

Many studies pointed to il-6 as a hall marker for severity and prognosis of covid-19 patients and represent the most important cornerstone at the discovery of many drugs for inhibition of it for switch-off of cytokine storm which is the concern of all scientists and patients together and a new disease at future medicine as covid-19 begin at last of December 2019. The sources of il-6 after viral stimulation are from macrophages and monocytes at many inflammatory sites or from stimulation of the HPA axis (endocrine il-6 ACTH stimulated) or respiratory il-6 stimulated by strenuous resistive breathing because contracting of respiratory muscles is considered like exercise and produces cytokines due to glycogen depletion The Discovery of a non-invasive and easy method to examine il-6 which is the most important marker for severity and cytokine storm represent a new horizon for future viruses and modern medicine and that accelerates the intervention and depression of cytokine storm as early as possible and open the door for the discovery of many drugs work on this exhaled il-6 so our method for examination of il-6 at exhaled of covid and postcovid-19 patients help doctors for rapid categorization of patients and suspicion of severity. So, our study is a novel method for examination of il-6 Herein we intend to investigate the level of IL-6 in a breath of COVID-19 patients for the diagnosis of the early stages of lung inflammation and fibrosis. LTB4 is a potent chemoattractant and stimulator of neutrophils, without any significant effect on airway muscle. And increased in exhaled of children with mild and moderate to severe persistent asthma.

COVID-19 has emerged as a global pandemic. It is mainly manifested as pneumonia which may deteriorate into severe respiratory failure. The major hallmark of the disease is the systemic inflammatory immune response characterized by Cytokine Storm (CS). CS is marked by elevated levels of inflammatory cytokines, mainly interleukin-6 (IL-6), IL-8, IL-10, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interferon- $\gamma$  (IFN- $\gamma$ ). Of these, IL-6 is found to be significantly associated with higher mortality. IL-6 is also a robust marker for predicting disease prognosis and deterioration of clinical profile. (1) IL-6 was detectable in the breath condensate of all the healthy non-smokers but was significantly higher in the COPD patient. Exhaled breath condensate is totally non-invasive and highly acceptable to patients. The collection procedure does not affect airway function or inflammation, and there is growing evidence that abnormalities in condensate composition may reflect biochemical changes in airway lining fluid. This method has been successfully used in previous studies to investigate several inflammatory markers in COPD and asthmatic patients. (2) IL-6 is produced in the lung by interstitial fibroblasts, alveolar macrophages, and large-vessel and bronchial epithelial cells. IL-6 levels are high in chronic inflammatory conditions of the lung, such as those due to allogeneic transplantation, bleomycin-induced fibrosis, and a variety of human interstitial lung diseases. High levels of IL-6 have been found in the induced sputum of patients with COPD, particularly during exacerbation. Park et al. found increased IL-6 levels in the Bronchioalveolar lavage fluid of patients with non-specific interstitial pneumonia/fibrosis and some patients with interstitial

pneumonia. (3) Dowlati et al. have reported increased levels of IL-6 in the serum and BAL fluid of patients with lung cancer. (4) A recent study by Bhowmik et al. found increased IL-6 and IL-8 levels in the sputum of COPD patients with frequent exacerbations. (5) Also, in another study Exhaled interleukin-6 and leukotriene B4 levels may be useful noninvasive markers of airway inflammation in cigarette smokers. (6) These studies and our novel method after clinical trials may open the field for future therapies for covid-19 and post covid-19 lung fibrosis by inhaler transport medicines as a new challenge for overcoming sequels of this pandemic. And this suggested new procedure for measurement of exhaled il-6 takes us to study which is IL-6 is risky is IL-6 produced from the airway or endocrine IL-6 or immune IL-6 From previous studies we need a procedure acceptable to patients and easy, noninvasive, sensitive study involved 20 healthy controls and 20 patients with moderate to severe covid-19 according to CDC classification and 20 patients post covid-19 with lung fibrosis to estimate the measurement of interleukin-6 at exhaled condensate, this clinical randomized control study consists of 3 arms for 6 months ( all participants above 18 years nonpregnant humans )

<https://europepmc.org/article/PPR/PPR443651v>

<https://doi.org/10.18103/mra.v10i2.2667>

[NCT05157204](https://clinicaltrials.gov/ct2/show/study/NCT05157204)