

Obesity-Related Inflammation and Covid-19 Prognosis: Is the White Adipose the Villain?

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Abstract

The emergence novel coronavirus (SARS-CoV-2/COVID-19) has become a worldwide pandemic health threat, causing severe respiratory syndrome in humans. COVID-19 effects, which were first observed in the respiratory tract, are continuously being found and characterized in different organs, and the disease now considered systemic. Recent studies show COVID-19 to have repercussions in the heart, central nervous system, liver, and kidney. Also, it is becoming increasingly clear that the presence of comorbidities is associated with COVID-19 severity and lethality. Thus, the highest fatality rates in infected patients with COVID-19 are related to the presence of diabetes mellitus, cardiovascular diseases (CVD), cancer, and chronic respiratory disease. An unbalanced immune reaction underlines the release of inflammatory cytokines, such as IL-6, IL-1 β , IFN γ , inducing the “cytokine storm” in infected patients

The white adipose tissue has not, to the best of our knowledge, been the focus of studies examining its potential contribution to the cytokine storm, albeit some opinion papers postulate this possibility. Early data obtained from infected patients from China and Italy regarding the correlation of comorbidities with COVID-19 infection outcome failed to provide detailed information on patient adiposity. The first report addressing body mass index in infected patients was a study carried out in the region of Seattle, which showed a mortality of around 60% percent among obese patients. Recent research suggests that overweight and obese adult people could be more prone to developing the severe form of COVID-19. Indeed, a multivariate linear regression analysis in infected patients from the USA, demonstrated a significant correlation between COVID-19 infection, age and BMI, the latter of which also impacting infection severity in children, adolescents and young adults, with higher incidence in those who were overweight or obese. Moreover, recent analyses in 4,013 COVID-19 patients in New York City also predicted obesity as a strong factor associated with critical illness. In Shenzhen, analyses carried out with 383 COVID-19 patients showed that obese patients were at higher risk to develop severe pneumonia, when compared with eutrophic patients. Thus, it is clear that higher adiposity and obesity are presently considered the main conditions associated with higher severity of COVID-19 and with mortality in patients less than 50 years of age. Unfortunately, the molecular mechanisms and biological processes underlining obesity impact on COVID-19 remain unclear.

By using transcriptomic data available in the Gene Expression Omnibus (GEO) repository (Supplementary Table 1), we have found that lung epithelial cells infected with SARS-CoV-2 (GSE147507) show increased expression of 161 genes, including of major mediators of the cytokine response, cellular response to type I

interferon, and neutrophil mediated immunity. The analysis of transcriptomic data of adipose tissue obtained from obese GEO individuals (GSE48964) revealed common genes with enhanced expression in SARS-CoV-2 infected lung epithelial cells. The retrieved genes in the analysis are those related with the immune response. Therefore, augmented inflammatory cytokine secretion by the white adipose tissue might be the missing molecular link between obesity and aggravation of COVID-19 symptoms. This integrative re-analysis demonstrates a set of 13 elevated common cytokines in lung epithelial cells infected with SARS-CoV-2 and in adipose tissue obtained from obese individuals, including CCL20, CXCL2, HBEGF, I-CAM1, IL1A, IL-1 β , IL-6, LIF, NFKBIA, NFKBIZ, SERPINB2, SOD2, and TNFAIP3. Thus, we suggest that the adding effect of cytokines expressed by infected lung cells and by white adipose tissue may partly explain the inflammatory dimension reached within the cytokine storm when obesity is present in COVID-19 patients.

In conclusion, taking into account the worldwide high prevalence of obesity (over 13%) and its plausible link with the global COVID-19 pandemic, we propose common pulmonary and WAT cytokine-mediated signalling pathway genes, whose increased expression may be the element connecting obesity and severe COVID-19