.000018