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Sequencing of SARS-COV-2 and Assessment the Level of Pro Inflammatory Cytokine during COVID-19 Infection in Diyala Governorate

A Thesis

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1.1 Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious respiratory disease resulting from a life-threatening novel coronavirus, sever acute respiratory syndrome - corona virus-2 (SARS-CoV-2). As of 20th February 2021, there have been 110,743,440 confirmed cases and 2.452.437 deaths by the SARS-CoV-2 disease worldwide (CSSE, 2021).

Sever acute respiratory syndrome - corona virus-2 is an enveloped, non-segmented, single-stranded, positive sense RNA virus (+ssRNA). The genome size ranges from (27 to 32 kb) a cap structure at the 5′ end followed by a reader sequence of about 70 bases, several open reading frames (ORFs) coding various proteins, and a non-translated region including a poly-A sequence at the 3′ end (Khailany *et al*., 2020).

The main transmission route of SARS-CoV-2 through direct, indirect, or close contact with infected people through saliva and respiratory secretions or their respiratory droplets, which are expelled during coughs, sneezes, talks or sings (Pung *et al*., 2020). Sever acute respiratory syndrome - corona virus-2 RNA has also been detected in other biological samples, including the urine and feces of some patients (Pan *et al*., 2020).

The SARS-CoV-2 infection mainly presents flu-like symptoms such as cough, fever, fatigue and myalgia. Patients may initially present with diarrhea and nausea a few days before developing a fever. This suggests that fever, is dominant but not the premier symptom of infection. A small number of patients have headache or hemoptysis (Wang *et al.*, 2020a). The clinical presentation of SARS-CoV-2 start within 14 days of exposure; however, in most cases symptoms present after about 5 days and symptom onset is within 11 days in 97.5% of individuals (Lauer *et al.*, 2020). Clinical data show that an increasing

number of SARS-CoV-2 patients present circulatory symptoms (palpitations, chest tightness, short of breath) as the initial symptoms (Huang *et al.*, 2020).

The inflammatory cytokine storm during SARS-CoV-2 infection is closely related to the development and progression of acute respiratory distress syndrome (ARDS). The serum levels of cytokines are significantly increased in patients with ARDS. Degree of increase is positively correlated with mortality rate (Parsons *et al.*, 2005). Cytokine storm characterized by a high level of interleukin-6 (IL-6) in the serum and the levels in the sever group were higher than those in the moderate group in many recent clinical trials (Chen *et al.*, 2020a). Several studies show high level of pro-inflammatory cytokine in patient with SARS-COV-2 these include IL-1, IL-2, IL-6, IL-8, IL-17, Granulocyte colony-stimulating factor (GCSF), Granulocyte-macrophage colony-stimulating factor (GM-CSF)) and chemokine's like interferon gamma-induced protein-10 (IP-10) and monocyte chemo attractant protein-1 (MCP-1) in the sera during the disease and may play a key role in the development of lung dysfunction by leading to the accumulation of immune cells within the lungs (Cao, 2020; Shi *et al.*, 2020). There is emerging evidence supporting the role of IL-17 in SARS-CoV-2 pathogenesis, including a report on the first anatomopathological lung analysis with a high number of T helper-17 lymphocytes in the alveolar space (Xu *et al.*, 2020). Furthermore, IL-17 promotes viral survival by inhibiting apoptosis in concert with IL-6 (Hou *et al.*, 2014).

Several studies have been conducted in various Iraqi cities such as that of Hussein *et al.*, (2020) who studied the effect of SARS-COV-2 outbreak among patient with kidney diseases in Kirkuk city, while Al-Malkey and Al-Sammak (2020) who determine the epidemiology status of SARS-COV-2 in Iraq.

1.2 Aims of Study

1. To determine the rate and sequencing of SARS-COV-2 infection among patients with respiratory symptoms using reverse transcriptase polymerase chain reaction in Diyala Governorate.

2. To evaluate the level of Pro-inflammatory cytokines such as IL-6 and IL-17 among patients with SARS-COV-2.

3. Investigating the correlation between SARS-COV-2 infection and patient's descriptive data such as gender, age, residence, education level, state of work, clinical signs, vital signs (Spo2, bpm, and BP), blood groups, contact with COVID-19 patient, having other disease and smoking habit.