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# Impact of IL-22 SNP (rs761162880), Serum Ferritin, D-Dimer and C-Reactive Protein in Sever COVID-19 Patients

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**Abstract:** People with COVID-19 infection experience a range of problems, each with differing degrees of severity. Because of this, assessing its analytical values is essential to anticipating and minimizing the dangers and difficulties associated with this condition. This study was conducted to determine whether the COVID-19 severity is correlated with the polymorphisms of SNP(rs761162880), in the IL-22 gene. Investigations the role of serum ferritin, D-dimer and C-reactive protein in COVID-19 severity. For the detection of SARS-COV-2, RT-PCR was used. The samples were subjected to D-dimer, ferritin, and CRP tests. Polymerase Chain Reaction (PCR) and DNA sequencing was used for genotyping. The findings showed that there was a significant increase in ferritin, D-dimer and CRP (p value <0.01). In order to forecast and avoid potential COVID-19 consequences. It was concluded the crucial to analyse the biochemical parameters of individuals infected with the virus in order to evaluate the severity and course of the illness. COVID-19 severity is not correlated with the polymorphisms of SNP(rs761162880).

**Keywords:** RT-PCR; DNA Sequencing; SNP; COVID-19; C-reactive protein; D-dimer; ferritins.

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## Introduction

SARS-CoV-2 that causes the 2019 Coronavirus Disease (COVID-19) is a pandemic of infectious diseases that causes severe acute respiratory syndrome (ARDS) (1). This 2019-CoV is the third and deadliest human virus after an epidemic of Transmission by zoonotic agents of CoV, 2003's SARS-CoV, and 2012's MERS-CoV (2,3).Patients with COVID-19 may have a range of symptoms. Although not all of the symptoms have been identified, at least 26 of them have been identified. It is imperative to underscore the large number of presentations since broad language, including neurological and skin-related signs, point to a variety of distinct reactions. This may lead to an increase in the quantity of indications and symptoms. Fever, headaches, dyspnea, and coughing are the most prevalent, non-specific symptoms of SARS-CoV-2 (4,5).The 2019 coronavirus disease is categorised into three severity levels. For instance, viral pneumonia and viral infection can cause the flu, which can result in first-stage illness for which patients may need to be hospitalised or kept on a ventilator for an extended period of time. Additionally, the second stage makes a distinction between coagulopathy and pulmonary inflammation, which can occur simultaneously but frequently overlap.

Fibrosis is the final stage of the illness. There are two respiratory phenotypes that can be identified in patients who need mechanical ventilation: low and high elastance. The H-type has more lung edoema, which increases pulmonary weight and decreases lung compliance (6).Given the significant role the respiratory system plays in suspected COVID-19 patients, a chest CT scan is highly recommended for both initial and follow-up screening. Even though CT scans can be performed before symptoms appear, X-rays of the chest are not very useful for diagnosis in the early stages. Moreover, CT results were shown to be diagnostic in a few instances after a real-time reverse-transcriptase polymerase chain reaction (RT-PCR) false-negative result was obtained (7).Biomarker testing dependability is one of the major obstacles to enabling public health initiatives. When dealing with acute respiratory infections, real-time PCR is frequently used to detect the causative viruses in respiratory secretions (8).Laboratory biomarkers that forecast the severity of COVID-19 are essential in the case of a pandemic. because the distribution of resources must be carefully considered, especially in the case of respiratory aid readiness. Using a systematic review and meta-analysis, we looked at the relationship between a range of biomarkers and the severity of COVID-19, such as serum ferritin, D-dimer, and C-reactive protein. Interleukin-22 (IL-22) plays a significant role in tissue healing as well as host defense at mucosal surfaces (9).Has been found to play a role in several tissues, including the lung, kidney, liver, intestines, thymus, pancreas, and skin(10). Studies have shown that IL-22 can lessen the severity of pneumonia by regulating the immune system and performing tissue-protective or -regenerative actions. It is plausible to assume that IL-22 may also help to lessen the severity of COVID-19 because it is a respiratory ailment with symptoms and pathological traits that are comparable to those of other severe pulmonary virus infections. What's more, recent research has demonstrated that IL-22 has strong immune-stimulating, antiviral, and antibacterial characteristics to respiratory syncytial virus, which could possibly extend to managing SARS-CoV-2 infection (10). The development of potentially effective treatments and the prevention of infection transmission are both aided by polymophisms linked to disease origin study. SNPs are a typical sort of these polymorphisms that are acknowledged to be active to play a significant role in the pathogenicity of a microbial agent, disease immunity, susceptibility, and severity of diseases (5). A growing body of evidence points to genetic variations in genes connected to immunological illnesses, various infections, or both as potential causes of COVID-19's severe symptoms (11). We looked examined the association between an IL-22 SNP (rs761162880) and number of biomarkers using a systematic review and meta-analysis, including as serum ferritin, D-dimer and C-reactive protein with the COVID-19 severity.

## Materials and methods

### Samples collection

This research was achieved in Al Yarmuk Teaching Hospital, during the period from December 2022 to the end of June 2023. The Ethics Committee, Department of Biology, (CSEC/1022/0137). Ninety Iraqi patients who were admitted to various isolation units and exhibited favorable SARS-CoV nasal swaps assessed by real-time reverse transcriptase PCR were included in the study. The hospital

was visited by those who had low oxygen saturation, weakness, vomiting, diarrhoea, and systemic illnesses. Each patient had their venous blood drawn on the second day of their admission to the hospital, and four tubes containing three milliliters of whole blood were used to collect blood specimens. The (Nyco Card kit from Abbott USA) is a non-heparinized tube (gel tube) that is used to test for C-reactive protein. The serum is extracted and purified from the tube by centrifuging it for ten minutes at 3000 RPM (rpm). The second tube contains sodium citrate, an anticoagulant, which is used to test D-dimer (Cardiac AFIAS D-Dimer kit from United Medical Company, China). The third tube (a Boditech AFIAS Ferritin kit from United Medical Company, China) is used to test ferratin using plasma. Fourth one is EDTA-heparinized tube which used for human DNA extraction.

**RNA extraction**

Following the directions on Nucleic acid extraction kit (Magnetic Bead Method) from Zybio Inc/China. (YXB20180096). For the extraction and processing of SARSCoV-2 RNA, a 200 µL sample volume is strongly suggested. Manual, semi-automated, and automatic approaches are available. Nucleic acid extraction is being carried out simultaneously for the Positive Control for SARS-CoV-2 and the Negative Control for SARSCOV-2.

**RT-PCR assay for SARS-COV-2 detection**

The PCR Rotor Gene Q Zybio Kit from China Company was utilised to perform Real-Time Polymerase Chain Reaction (PCR) in order to detect SARS-COV-2 RNA in samples taken from the Nasopharyngeal Swap. This product qualitatively detected SARS-CoV-2 RNA in the samples by measuring the intensity of fluorescence signals during RT-PCR amplification using certain primers and probes against the conserved areas of the N, RdRP, and s genes.Each PCR reaction tube with filter tips held ten microliters of the SARS-CoV-2 Positive Control and SARSCOV-2 Negative Control nucleic acid samples. After transitory centrifugation to avoid creating bubbles in tubes, they were transferred to the amplification detection zone and capped with caps.Tubes for PCR reactions were used. The number and sequence of the sample were recorded in a fluorescent PCR device, and the ABI 7500 was used as an example to choose the following PCR amplification settings as seen in (Table 1).

**Table (1): RT-PCR protocol used to detect SARS-CoV-2.**

| Steps | Temperature | Time | Cycle |
|---|---|---|---|
| **UNG reaction** | 37°C | 1 min | 1 |
| **Reverse transcription** | 50°C | 5 min | 1 |
| **Initial denaturation** | 95°C | 2 min | 1 |
| **Denaturation** | 95°C | 5 sec | 45 with Amplification and fluorescence detection step |
| **Amplification and fluorescence detection** | 60°C | 30 sec | |

Report Fluorescence Setting: Passive Reference Setting None, Quenching Fluorescence Setting None, FAM, ROX, CY5, and Vic. Step 5 Report Fluorescence Setting: FAM, ROX, CY5, and Vic; Quenching Fluorescence Setting: None; Passive Reference Setting: None; Fluorescence Detection.

**Human genomic DNA isolation**

To isolate DNA of COVID -19 patients and healthy people, the EasyPure Genomic DNA Kit was used in order to extract the genomic DNA.

At -20°C, the pure DNA was kept. After that, agarose gel electrophoresis was performed on the isolated DNA to verify its integrity and existence (12).

**Molecular detection of IL-22 SNP (rs761162880)**

**Primers of pcr**

Primer used in this study were designed according to their reference sequence in the database of the National Centre for Biotechnology Information (NCBI). The Primer 3 plus, V4 and University Code of Student Conduct (UCSC) programs were used to design the primers and synthesized by Alpha DNA, S.E.N.C. (Montreal) and stored lyophilized. The sequences of primers used in the experiments in this study are shown in (Table 2).

**Table (2): Designed Primer used in the study**

| Primer | Sequence (5′→3′ direction) |
|---|---|
| **Forward** | TTTCTGATCACCTCCAATGAGA |
| **Reverse** | CCTCCTTAGCCAGCATGAAG |

**Primer sequence matching:**

Detecting primers for (rs761162880) genotyping were prepared. The primer sequences were designed in accordance with their reference sequences (rs) in the NCBI (National Center for Biotechnology Information) database. The genotyping primer sequences were matched by NCBI's bioinformatics programs.

**Master mix of PCR**

The 2xEasyTaq PCR SuperMix components.

- Taq DNA polymerase
- dNTPs
- Optimized reaction buffer

**Program of PCR**

PCR reactions were carried out in a 25 µl final volume and according to the manufacturer's instructions. As Fellows:

1. The master mix was thawed at room temperature (25°C).
2. The component volumes needed to prepare the required reaction numbers were calculated according to the (Table 3).
3. The tube containing all of the components was briefly centrifuged to spin the contents down and eliminate any air bubbles.
4. The tube was set inside the PCR well and the program was run.
5. The PCR program conditions were designed for this study as shown in (Table 4).

**Table (3): The components and volumes of PCR reaction.**

| Component | Volume 25 µl |
|---|---|
| 2xEasy*Taq*® PCR SuperMix | 12.5µl |
| Forward primer | 1 µl |
| Revers primer | 1 µl |
| DNA | 4µl |
| Nuclease free water | 6.5µl |

**Table (4): PCR program.**

| Step | Temperature (°C) | Time | cycle |
|---|---|---|---|
| **Denaturation** | 94 | 5 min | 1 |
| **Denaturation** | 94 | 30 sec | 35 |
| **annealing** | 60 | 30 sec | |
| **Extension** | 72 | 30 sec | |
| **Extension** | 72 | 5 min | 1 |

**Analysis of PCR product**

The generated PCR fragments were subjected to Sanger sequencing using an ABI3730XL automated DNA sequencer (Macrogen Corporation, Korea). Once aligned with a reference sequence in the Gene Bank, the genotypes were shown by the Bioedit software.

**Estimation of ferritin**

With a pipette, a handered microliter of sample was taken and put into the cartridge's sample well. In the cartridge holder, the cartridge was inserted. A tip was put into the cartridge's tip hole. On the screen, the 'START' symbol was tapped. After 10 minutes the test result was presented on the screen.

**Estimation of D-dimer**

With a pipette, a handered microliter of sample was taken and put into the cartridge's sample well. In the cartridge holder, the cartridge was inserted. A tip was put into the cartridge's tip hole. On the screen, the 'START' symbol was tapped. After 12 minutes the test result was presented on the screen.

**Estimation of C- reactive protein**

Five microliters of patient sample or Afinion CRP Control were put into a capillary and placed into a tube of R1/dilution liquid. The tube was tightly closed and thoroughly stirred for 10 seconds. On the TD/test apparatus, fifty microliters of diluted sample or diluted Afinion CRP Control were administered. The material was allowed to soak into the membrane for a period of time (approx. 30 seconds). On the TD/test device, one drop of R3/washing solution was given. For (approx .20 seconds) of time, the reagent was allowed to soak into the membrane. The NycoCard Reader II was used to read the results within 5 minutes. And the Reader II User Instruction Manual was followed.

**Statistical analysis**

The Statistical Analysis IBM SPSS Statistics 26 program was used to detect the effect of different factors on study parameters. One-way ANOVA and T-test was used to significantly compare between means. Chi-square test was used to significantly compare between percentage (0.05 and 0.01 probability).

**Results and discussion**

In this study, 90 Iraqi patients between the ages of 16 and 92 had COVID-19 infections, which were categorised into three severity categories based on their symptoms according WHO classification and doctor’s evaluation (mild, moderate, severe, and critical) (Table 5). Real-time PCR was used to identify SARS-CoV-2 in all samples based on a nasopharyngeal swab. D-Dimer, and AFIAS A sandwich immunodetection technique was employed in the test. Using the NycoCard CRP sandwich structure, an immunometric assay. There was statistical difference (high significant different) ($p$ value <0.01) between the patient and the control group. As seen in the (Table 6) for all parameters Mean±SE Ferritin (519.37± 215.46), D-dimer (3.40± 1.12) and C-reactive protein (41.09± 16.07).

**Table (5): Distribution of patient according to the severity of diseas.**

| Group | | Frequency | Percent |
|---|---|---|---|
| Patients | Moderate | 30 | 33.3% |
| | Sever | 30 | 33.3% |
| | Critical | 30 | 33.3% |
| | Total | 90 | 100.0% |
| Control | Control | 30 | 100.0% |

**Table (6): Statistical analysis results of Ferritin, D. Dimer and C-reactive protein in patient and control group**

| Group | | Ferritin | D-Dimer | CRP |
|---|---|---|---|---|
| Patients | Mean | 519.37 | 3.40 | 41.09 |
| | Std. Deviation | 215.46 | 1.12 | 16.07 |
| Control | Mean | 56.70 | 0.75 | 0.22 |
| | Std. Deviation | 24.60 | 0.77 | 0.09 |
| p-value | | 0.001** | 0.001** | 0.001** |

Ferritin levels increased significantly across a range of severity levels, with very significant increases (p value <0.01) between moderate group and sever, critical groups as shown in (Table 8); mean ± SE (369.61 ±137.29) in the mild or moderate group, (584.79 ± 88.54) in the severe group, and (593.11 ± 303.33) in the critical group. Current study suggests that elevated ferritin levels may be observed during the acute phase of a reaction and that it may contribute to inflammation during a cytokine storm(13). Serum ferritin levels were found to be significantly higher in extreme cases. Ferritin levels were higher in non-survivors among a previous study, which was consistent with our results(14).Furthermore, it was demonstrated that ferritin levels increased in direct proportion to the illness's severity(15).Moreover, serum ferritin levels above 300 ng/mL were linked to a higher risk of death compared to ferritin levels below 300 ng/mL.(16).As seen in the (Table 7) there was no significant influence of sex on the parameters .With varying degrees of severity, a substantial rise in D-dimer was discovered with highly significant (p value, 0.01) differences between moderate, sever groups and critical group. Mean ± SE (2.99 ±1.05) in mild or moderate group, (3.26 ± 1.00) in severe group while (3.88 ± 0.86) in critical group as seen in the (Table 8) COVID-19 patients with severe symptoms exhibited a higher D-dimer level than those with lesser symptoms. Elevated D-dimer was found more frequently in COVID-19 dead patients, and levels greater than 1 g/ml were associated with a higher risk of hospital death(16).D-dimer tests are frequently employed in clinical practise to rule out the diagnosis of embolism pulmonary or deep vein thrombosis. Elevated D-dimer levels indicate an increased chance of atypical blood coagulation. Elevated D-dimer levels have also been associated with a higher death risk from community-acquired pneumonia.(17). Patients with severe community-acquired pneumonia had significantly greater D-dimer levels, whereas those with normal D-dimer values had a lower risk of sequelae(18).as can be seen in (Table 7). There was no significant influence of gender on the D-dimer with varying degrees of severity, a substantial rise in CRP was identified with a very significant (p value< 0.01) difference between moderate group and sever, critical groups. Mean ± SE (33.75 ±6.02) in mild or moderate group, (43.94 ± 18.56) in severe group, while ( 45.60 ± 18.08) in critical group as seen in the (Table 8). It was discovered that 86 percent or more of severe COVID19 patients had increased CRP levels(19).Compared to patients with mild or non-severe infections, those with severe infections had significantly higher CRP levels. Another study found that the average CRP value for individuals with severe symptoms was 39.4 mg/L, while the average CRP value for those with mild symptoms was 18.8 mg/L(20).In a different study, the mean CRP levels of

severe patients were significantly higher (46 mg/L) than those of non-severe patients (23 mg/L) (21).The median CRP levels of COVID-19 patients who died were 10 times greater than those of those who survived (100 vs. 9.6 mg/L)(22).A recent study found that 7.7% of non-severe COVID19 patients progressed to severe disease courses after being admitted to the hospital.In comparison to non-severe cases, patients with worsened conditions had significantly higher CRP values (43.8mg/L vs. 12.1 mg/L). The authors proposed CRP as a useful indicator for predicting COVID19 aggravation in non-severe COVID19 patients after it was demonstrated that CRP values had a high correlation with the worsening of non-severe COVID19 patients. The ideal threshold value for CRP is 26.9 mg/L.

The risk of severe episodes rises by 5% for every unit increase in CRP levels in COVID-19 patients(23).as seen in the (Table 7). There was no discernible variation in the impact of gender on the parameters.

**Table (7): Statistical analysis results of Ferritin, D. Dimer and C-reactive protein in patient according to the Sex.**

| Group | Sex | | Ferritin | D-Dimer | CRP |
|---|---|---|---|---|---|
| Patients | Male | Mean | 558.59 | 3.33 | 38.39 |
| | | Std. Deviation | 473.98 | 3.89 | 43.68 |
| | Female | Mean | 502.05 | 3.94 | 36.67 |
| | | Std. Deviation | 409.90 | 4.93 | 39.97 |
| | P-value | | 0.5 | 0.5 | 0.8 |

**Table (8): Statistical analysis results of Ferritin, D. Dimer and C-reactive protein in patient according to the severity of disease.**

| Type of severity | | Ferritin | D-Dimer | CRP |
|---|---|---|---|---|
| Moderate | Mean | 369.61b | 2.99 b | 33.75 b |
| | Std. Deviation | 137.29 | 1.05 | 6.02 |
| Sever | Mean | 584.79 a | 3.26 a | 43.94 a |
| | Std. Deviation | 88.54 | 1.00 | 18.56 |
| Critical | Mean | 593.11 a | 3.88 a | 45.60 a |
| | Std. Deviation | 303.33 | 0.86 | 18.08 |
| p-value | | 0.001** | 0.002** | 0.007** |

**Means followed by different letters are significantly different according to Duncan's multiple range comparisons (DMRTs), Means followed by the same letter are not significantly different**

As shown in (Table 9) the influence of age on parameters is significant. (P-value<0.01) for ferritin, D-dimer and CRP.

**Table (9): Statistical analysis results of Ferritin, D. Dimer and C-reactive protein in patient according to the Age**

| Group | Age | | Ferritin | D-Dimer | CRP |
|---|---|---|---|---|---|
| Patients | <40 | Mean | 327.38 b | 1.69 b | 29.83 b |
| | | Std. Deviation | 188.98 | 0.70 | 12.76 |
| | 40-60 | Mean | 556.39 a | 3.71 a | 34.29 a |
| | | Std. Deviation | 239.42 | 1.89 | 13.24 |
| | >60 | Mean | 570.72 a | 4.15 a | 42.23 a |
| | | Std. Deviation | 250.47 | 1.53 | 17.78 |
| | p-value | | 0.001** | 0.01** | 0.01** |

**Means followed by different letters are significantly different according to Duncan's multiple range comparisons (DMRTs), Means followed by the same letter are not significantly different.**

Numerous studies have reported a high fatality rate from SARS-CoV-2 infection, especially in older adults with concomitant illnesses. The expected increase in severity with age has been seen in a few cases. Estimates indicate that, with an average age range of 50 to 60 years(24).Patients over 60 are more prone to get respiratory failure. This demonstrated that COVID-19 patients with advanced age had a more serious illness than those with earlier age(25).Additionally, the current study found that COVID-19 cases in the 50–60 age range tended to be more severe than cases in younger age groups.It has been demonstrated that older patients had pathologically higher levels of CRP, D-dimer, and ferritin than younger ones.The current study found that, as compared to a control group, individuals with varied degrees of severity (mild or moderate, severe, critical) had significantly higher levels of ferritin, D-dimer, and CRP (c-reactive protein). While the influence of gender is not significant in any of the characteristics, the effect of age is highly significant in all of them.

**Genotype and allele frequencies**

There was no significant correlation between rs761162880 and the severity of COVID-19 for both of genotypes GT, TT P-value 0.4,0.9 respectively (p-value >0.05) as seen in (Table 10).

**Table (10): Genotype and allele frequencies detected by Hardy-Weinberg equilibrium law of rs761162880 SNP between patient group and control group.**

| Genotype rs761162880 | Patient group No.=90 | Control group No.=30 | P-value | OR | CI 95% |
|---|---|---|---|---|---|
| **GG** | 60 (66.7%) | 22 (73.3%) | -- | 1.00 | (Reference) |
| **GT** | 24 (26.7%) | 6 (20.0%) | 0.4 | 1.4 | 0.5292 to 4.0645 |
| **TT** | 6 (6.7%) | 2 (6.7%) | 0.9 | 1.1 | 0.2064 to 5.8623 |
| **Total** | 90 | 30 | -- | -- | -- |
| **Allele Frequency** | | | | | |
| **G** | 80.0% (144) | 83.3% (50) | -- | 1.00 | (Reference) |
| **T** | 20.0% (36) | 16.7% (10) | 0.5 | 1.2 | 0.5782 to 2.7023 |

The frequency of the GT genotype and the severity of COVID-19 showed a significant correlation, showing an increased risk in the moderate (p-value= 0.05) and OR=3.1 more risk factor from other while no significant correlation between the frequency of TT genotype and severity of COVID-19 (p value= 0.2 , p > 0.05) and Control group as seen in (Table11).

**Table (11):Genotype and allele frequencies detected by hardy-Weinberg equilibrium law of rs761162880 SNP between patient (Moderate) group and control group.**

| Genotype rs761162880 | Moderate No.=30 | Control group No.=30 | P-value | OR | CI 95% |
|---|---|---|---|---|---|
| **GG** | 14 (46.7%) | 22 (73.3%) | -- | 1.00 | (Reference) |
| **GT** | 12 (40.0%) | 6 (20.0%) | 0.05 | 3.1 | 0.9588 to 10.3018 |
| **TT** | 4 (13.3%) | 2 (6.7%) | 0.2 | 3.1 | 0.5067 to 19.492 |
| **Allele Frequency** | | | | | |
| **G** | 66.7% (40) | 83.3% (50) | -- | 1.00 | (Reference) |
| **T** | 33.3% (20) | 16.7% (10) | 0.03 | 2.5 | 1.0521 to 5.94 |

There was no significant correlation with sever group for both of genotypes GT, TT p-value 0.5,0.9 respectively (p-value >0.05) as seen in (Table 12).

**Table (12): Genotype and allele frequencies detected by Hardy-Weinberg equilibrium law of rs761162880 SNP between patient Sever group and control group.**

| Genotype rs761162880 | Sever No.=30 | Control group No.=30 | P-value | OR | CI 95% |
|---|---|---|---|---|---|
| **GG** | 20 (66.7%) | 22 (73.3%) | -- | 1.00 | (Reference) |
| **GT** | 8 (26.7%) | 6 (20.0%) | 0.5 | 1.4 | 0.4332 to 4.965 |
| **TT** | 2 (6.7%) | 2 (6.7%) | 0.9 | 1.1 | 0.1414 to 8.55 |
| **Allele Frequency** | | | | | |
| **G** | 80.0% (48) | 83.3% (50) | -- | 1.00 | (Reference) |
| **T** | 20.0% (12) | 16.7% (10) | 0.6 | 1.2 | 0.4942 to 3.16 |

There was no significant correlation with Moderate group for both of genotypes TG, GG p-value 0.2,0.5 respectively (p-value >0.05) as seen in (Table 13).

**Table (13): Genotype and allele frequencies detected by Hardy-Weinberg equilibrium law of rs761162880 SNP between patient Critical group and control group.**

| Genotype rs761162880 | Critical No.=30 | Control group No.=30 | P-value | OR | CI 95% |
|---|---|---|---|---|---|
| **GG** | 26 (86.7%) | 22 (73.3%) | -- | 1.00 | (Reference) |
| **GT** | 4 (13.3%) | 6 (20.0%) | 0.4 | 0.5 | 0.1410 to 2.25 |
| **TT** | 0 | 2 (6.7%) | 0.2 | 0.1 | 0.0077 to 3.72 |
| **Allele Frequency** | | | | | |
| **G** | 93.3% (56) | 83.3% (50) | -- | 1.00 | (Reference) |
| **T** | 6.7% (4) | 16.7% (10) | 0.09 | 0.3 | 0.1054 to 1.21 |

To the best of the information we have, this study is the first to show a connection between the polymorphisms in IL-22 (rs761162880) with the prognosis of COVID-19 and ARDS. The risk of ARDS and the prognosis for COVID-19 were shown to be not associated with polymorphisms of IL-22, rs761162880 in the current study.

## Conclusion

Serum ferritin, C-reactive protein, and D-dimer analytical values were altered in the patients with significant symptoms. In individuals with severe symptoms, there were significant changes in all of these indicators. In order to forecast and avoid potential COVID-19 consequences, it is crucial to analyses the biochemical parameters of individuals infected with the virus in order to evaluate the severity and course of the illness. COVID-19 severity is not correlated with the polymorphisms of SNP(rs761162880).

## References


1. Farah, H. and Ali, I. A. (2023). Molecular Detection of Candida spp. Isolated from Female Patients Infected with COVID-19 in Baghdad City. Iraqi Journal of Biotechnology, 22(1).
2. AL, A. D. A. A. N. (2022). Determination of Angiotensin-Converting Enzyme 2 (ACE2) Receptor Level in Samples of Iraqi Patients Infected with COVID-19. Iraqi Journal of Biotechnology, 21(2).
3. Hussein, T. A. A. and Fadhil, H. Y. (2023). Impact of inflammatory markers, dread diseases and cycle threshold (Ct) Values in COVID-19 progression. Bionatura.
4. Mahmood, Z. S.; Fadhil, H. Y. and Ad, A. H. (2021). Estimation of hematological parameters of disease severity in Iraqi patients with COVID-19. Iraqi Journal of Science, 3487-3496.
5. Al-Suhail, R. G. A. and Ali, L. F. (2021). Statistical Analysis of COVID-19 Pandemic Across the Provinces of Iraq. Iraqi Journal of Science, 811-824.
6. Ghahramani, S.; Tabrizi, R.; Lankarani, K. B.; Kashani, S. M. A.; Rezaei, S., Zeidi, N., *et al*. (2020). Laboratory features of severe vs. non-severe COVID-19 patients in Asian populations: a systematic review and meta-

analysis. European Journal of Medical Research, 25(1):1-10.
7. Salehi-Abari, I.; Khazaeli, S.; Salehi-Abari, F. and Salehi-Abari, A. (2020). Practical guideline for screening the patients with SARS-CoV-2 infection and Persian Gulf criteria for diagnosis of COVID-19. Advances in Infectious Diseases, 10(03): 67.
8. Yang, A. P.; Liu, J. P.; Tao, W. Q. and Li, H. M. (2020). The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. International Immunopharmacology, 84: 106504.
9. Rutz, S.; Eidenschenk, C. and Ouyang, W. (2013). IL-22, not simply a Th17 cytokine. Immunological Reviews, 252(1): 116-132.
10. Fang, S.; Ju, D.; Lin, Y. and Chen, W. (2022). The role of interleukin-22 in lung health and its therapeutic potential for COVID-19. Frontiers in Immunology, 13: 951107.
11. Zhou, P.; Yang, X. L.; Wang, X. G.; Hu, B.; Zhang, L.; Zhang, W., *et al*. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature, 579(7798): 270-273.
12. Sambrook, J. and Russell, D. W. (2001). Molecular Cloning: Ch. 8. In Vitro amplification of DNA by the polymerase chain reaction (Vol. 2). Cold Spring Harbor Laboratory Press.
13. Kernan, K. F. and Carcillo, J. A. (2017). Hyperferritinemia and inflammation. International Immunology, 29(9): 401-409.
14. Taneri, P. E.; Gómez-Ochoa, S. A.; Llanaj, E.; Raguindin, P. F.; Rojas, L. Z.; Roa-Díaz, Z. M., *et al*. (2020). Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. European Journal of Epidemiology, 35: 763-773.
15. Li, X.; Xu, S.; Yu, M.; Wang, K.; Tao, Y.; Zhou, Y., *et al*. (2020). Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. Journal of Allergy and Clinical Immunology, 146(1): 110-118.
16. Zhou, F.; Yu, T.; Du, R.; Fan, G.; Liu, Y.; Liu, Z., *et al*. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet, 395(10229): 1054-1062.
17. Querol-Ribelles, J. M.; Tenias, J. M.; Grau, E.; Querol-Borras, J. M.; Climent, J. L.; Gomez, E. *et al*. (2004). Plasma d-dimer levels correlate with outcomes in patients with community-acquired pneumonia. Chest, 126(4): 1087-1092.
18. Snijders, D.; Schoorl, M.; Schoorl, M.; Bartels, P. C., van der Werf, T. S. and Boersma, W. G. (2012). D-dimer levels in assessing severity and clinical outcome in patients with community-acquired pneumonia. A secondary analysis of a randomised clinical trial. European Journal of Internal Medicine, 23(5): 436-441.
19. Chen, N.; Zhou, M.; Dong, X.; Qu, J.; Gong, F.; Han, Y., *et al*. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet, 395(10223): 507-513.
20. Gao, Y.; Li, T.; Han, M.; Li, X.; Wu, D.; Xu, Y., *et al*. (2020). Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. Journal of Medical Virology, 92(7): 791-796.
21. Mo, P.; Xing, Y.; Xiao, Y.; Deng, L.; Zhao, Q.; Wang, H., *et al*, Y. (2021). Clinical characteristics of refractory coronavirus disease 2019 in Wuhan, China. Clinical Infectious Diseases, 73(11): e4208-e4213.
22. Luo, X.; Zhou, W.; Yan, X.; Guo, T.; Wang, B.; Xia, H., *et al*. (2020). Prognostic value of C-reactive protein in patients with coronavirus 2019. Clinical Infectious Diseases, 71(16): 2174-2179.
23. Wang, G.; Wu, C.; Zhang, Q.; Wu, F.; Yu, B.; Lv, J., *et al*., (2020, May). C-reactive protein level may predict the risk of COVID-19 aggravation. In Open forum infectious diseases, US: Oxford University Press, 7 (5) :153.
24. Verity, R.; Okell, L. C.; Dorigatti, I.; Winskill, P.; Whittaker, C.; Imai, N., *et al*., (2020). Estimates of the severity of coronavirus disease 2019: a model-based analysis. The Lancet Infectious Diseases, 20(6):669-677.
25. Liu, Y.; Mao, B.; Liang, S.; Yang, J. W.; Lu, H. W.; Chai, Y. H.; *et al*., (2020). Association between age and clinical characteristics and outcomes of COVID-19. European Respiratory Journal, 55(5):1-4.