

## Obesity and COVID-19: Impact on Immunity, Infection and Vaccination

*Obesidade e COVID-10: Impacto na Imunidade, Infecção e Vacinação*

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Obesity is a complex and multifactorial pathology that has been increasing significantly in recent decades, becoming a serious public health problem. It can be characterized by an energy and metabolic imbalance that compromises the health of individuals. Obesity can be complicated by other diseases or be associated with the development of comorbidities, such as diabetes mellitus, cardiovascular disease, hypertension, dyslipidemia, hepatic steatosis, in addition to various types of cancer.<sup>1</sup>

It is important to say that obesity also causes dysregulation of the immune system, which impairs the response of innate and adaptive immunity cells, alteration in the phenotype of macrophages and T lymphocytes, dysregulation in the production of cytokines and chemokines, cellular senescence, and alteration in the production of immunoglobulins. Another aspect to highlight is that obese individuals are at greater risk of developing bacterial, fungal, and viral infections, or are associated with a worse prognosis. This greater susceptibility may be associated with the modulation of the immune response, as well as anatomical and physiological changes in the respiratory system, and changes in the healing process, which contributes to an increased risk of post-surgery infections.<sup>2</sup>

Due to the large number of obese people in the

world, their susceptibility to infections and the COVID-19 pandemic, several studies have shown that various diseases such as diabetes, kidney, and cardiovascular diseases, as well as obesity are related to a greater risk of developing more severe symptoms of SARS-CoV-2 infection. Thus, it has been shown that obese patients have a higher mortality rate and are associated with a longer stay in intensive care units (ICU).<sup>3</sup> A systematic review of several studies indicated that 32% of patients with cases of reinfection were obese, showing that obesity can be a contributing factor to the severity and reinfection of SARS-CoV-2.<sup>4</sup>

Besides the effects during the symptomatic phase, several individuals had chronic post-COVID-19 syndrome, such as cases of pain, chronic fatigue, weakness, mental disorders such as sleep disturbance and depression. During the pandemic, a reduction in physical activity was also observed, which is accompanied by loss of muscle mass and an increase in central adipose tissue, contributing to insulin resistance and dyslipidemia. In addition to the biological effects of COVID-19, the physical, emotional, and social aspects also contributed to a change in lifestyle and an increase in cases of obesity. Those obese individuals who required surgical treatment were also harmed by the reduction in the number of bariatric

surgical procedures.<sup>5</sup>

Obesity is characterized as a low-grade inflammatory state, which may contribute to the development of more severe forms of COVID-19. The relationship between disease severity and obesity can be explained because ACE2 is highly expressed in adipocytes and adipocyte-like cells found in lung tissue. Furthermore, in murine experimental studies, it was demonstrated that obese mice had a higher expression of ACE2 and TMPRSS2 in the trachea and lungs, which may facilitate the entry of the virus into cells.<sup>6,7</sup> This chronic low-grade inflammation associated with the immune response due to cell activation and production of pro-inflammatory cytokines may contribute to the amplification and worsening of the disease caused by the "cytokine storm".<sup>6</sup>

Furthermore, obese individuals have an accumulation of leptin-induced M1 macrophages (hormone produced by adipose tissue), neutrophils with impaired microbicidal activity, and a reduction in NK cells, in addition to an increase in the production of TNF- $\alpha$ , IL-6, IL-12, IL-1 $\beta$  and TGF- $\beta$ . Interestingly, obesity can lead to depletion of CD8+ T cells, a decrease in B lymphocytes and differentiation of helper T cells.<sup>6</sup>

Vaccination against COVID-19 has been shown to be effective, with an increase in the humoral immune response and a reduction in severe cases of the disease. Obesity is associated with a low immune response to tetanus, influenza, and hepatitis B vaccines. When comparing obese and non-obese individuals, it was shown that despite being effective, obese individuals had a lower rate of anti-SARS-CoV-2 neutralizing antibodies, and after 90 days, they had reduced specific antibodies, showing even more the importance of doses of reinforcement, especially for this group of people.<sup>8</sup>

A population-based cohort study from England showed that the first and second doses of COVID-19 vaccines were effective for obese and normal individuals, but not for those with low BMI. However, this research also showed that individuals with lower or higher BMI present a greater risk of developing severe cases of COVID-19, even after two doses of the vaccine.<sup>9</sup>

In obesity, the decrease in immunogenicity to long-term vaccination can be explained in different ways. For example, inhibition of thymopoiesis, leading to a reduction in the T lymphocyte repertoire; a reduction in memory T and B cells, which may be associated with a decrease in telomeres; an increase in the expression of PD-1 and PD-L1, inducing the exhaustion of these cells. In addition, long-term humoral immunity induced by vaccination may also be impaired, due to reduced antibody class switching and depletion of memory B cells. However, most studies of mechanisms of action are based on influenza vaccination.<sup>10</sup>

Thus, it is possible to observe the great complexity of obesity and its impact on several diseases, such as COVID-19. Interestingly, obesity can modulate the immune response of individuals, compromising a protective response against SARS-CoV-2 infection or the response to vaccines. However, more studies need to be performed to elucidate the mechanisms of low long-term

immunogenicity for SARS-CoV-2 and the different types of vaccines and doses.

**Keywords:** *Obesity. SARS-CoV-2. Immunity. Vaccination.*

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## CONTRIBUIÇÕES DO AUTOR

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