

**Characteristics and Outcomes of COVID-19 in Pediatric Patients with Chronic Diseases Attending Qena University Hospital, Upper Egypt**

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**Abstract**

**Background:** Considering the global SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) outbreak, comorbid conditions in children may enhance the risk of COVID-19-related severe morbidity and mortality with failure of chronic disease management.

**Objectives:** To explore the various clinical, laboratory, and radiological presentations of COVID-19 among pediatric patients having chronic diseases and correlate the data with the outcomes of the included patients.

**Patients and Methods:** This study was a descriptive study that was carried out on 36 pediatric patients with COVID-19 who have chronic diseases (16 cardiac patients, 8 neurological patients, 6 renal patients, 4 patients with genetic disorders, and 2 rheumatological patients) attending Pediatrics Department at Qena University Hospital. Clinical, laboratory, and radiological assessments of the included patients were performed. Serum angiotensin converting enzyme-2 (ACE-2) and tumor necrosis factor-alpha (TNF- $\alpha$ ) were measured using commercially available ELISA kits.

**Results:** Our study was conducted on 36 children, 22.22% of the studied cases were confirmed to have COVID-19, and 77.78% of cases were suspected. Regarding disease severity, 11.11% of cases were critical, 16.67% were severe, 44.44% were moderate and 27.78% were mild. The main symptoms were fever in 88.89%, dyspnea in 72.22%, and dry cough in 61.11%. The lymphocytic count was normal, decreased, and increased in 44.4%, 33.3%, and 22.2% of cases respectively. The neutrophilic count was increased, normal, and decreased in 55.56%, 27.7%, and 16.6% of cases respectively. TNF-alpha levels were higher in rheumatologic and neurologic groups. CT findings of COVID-19 were detected in 44.44% of cases. Regarding the outcome; 77.8% recovered, 11.11% had complications, and 5.6% died.

**Conclusion:** Although the clinical pattern of COVID-19 among pediatric patients with chronic diseases is more or less similar to adult pattern, laboratory and imaging findings differ, so this may be helpful for early detection of COVID-19 in pediatric patients with chronic disease to avoid unwanted outcomes.

**Keywords:** Characteristics, Pediatrics, Chronic diseases, COVID-19, Qena University Hospital (QUH).

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## Introduction

In late 2019, a study conducted by **Wu et al. (2020)** identified severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) as the etiological agent responsible for a series of severe pneumonia cases originating in Wuhan City, located in the Hubei Province of China. This assertion was substantiated by the identification of SARS-CoV2 as the causative agent behind several instances of severe pneumonia. The illness is often known as COVID-19, a novel coronavirus disease that emerged in 2019. Given its global transmission, the World Health Organization (WHO) officially declared it a pandemic on March 11, 2020 (**Hassany et al., 2020**). The sickness is often known as COVID-19, which stands for coronavirus disease 2019. Due to the extensive prevalence of the illness, it has been designated with this classification. SARS-CoV-2 belongs to the  $\alpha$ -coronavirus family, similar to prior iterations such as SARS-CoV and MERS-CoV can induce deadly infections (**Zaki et al., 2012**). The aforementioned strain has been associated with a severe respiratory ailment known as severe acute respiratory syndrome (SARS).

The incidence of SARS-CoV-2 infection is much lower in children compared to adults, and when infection does occur, it often manifests as a less severe illness with a lower mortality rate than seen in the adult population (**Su et al., 2020**). **Qiu et al. (2020)** conducted a study that revealed that the clinical manifestations of COVID-19 in pediatric patients have a resemblance to those seen in other respiratory viral infections. Some of the symptoms that individuals may encounter include fever, cough, shortness of breath, sore throat, diarrhea, nausea, vomiting, anorexia, and myalgia. Based on the findings of many studies, it has been shown that a considerable proportion of children who test positive for COVID-19 do not manifest any symptomatic indications at the time of first diagnosis (**Livingston et al., 2020**). A recent study conducted by **Hoffmann et al. (2020)** showed that SARS-CoV-2 utilizes the ACE2 receptor, similar to SARS-CoV, to facilitate cellular entry. This process is facilitated by the serine protease called TMPRSS2 (Transmembrane Serine Protease 2), which primes the S-protein. The aforementioned knowledge was disseminated in the scholarly publication *Virus Research*. The interaction between the surface of SARS-CoV-2 and ACE2 via the receptor binding domain (RBD) of the S-protein plays a crucial role in facilitating the transmission of the viral infection. The need for ACE2 is attributed to its role in facilitating the propagation of the infection.

In a research done by **Wrapp et al. (2020)**, it was shown that the interaction between ACE2 and the RBD of the SARS-CoV-2 virus is much more potent, ranging from 10 to 20 times greater, compared to prior strains of SARS-CoVs. This elucidates the mechanisms by which the virus exhibits heightened aggressiveness. The potential impact of cytokine storms on the pathogenesis of COVID-19 has been suggested by many lines of evidence. Elevated levels of various serum cytokines have been observed in patients experiencing cytokine storms associated with COVID-19. These cytokines include IL-1 $\beta$ , IL-6, interferon  $\gamma$ -induced protein-10 (IP-10), TNF- $\alpha$ , interferon- $\gamma$  (IFN- $\gamma$ ), macrophage inflammatory protein (MIP) -1 $\alpha$  and -1 $\beta$ , and vascular endothelial growth factor (VEGF) (**Wrapp et al., 2020; Merad and Martin, 2020; Rahmati et al., 2020; Neumann et al., 2020; Ahmed et al., 2023**). Children who experience comorbidity of many chronic illnesses are at an elevated risk of contracting COVID-19 and encountering suboptimal care for their pre-existing medical conditions. As a result of this, there is an increased prioritization of managing patients with chronic conditions throughout the pandemic. According to the studies conducted by **Lu et al. (2020)** and **Sun et al. (2020)**, it was observed that 40 % of the participants in the pediatric clinic with severe illness had concomitant chronic conditions. The aforementioned conclusions were derived from a comprehensive research study. The findings presented here are in alignment with data collected from many regions worldwide.

The aim of this work was to explore the various clinical, laboratory, and radiological presentations of COVID-19 among pediatric patients who had chronic diseases and attended the Pediatrics Department, Qena University Hospitals and correlate the laboratory and radiological data with the clinical criteria, disease severity, and outcomes of the included patients.

## Patients and methods

This was a descriptive study that was conducted in the Pediatrics Department of Qena University Hospitals including 36 children with COVID-19 who had comorbid chronic diseases during the period between January 2022 to January 2023.

**Inclusion criteria:** All children were less than 18 years of age, were infected with SARS-CoVs, and already had chronic diseases.

**Exclusion criteria:** Patients >18 years old or who refused to participate in the study.

## Methodology

1. All patients were subjected to the following:

- Complete history and full clinical examination .
  - Laboratory Investigations:
    - (A) Routine laboratory investigations:
      - Complete Blood Count (CBC): by Erma Automated Blood Count Machine (Tokyo, Japan).
      - Coagulation profile (PT, PC, and INR) and D-dimmer: by immune turbidimetry assay with the coagulational laboratory auto-analyzer (ACL 2000; Instrumentation Laboratory, Milan, Italy) (**Schafer et al., 2022**).
      - Kidney function test (serum creatinine) Liver profile (ALT, AST, and serum albumin), CRP, and LDH were measured by using a photometric unit of the auto-analyzer, the Cobas 6000 analyzer (c501 module) (**Kumar and Kaistha, 2023**).
      - Serum ferritin and troponin I by TOSOH AIA-360 Automated Immunoassay Analyzer, JAPAN) (**Singh et al., 2021; Garcia et al., 2021**).
    - (B) Specific biochemical assay: serum ACE2 and TNF-alpha were performed using commercial ELISA kits from Elabscience company, USA (catalog No: E-EL-H0281 96T for ACE2 and catalog No: E-EL-H0109 96T for TNF-alpha). Assays were performed using a microplate ELISA reader (EMR-500, USA) according to the manufacturer's detailed instructions.
    - (C) Laboratory investigation for COVID-19: all patients were tested for serum COVID-19 immunoglobulin (IgG and IgM), rapid SARS-COV-2 antigen serum testing, and RT-PCR confirmation from nasopharyngeal swab.
  - Radiological investigation: A non-enhanced computerized tomography (CT) scan of the chest was done using scanner Gantry Model CGGT-021A Japan. Severity was assessed using CORADS (Coronavirus Disease 2019-Reporting and Data System) (**Penha et al., 2021**).
2. All patients were diagnosed to have a recent COVID-19 with assessment of disease severity according to **Mostafa et al.(2020)**.
  3. All patients received medical treatment according to the algorithm for management of a child with COVID-19 (**Fig.1**) (**Mostafa et al., 2020**).

### Ethical aspects

The parents or caregivers of the participants provided written informed permission, and the researcher received approval from the local Ethics Committee at Qena Faculty of Medicine, South Valley University. All participants' parents in the present study were provided with comprehensive information on the purpose and specifics of the research, including the assurance that the findings would remain secret. Ethical approval code (SVU.MED.PED025.2.23.9.731).

### Statistical analysis

The analysis of the acquired data was conducted using version 26 of the Statistics Package for the Social Sciences (SPSS), a well-recognized statistical program. A comprehensive analysis was conducted to assess the normal distribution of the data, using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The results of these tests indicated that the data pertaining to Pulse, RR, Hb, MCV, HCT, Neutrophil/total WBCs, and S. albumin had a normal distribution. On the other hand, the data pertaining to other variables exhibited no adherence to a normal distribution in any manner. The data was provided to the reader in many ways, including raw numerical values, percentages, the arithmetic mean, and the standard deviation. Both the chi-square test and the Fisher exact test were used to achieve the objective of comparing different qualitative features. The continuous data were provided in two formats: either as the mean accompanied by the standard deviation (Mean+SD), or as the median together with the interquartile range (Median(IQR)). Both of these forms are often known as "Mean." The Kruskal-Wallis test was used to analyze the parametric data, while the One-Way ANOVA test was applied for the analysis of the non-parametric data in this work. Both of these tests demonstrated significant differences among all of the groups. The assessment of differences between each set of groups was conducted by using the independent samples T-test for data with parametric distributions, and the Mann-Whitney test for data without parametric distributions. The data in nominal form were presented as percentages, and the Chi-square test was used to ascertain the presence of any statistically significant variations among the groups. For a result to be deemed statistically significant, it is necessary for the p-value to be less than 0.05.

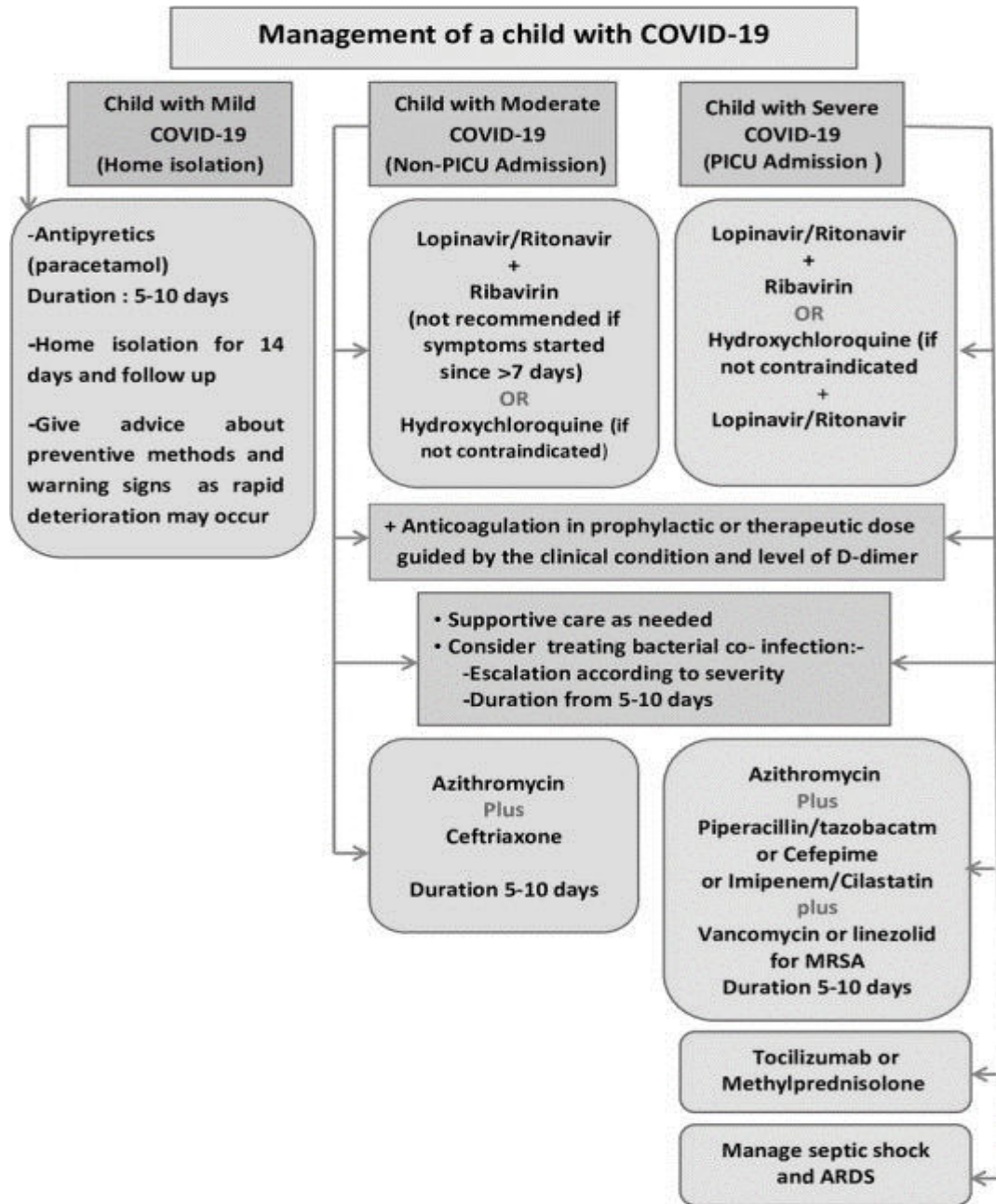


Fig.1. Algorithm for management of a child with COVID-19 (Mostafa et al., 2020).

**Results**

According to the studied pediatric patients’ classification, most patients were suspected of

COVID-19 according to case definition and most of the cases were moderate according to severity. (Table 1).

Table 1. Studied pediatric patients’ classification according to case definition and severity:

| Patients’ classifications                          | No. (n=36) | (%)   |
|--|------------|-------|
| <b>Classification according to case definition</b> |            |       |
| Confirmed  | 8          | 22.22 |
| Suspected  | 28         | 77.78 |
| <b>Classification according to severity</b>        |            |       |
| Mild   | 10         | 27.78 |
| Moderate   | 16         | 44.44 |
| Severe   | 6          | 16.67 |
| Critical   | 4          | 11.11 |

**Data analysis of the included pediatric patients with COVID-19:**

**Demographic and clinical data:** There were 24 males (66.6%) and 12 females (33.3%). The median age was 2 years (IQR of 0.75 – 5 years). There were 16 patients (44.4%) of low

social state and 20 patients (55.5%) of moderate social state in the studied patients. Clinical features of pediatric patients with COVID-19 disease were presented in (Table.2).

Table 2. Clinical manifestations

| Clinical features                                  | Patients no = 36  |
|--|-------------------|
| <b>(A) Symptoms:</b>                               |                   |
| <b>General manifestations:</b>                     |                   |
| <b>History of contact: No. (%)*</b>                | 4 (11.1%)         |
| <b>Fever:</b>                                      |                   |
| No. (%)  | 32 (88.8%)        |
| Duration (days): median (IQR)                      | 5 (3.25 – 7.75)   |
| <b>Respiratory manifestations:</b>                 |                   |
| <b>Rhinorrhea: No. (%)</b>                         | 6 (16.6 %)        |
| Duration (days): mean $\pm$ SD                     | (11.5 $\pm$ 1.73) |
| <b>Dry cough:</b>                                  |                   |
| No. (%)  | 22 (61.1 %)       |
| Duration (days): median (IQR)                      | 6 (5 – 12)        |
| <b>Dyspnea:</b>                                    |                   |
| No. (%)  | 26 (72.2 %)       |
| Duration days: median (IQR)                        | 7 (3.5 – 9.25)    |
| <b>GIT manifestations:</b>                         |                   |
| <b>Vomiting:</b>                                   |                   |
| No. (%)  | 6 (16.6 %)        |
| Duration (days): median (IQR)                      | 8.5 (5 – 12)      |
| <b>Diarrhea:</b>                                   |                   |
| No. (%)  | 4 (11.1 %)        |
| Duration (days): mean $\pm$ SD                     | (11.5 $\pm$ 1.73) |
| <b>Abdominal pain:</b>                             |                   |
| No. (%)  | 4 (11.1 %)        |
| Duration (days): median (IQR)                      | 8.5 (5 – 12)      |
| <b>Renal manifestations: No. (%)</b>               | 6 (16.6 %)        |
| <b>Neurological manifestations:</b>                |                   |
| <b>Convulsions: No. (%)</b>                        | 8 8 (22.2%)       |
| <b>DCL: No. (%)</b>                                | 4 (11.1 %)        |
| <b>Hospital LOS (days): median (IQR)</b>           | 17.5 (14-21)      |
| <b>(B) Signs:</b>                                  |                   |
| <b>Pulse (beats/min): mean <math>\pm</math>SD</b>  | 114.2 $\pm$ 21.03 |
| <b>SBP (mmHg): mean <math>\pm</math>SD</b>         | 90.5 $\pm$ 12.4   |
| <b>DBP (mmHg): mean <math>\pm</math>SD</b>         | 57.7 $\pm$ 9.2    |
| <b>Temperature (°c): mean <math>\pm</math>SD</b>   | 38.1 $\pm$ 0.69   |
| <b>RR (cycles/minute): mean <math>\pm</math>SD</b> | 37.2 $\pm$ 9.13   |
| <b>Pallor: No. (%)</b>                             | 20 (55.5 %)       |
| <b>Respiratory distress: No. (%)</b>               | 26 (72.2 %)       |
| <b>Grade I</b>                                     | 2 (5.56 %)        |
| <b>Grade II</b>                                    | 16 (44.44 %)      |
| <b>Grade III</b>                                   | 8 (22.22 %)       |
| <b>Pneumonia: No. (%)</b>                          | 24 (66.67%)       |
| <b>Respiratory failure: No. (%)</b>                | 4 (11.11 %)       |
| <b>Connection to MV: No. (%)</b>                   | 4 (11.11 %)       |
| <b>Murmur: No. (%)</b>                             | 14 (38.89 %)      |
| <b>Heart failure: No. (%)</b>                      | 4 (11.1 %)        |
| <b>Hepatomegaly: No. (%)</b>                       | 6 (16.6 %)        |
| <b>Splenomegaly: No. (%)</b>                       | 2 (5.5 %)         |
| <b>GCS: Mean <math>\pm</math>SD</b>                | 14.6 $\pm$ 0.9    |

\* No. (%): indicates the number and percentage of the patients with the corresponding clinical feature.

**Laboratory investigations:** Complete Blood Count (CBC): There was anemia in 20 patients (55.5%). The mean  $\pm$ SD Hb and RBCs were (10.5  $\pm$  2.1 g/dl) and (4.1  $\pm$  0.62  $\times 10^6$  / $\mu$ g) respectively. PLT count was normal and increased in 38.8% and 61.1% of the patients respectively. WBCs were normal,

increased, and decreased in 50%, 44.4%, and 5.5% of the patients respectively. Lymph/total WBC was normal, increased, and decreased in 44.4%, 22.2%, and 33.3% of the patients respectively. Neutrophil/total WBC was normal, increased, and decreased in 27.7%, 55.5%, and 16.6% of the patients respectively.

Coagulation and inflammatory parameters: The mean  $\pm$ SD PT, PC, and INR were ( $12.8 \pm 1.7$  seconds), ( $88.3 \pm 14.2$  %), and ( $1.1 \pm 0.11$  ) respectively. CRP was positive in 24 patients (66.6%) while it was negative in 12 patients (33.3%). Ferritin was normal in 12 patients (33.3%) while it was increased in 24 patients (66.6%). LDH was increased in all studied patients (100%). Troponin I was increased in 20 patients (55.5%) while it was normal in 16 patients (44.4%). D-dimer was normal in 18 patients (50%) while it was increased in 6 patients (16.6%) and decreased in 12 patients (33.3%).

Liver and kidney function tests: Creatinine was normal in 32 patients (88.8%)

and was elevated in 4 patients (11.1%). Albumin was normal in 16 patients (44.4%) and was decreased in 20 patients (55.5%). AST and ALT were normal in 66.6% and 88.8% of the patients respectively while they were increased in 33.3% and 11.1% of the patients respectively.

Specific biochemical levels: The median TNF- $\alpha$  was 26.5 (pg/ml) with (IQR of 21.02 – 38.4) and the median ACE2 was 6.02 (ng/ml) with (IQR of 2.84 – 9.28).

Laboratory tests for COVID-19: COVID IgG, IgM, Ag, and PCR were positive in 33.3%, 72.2%, 16.6%, and 5.5% of the patients respectively. (Fig.2).

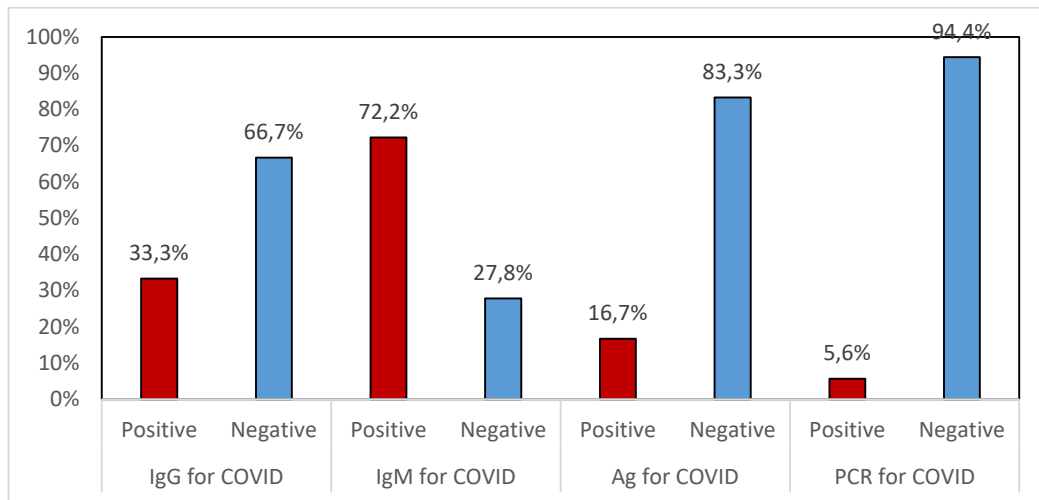


Fig.2. Laboratory tests for COVID-19 in all studied patients.

**Radiological findings in the studied patients:** There were chest CT findings in 16 patients (44.4%), 6 patients (16.7%) showed CORAD 4

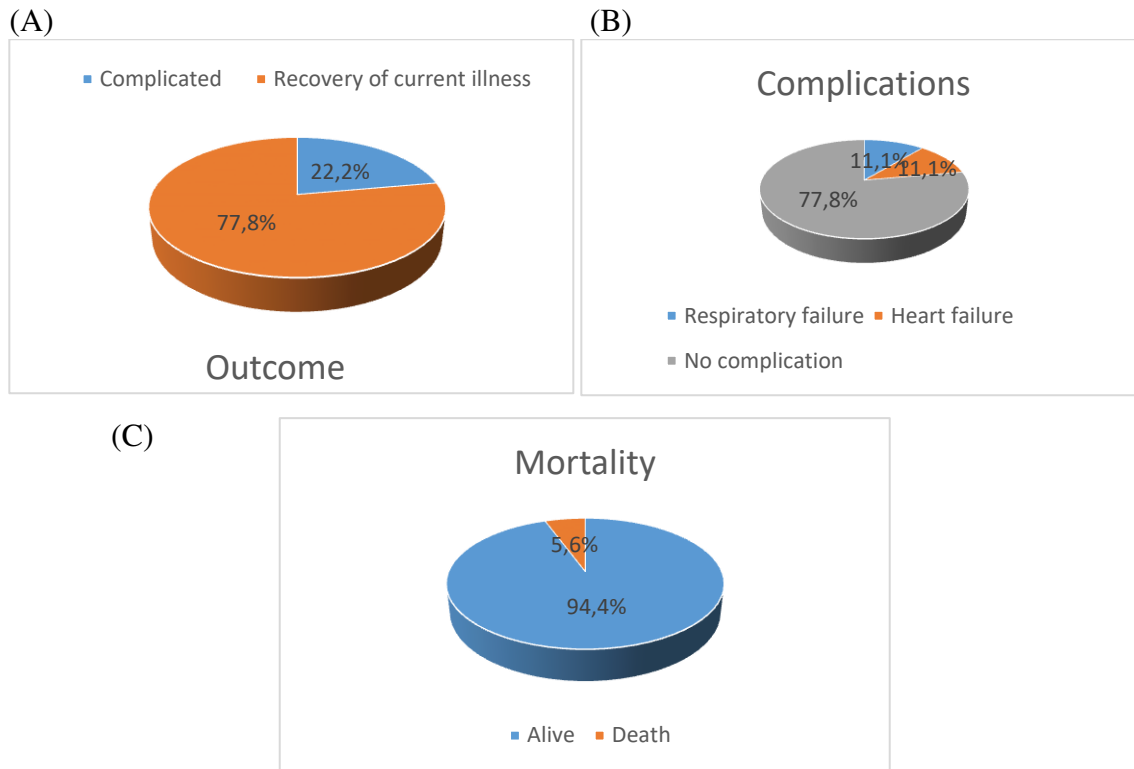
and 10 patients (27.8%) showed CORAD 5, as seen in (Table 3).

Table 3. CT findings of the included pediatric patients:

| CT finding and its severity           | Patients No.=36 (%) |
|---------------------------------------|---------------------|
| <b>CT chest findings of COVID-19:</b> |                     |
| Yes                                   | 16 (44.44 %)        |
| No                                    | 20 (55.56 %)        |
| <b>CT severity:</b>                   |                     |
| CORAD 4                               | 6 (16.70 %)         |
| CORAD 5                               | 10 (27.80 %)        |
| None                                  | 20 (55.60 %)        |

**Outcome and mortality among the included patients:** As regards outcome, there were 8 complicated patients (22.2%) and 28 patients (77.8%) recovered. The complicated cases showed respiratory failure in 4 patients (11.1%) and heart failure in 4 patients

(11.1%) (Fig.3. A and B). As regards mortality, 2 patients died (5.6%) and 34 still alive patients (94.4%) among the studied patients (Fig.3.C).

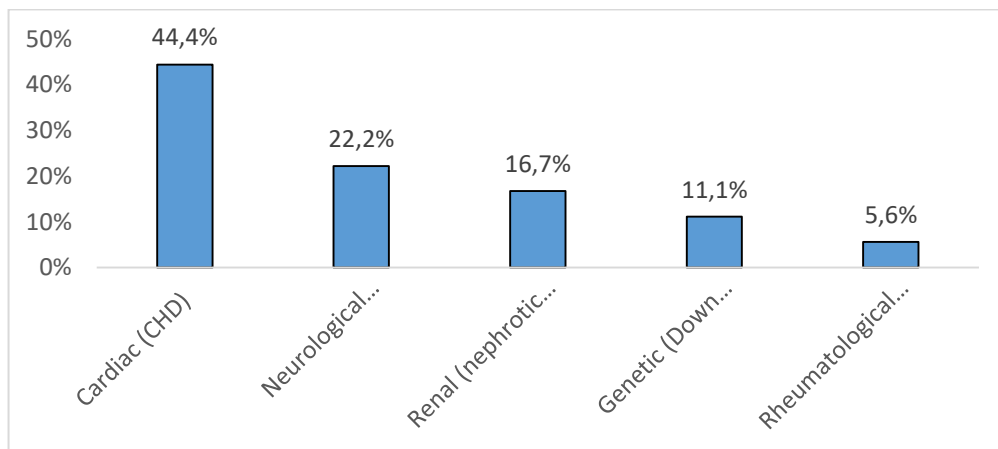


**Fig.3. Outcome and mortality among the studied patients; A) Outcomes; B) Complications; C) Mortality.**

**Data analysis of the included patients according to type of chronic disease:**

Among the included 36 patients, there were 16 patients (44.4%) with CHD, 8 patients (22.2%) with epilepsy, 6 patients (16.7%) with nephrotic syndrome, 4 patients (11.1%)

with Down syndrome and 2 patients (5.6%) with JRA in the studied patients as seen in (Fig.4). Demographic data distribution between patients' groups was seen in (Table 4):



**Fig.4. Type of chronic diseases among the included pediatric patients with COVID-19**

**Table 4. Demographic data distribution between patients' groups**

| Demographic data         | Cardiac (n=16) | Neurological (n=8) | Renal (n=6) | Genetic disease (n=4) | Rheumatological (n=2) | P. value |
|--------------------------|----------------|--------------------|-------------|-----------------------|-----------------------|----------|
| Age(years): Median (IQR) | 0.67(0.3-2.45) | 3.35(1.55-6.5)     | 5(3-7)      | 0.88(0.75-1)          | 8(8-8)                | 0.005**  |
| Sex:                     |                |                    |             |                       |                       |          |
| Male                     | 12(75%)        | 4(50%)             | 6(100%)     | 0(0%)                 | 2(100%)               | 0.009**  |
| Female                   | 4(25%)         | 4(50%)             | 0(0%)       | 4(100%)               | 0(0%)                 |          |
| Social status:           |                |                    |             |                       |                       |          |
| Low                      | 6(37.5%)       | 4(50%)             | 2(33.33%)   | 4(100%)               | 0(0%)                 | 0.120    |
| Moderate                 | 10(62.5%)      | 4(50%)             | 4(66.67%)   | 0(0%)                 | 2(100%)               |          |

### *Clinical data distribution between patients' groups*

(A) Symptoms are described in (Table 5). There was a statistically significant difference (p-value = 0.001) between the studied groups as regards cough and dyspnea. There were 14 patients (87.5%) with dry cough in the cardiac group, 4 patients (50%) in the neurological group, 4 patients (100%) in the genetic disease group, and no patients in the renal and rheumatological group. There were 16 patients (100%) with dyspnea in the cardiac

group versus 4 patients (50%) in the neurological group, 4 patients (100%) in the genetic disease group, 2 patients (100%) in the rheumatological group, and no patients in the renal group. There was a statistically significant difference (p-value = 0.03) between the studied groups as regards diarrhea. There were 2 patients (25%) with diarrhea in the neurological group, 2 patients (50%) in the genetic disease group, and no patients in the cardiac, renal, and rheumatological groups.

**Table 5. Clinical symptoms distribution between patients' groups:**

| Clinical symptoms                             | Cardiac (n=16) | Neurological (n=8) | Renal (n=6) | Genetic disease (n=4) | Rheumatological (n=2) | P. value |
|---|----------------|--------------------|-------------|-----------------------|-----------------------|----------|
| <b>History of contact:</b>                    |                |                    |             |                       |                       |          |
| Yes   | 2(12.5%)       | 2(25%)             | 0(0%)       | 0(0%)                 | 0(0%)                 | 0.542    |
| No  | 14(87.5%)      | 6(75%)             | 6(100%)     | 4(100%)               | 2(100%)               |          |
| <b>Fever:</b>                                 |                |                    |             |                       |                       |          |
| Yes   | 14(87.5%)      | 8(100%)            | 4(66.67%)   | 4(100%)               | 2(100%)               | 0.310    |
| No  | 2(12.5%)       | 0(0%)              | 2(33.33%)   | 0(0%)                 | 0(0%)                 |          |
| <b>Rhinorrhea:</b>                            |                |                    |             |                       |                       |          |
| Yes   | 6(37.5%)       | 0(0%)              | 0(0%)       | 0(0%)                 | 0(0%)                 | 0.061    |
| No  | 10(62.5%)      | 8(100%)            | 6(100%)     | 4(100%)               | 2(100%)               |          |
| <b>Dry cough:</b>                             |                |                    |             |                       |                       |          |
| Yes   | 14(87.5%)      | 4(50%)             | 0(0%)       | 4(100%)               | 0(0%)                 | <0.001** |
| No  | 2(12.5%)       | 4(50%)             | 6(100%)     | 0(0%)                 | 2(100%)               |          |
| <b>Dyspnea:</b>                               |                |                    |             |                       |                       |          |
| Yes   | 16(100%)       | 4(50%)             | 0(0%)       | 4(100%)               | 2(100%)               | <0.001** |
| No  | 0(0%)          | 4(50%)             | 6(100%)     | 0(0%)                 | 0(0%)                 |          |
| <b>Vomiting:</b>                              |                |                    |             |                       |                       |          |
| Yes   | 2(12.5%)       | 2(25%)             | 0(0%)       | 2(50%)                | 0(0%)                 | 0.249    |
| No  | 14(87.5%)      | 6(75%)             | 6(100%)     | 2(50%)                | 2(100%)               |          |
| <b>Diarrhea:</b>                              |                |                    |             |                       |                       |          |
| Yes   | 0(0%)          | 2(25%)             | 0(0%)       | 2(50%)                | 0(0%)                 | 0.030*   |
| No  | 16(100%)       | 6(75%)             | 6(100%)     | 2(50%)                | 2(100%)               |          |
| <b>Abdominal pain:</b>                        |                |                    |             |                       |                       |          |
| Yes   | 2(12.5%)       | 2(25%)             | 0(0%)       | 0(0%)                 | 0(0%)                 | 0.542    |
| No  | 14(87.5%)      | 6(75%)             | 6(100%)     | 4(100%)               | 2(100%)               |          |
| <b>Dehydration:</b>                           |                |                    |             |                       |                       |          |
| No  | 16(100%)       | 8(100%)            | 6(100%)     | 4(100%)               | 2(100%)               | -        |
| <b>Total disease duration (days): Mean±SD</b> | 16.38±6.45     | 18.75±2.96         | 15±4.98     | 22.5±8.66             | 21±0                  | 0.104    |

Signs were presented in (Table 6). There was a highly statistically significant difference (p-value < 0.001) between the studied groups as regards respiratory distress. There were 16 patients (100%) with respiratory distress in the cardiac group versus 4 patients in the neurological group (50%) and genetic disease group (100%), 2 patients (100%) in the rheumatological group, and no patients (0%) in the renal group. There was a

statistically significant difference (p-value = 0.001) between the studied groups as regards signs of pneumonia. There were 14 patients (87.5%) with signs of pneumonia in the cardiac group versus 4 patients in the neurological group (50%) and genetic disease group (100%), 2 patients (100%) in the rheumatological group, and no patients (0%) in the renal group.



**Table 6. Clinical signs distribution between patients' groups:**

| Clinical signs                              | Cardiac<br>no=16 (%) | Neurological<br>no=8 (%) | Renal<br>no=6 (%) | Genetic<br>disease<br>no=4 (%) | Rheumatological<br>no=2 (%) | P. value |
|---|----------------------|--------------------------|-------------------|--------------------------------|-----------------------------|----------|
| <b>Pallor:</b>                              |                      |                          |                   |                                |                             |          |
| Yes   | 8(50%)               | 6(75%)                   | 4(66.67%)         | 0(0%)                          | 2(100%)                     | 0.080    |
| No  | 8(50%)               | 2(25%)                   | 2(33.33%)         | 4(100%)                        | 0(0%)                       |          |
| <b>Pulse (bpm): mean±SD</b>                 | 126.5±18.06          | 102.5±8.86               | 92.67±9.85        | 130±23.09                      | 96±0                        | <0.001** |
| <b>Systolic BP (mm Hg):<br/>mean±SD</b>     | 82.5±8.56            | 90±7.56                  | 106.67±5.16       | 90±11.55                       | 110±0                       | <0.001** |
| <b>Diastolic BP (mm Hg):<br/>mean±SD</b>    | 52.5±4.47            | 55±5.35                  | 73.33±5.16        | 55±5.77                        | 70±0                        | <0.001** |
| <b>Temperature (°C):<br/>mean±SD</b>        | 38.04±0.71           | 38.75±0.6                | 37.6±0.47         | 38.2±0.35                      | 37.8±0                      | 0.009    |
| <b>RR (breaths per minute):<br/>mean±SD</b> | 44.63±5.08           | 30.5±7.8                 | 27±1.55           | 37.5±8.66                      | 36±0                        | <0.001** |
| <b>Respiratory distress:</b>                |                      |                          |                   |                                |                             |          |
| Yes   | 16(100%)             | 4(50%)                   | 0(0%)             | 4(100%)                        | 2(100%)                     | <0.001** |
| No  | 0(0%)                | 4(50%)                   | 6(100%)           | 0(0%)                          | 0(0%)                       |          |
| <b>Its grades</b>                           |                      |                          |                   |                                |                             |          |
| None  | 0(0%)                | 4(50%)                   | 6(100%)           | 0(0%)                          | 0(0%)                       | <0.001** |
| I   | 0(0%)                | 2(25%)                   | 0(0%)             | 0(0%)                          | 0(0%)                       |          |
| II  | 10(62.5%)            | 2(25%)                   | 0(0%)             | 2(50%)                         | 2(100%)                     |          |
| III   | 6(37.5%)             | 0(0%)                    | 0(0%)             | 2(50%)                         | 0(0%)                       |          |
| <b>Signs of pneumonia:</b>                  |                      |                          |                   |                                |                             |          |
| Yes   | 14(87.5%)            | 4(50%)                   | 0(0%)             | 4(100%)                        | 2(100%)                     | 0.001**  |
| No  | 2(12.5%)             | 4(50%)                   | 6(100%)           | 0(0%)                          | 0(0%)                       |          |
| <b>Signs of respiratory failure:</b>        |                      |                          |                   |                                |                             |          |
| Yes   | 2(12.5%)             | 2(25%)                   | 0(0%)             | 0(0%)                          | 0(0%)                       | 0.542    |
| No  | 14(87.5%)            | 6(75%)                   | 6(100%)           | 4(100%)                        | 2(100%)                     |          |
| <b>Connection to MV:</b>                    |                      |                          |                   |                                |                             |          |
| Yes   | 2(12.5%)             | 2(25%)                   | 0(0%)             | 0(0%)                          | 0(0%)                       | 0.542    |
| No  | 14(87.5%)            | 6(75%)                   | 6(100%)           | 4(100%)                        | 2(100%)                     |          |
| <b>Murmur:</b>                              |                      |                          |                   |                                |                             |          |
| Yes   | 14(87.5%)            | 0(0%)                    | 0(0%)             | 0(0%)                          | 0(0%)                       | <0.001** |
| No  | 2(12.5%)             | 8(100%)                  | 6(100%)           | 4(100%)                        | 2(100%)                     |          |
| <b>Signs of heart failure:</b>              |                      |                          |                   |                                |                             |          |
| Yes   | 4(25%)               | 0(0%)                    | 0(0%)             | 0(0%)                          | 0(0%)                       | 0.229    |
| No  | 12(75%)              | 8(100%)                  | 6(100%)           | 4(100%)                        | 2(100%)                     |          |
| <b>Hepatomegally:</b>                       |                      |                          |                   |                                |                             |          |
| Yes   | 4(25%)               | 0(0%)                    | 0(0%)             | 2(50%)                         | 0(0%)                       | 0.126    |
| No  | 12(75%)              | 8(100%)                  | 6(100%)           | 2(50%)                         | 2(100%)                     |          |
| <b>Splenomegally:</b>                       |                      |                          |                   |                                |                             |          |
| Yes   | 2(12.5%)             | 0(0%)                    | 0(0%)             | 0(0%)                          | 0(0%)                       | 0.619    |
| No  | 14(87.5%)            | 8(100%)                  | 6(100%)           | 4(100%)                        | 2(100%)                     |          |
| <b>GCS: Mean±SD</b>                         | 14.75±0.68           | 13.75±1.39               | 15±0              | 15±0                           | 15±0                        | 0.054    |
| <b>Death</b>                                | 0(0%)                | 2(25%)                   | 0(0%)             | 0(0%)                          | 0(0%)                       | 0.116    |

**Laboratory data of different COVID-19 patients subgroups:**

Complete Blood Count was described in (Table 7): There were statistically significant differences (p-value = 0.032, 0.035, 0.032, 0.009, and 0.014) between the studied groups

as regards RBCs, MCV, MCH, PLT, and WBCs respectively. Also, there were statistically significant differences (p-value = 0.025 and 0.017) between the studied groups as regards lymph/WBCs (%) and neutrophil/total WBCs (%) respectively.

Table 7. CBC data distribution between the studied patients' groups

| CBC results   | Cardiac (n=16)                  | Neurological (n=8)         | Renal (n=6)                     | Genetic disease (n=4)     | Rheumatological (n=2)     | P. value |
|---|---------------------------------|----------------------------|---------------------------------|---------------------------|---------------------------|----------|
| <b>Hb(g/dl): mean±SD</b>  | 11.1±2.5                        | 9.2±1.58                   | 10.76±1.11                      | 12.05±0.52                | 8.7±0                     | 0.079    |
| <b>RBCs (×10<sup>6</sup>/μg): mean±SD</b>   | 4.49±0.7                        | 3.83±0.6                   | 4.02±0.36                       | 3.91±0.02                 | 3.89±0                    | 0.032*   |
| <b>MCV (fl): mean±SD</b>  | 78.15±8.67                      | 76.2±5.04                  | 81.8±1.25                       | 87.8±6.7                  | 71.2±0                    | 0.035*   |
| <b>MCH (pg): mean±SD</b>  | 24.9±4.7                        | 24.15±3.09                 | 26.93±0.6                       | 30.85±1.21                | 22.4±0                    | 0.032*   |
| <b>RDW (%): mean±SD</b>   | 14.81±1.74                      | 15.35±3.28                 | 13.83±1.25                      | 14.75±1.67                | 14.6±0                    | 0.918    |
| <b>HCT (%): mean±SD</b>   | 33.78±4.77                      | 29.03±4.11                 | 32.9±3.49                       | 34.4±2.89                 | 27.7±0                    | 0.055    |
| <b>Anemia:</b><br>yes<br>no   | 8(50%)<br>8(50%)                | 6(75%)<br>2(25%)           | 4(66.67%)<br>2(33.33%)          | 0(0%)<br>4(100%)          | 2(100%)<br>0(0%)          | 0.080    |
| <b>Type of anemia:</b><br>Microcytic<br>hypochromic<br>Normocytic<br>Normochromic | 8(50%)<br>8(50%)<br>8(50%)      | 6(75%)<br>2(25%)<br>2(25%) | 0(0%)<br>6(100%)                | 0(0%)<br>4(100%)          | 2(100%)<br>0(0%)          | 0.002**  |
| <b>PLT (×10<sup>3</sup>/μg):</b><br>Normal<br>Increased                           | 8(50%)<br>8(50%)                | 0(0%)<br>8(100%)           | 4(66.67%)<br>2(33.33%)          | 0(0%)<br>4(100%)          | 2(100%)<br>0(0%)          | 0.009**  |
| <b>Mean±SD</b>  | 394.86±116.45                   | 274±78.1                   | 456.63±40.5                     | 380.5±19.05               | 468±0                     | 0.019*   |
| <b>WBCs (×10<sup>3</sup>/μg):</b><br>Decreased<br>Normal<br>Increased             | 0(0%)<br>12(75%)<br>4(25%)      | 2(25%)<br>4(50%)<br>2(25%) | 0(0%)<br>2(33.33%)<br>4(66.67%) | 0(0%)<br>0(0%)<br>4(100%) | 0(0%)<br>0(0%)<br>2(100%) | 0.014*   |
| <b>Mean±SD</b>  | 10.76±4.94                      | 8.7±4.82                   | 11.24±1.96                      | 19.05±1.44                | 27.5±0                    | 0.006**  |
| <b>Lymphocytic count (×10<sup>3</sup>/μg): Median (IQR)</b>                       | 3.36(2.18-4.5)                  | 3.2(0.85-3.83)             | 2.92(1.99-3.8)                  | 4.1(3.2-5)                | 2.2(2.2-2.2)              | 0.350    |
| <b>Lymph/total WBCs(%):</b><br>Decreased<br>Normal<br>Increased                   | 2(12.5%)<br>10(62.5%)<br>4(25%) | 4(50%)<br>0(0%)<br>4(50%)  | 2(33.33%)<br>4(66.67%)<br>0(0%) | 2(50%)<br>2(50%)<br>0(0%) | 2(100%)<br>0(0%)<br>0(0%) | 0.025*   |
| <b>Median (IQ range)</b>  | 35.95(20.08-56.05)              | 30.55(10.08-46.83)         | 32.44(14.81-33.66)              | 21.3(17.9-24.7)           | 7.9(7.9-7.9)              | 0.196    |
| <b>Neutrophilic count(×10<sup>3</sup>/μg): Median (IQ range)</b>                  | 5.16(2.75-58.58)                | 3.65(2.6-9.2)              | 6.41(5.85-9.64)                 | 14.1(13.9-14.3)           | 24.4(24.4-24.4)           | 0.043*   |
| <b>Neutrophil/total WBCs (%):</b><br>Decreased<br>Normal<br>Increased             | 6(37.5%)<br>4(25%)<br>6(37.5%)  | 0(0%)<br>4(50%)<br>4(50%)  | 0(0%)<br>2(33.33%)<br>4(66.67%) | 0(0%)<br>0(0%)<br>4(100%) | 0(0%)<br>0(0%)<br>2(100%) | 0.083    |
| <b>Median (IQ range)</b>  | 48.85(20.52-66.45)              | 58.15(44.48-79.85)         | 64.93(56.77-71.72)              | 76.8(68.6-85)             | 88.7(88.7-88.7)           | 0.017*   |

Specific biochemical markers were described in (Table 8): There was a statistically significant difference (p-value =

0.001) between the studied groups as regards serum TNF-α with the highest values among the neurological group.

**Table 8.** Specific biochemical tests distribution between patients' groups:

| Specific biochemical Tests                | Cardiac (n=16)     | Neurological (n=8) | Renal (n=6)        | Genetic disease (n=4) | Rheumatological (n=2) | P. value |
|---|--------------------|--------------------|--------------------|-----------------------|-----------------------|----------|
| ELISA for TNF-alpha (pg/ml): median (IQR) | 21.68(18.34-27.13) | 40.45(37.02-42.52) | 25.34(23.58-30.22) | 24.9(19.45-30.34)     | 56.34(56.34-56.34)    | 0.001**  |
| ELISA for ACE2 (ng/ml): median (IQR)      | 6.22(3.34-9.18)    | 5.96(3.54-10.47)   | 5.75(1.31-10.24)   | 11.83(1.42-22.24)     | 6.38(6.38-6.38)       | 0.974    |

**Radiological data:** No statistically significant difference (p-value = 0.070) between the studied groups as regards CT chest findings of COVID-19. No statistically significant

difference (p-value = 0.241) between the studied groups as regards CT severity as seen in (Table.9).

**Table 9.** Chest CT finding and severity among the studied patients' groups:

| CT finding and severity      | Cardiac (n=16) | Neurological (n=8) | Renal (n=6) | Genetic disease (n=4) | Rheumatological (n=2) | P. value |
|------------------------------|----------------|--------------------|-------------|-----------------------|-----------------------|----------|
| CT chest finding of COVID-19 |                |                    |             |                       |                       |          |
| Yes                          | 10(62.5%)      | 4(50%)             | 0(0%)       | 2(50%)                | 0(0%)                 | 0.070    |
| No                           | 6(37.5%)       | 4(50%)             | 6(100%)     | 2(50%)                | 2(100%)               |          |
| CT severity                  |                |                    |             |                       |                       |          |
| CORAD 4                      | 4(25%)         | 2(25%)             | 0(0%)       | 0(0%)                 | 0(0%)                 | 0.241    |
| CORAD 5                      | 6(37.5%)       | 2(25%)             | 0(0%)       | 2(50%)                | 0(0%)                 |          |
| None                         | 6(37.5%)       | 4(50%)             | 6(100%)     | 2(50%)                | 2(100%)               |          |

5. Outcome and mortality distribution are described in (Table10). There was a highly statistically significant difference (p-value < 0.001) between the studied groups as regards complications. In the cardiac group, there was respiratory failure in 12.5% of patients & heart failure in 25% of patients, and in the neurological group, there was respiratory failure in 25% of patients and no patients had heart failure. There was no respiratory failure or heart failure in renal, genetic, or rheumatological groups. No statistically significant difference (p-value = 0.116) between the studied groups as regards mortality.

**Table 10.** Outcome and mortality distribution between the studied groups according to the type of chronic disease.

|                             | Cardiac (n=16) | Neurological (n=8) | Renal (n=6) | Genetic disease (n=4) | Rheumatological (n=2) | P. value |
|-----------------------------|----------------|--------------------|-------------|-----------------------|-----------------------|----------|
| ❖ Outcome                   |                |                    |             |                       |                       |          |
| Complicated                 | 6(37.5%)       | 2(25%)             | 0(0%)       | 0(0%)                 | 0(0%)                 | 0.229    |
| Recovery of current illness | 10(62.5%)      | 6(75%)             | 6(100%)     | 4(100%)               | 2(100%)               |          |
| Complications:              |                |                    |             |                       |                       |          |
| Respiratory failure         | 2(12.5%)       | 2(25%)             | 0(0%)       | 0(0%)                 | 0(0%)                 | <0.001** |
| Heart failure               | 4(25%)         | 0(0%)              | 0(0%)       | 0(0%)                 | 0(0%)                 |          |
| ❖ Mortality                 |                |                    |             |                       |                       |          |
| Alive                       | 16(100%)       | 6(75%)             | 6(100%)     | 4(100%)               | 2(100%)               | 0.116    |
| Death                       | 0(0%)          | 2(25%)             | 0(0%)       | 0(0%)                 | 0(0%)                 |          |

## Discussion

This study examined 36 pediatric COVID-19 patients with chronic diseases. Participants were treated in Qena University Hospitals' Pediatrics Department. More than three-fourths of the children in the study had recovered. Our study sought to add to the current data on COVID-19 in children.

Children with several chronic conditions are more likely to get COVID-19 and have

poor symptom management. Also, they are more prone to be misdiagnosed as medical professionals may have trouble separating virus-related symptoms from those caused by pre-existing disorders.

Our analysis found that 77.7% of pediatric patients had a plausible chance of having COVID-19, while 22.2% had been diagnosed with it. A large percentage of individuals exhibited minor illness symptoms throughout

our assessment. **Hu et al. (2020)** found that age and comorbidities affect COVID-19 severity and effects. According to **Hoste et al. (2023)**, SARS-CoV-2 infections can have different clinical symptoms. Additionally, severe COVID-19 instances in children and teenagers are rare. Conversely, chronically unwell children may be more likely to develop the illness. Immunological explanations (**Zimmermann et al., 2020 and Brodin, 2021**) explaining young people's relative resistance to COVID-19, including those with chronic illnesses, remain unanswered.

Our study found that most participants were male and ranged in age from 0.75 to 5 years, with a median of 2 years. Even though 66.67% of the cardiac group, 50% of the neurological group, and 100% of the renal and rheumatological groups were male, all genetic groups only contained females. Down syndrome occurrence is more common in males according to many studies as **Soriano et al. (2022)** so female predominance in our study may be explained by the small studied sample size. The above result matches **Maryam et al. (2022)** which found that 55 of 91 patients were males and 36 were females. The median patient age was 32 months, with the interquartile range being 11 to 91 months. Differences in genetics, hormones, immune systems, and ACE2 expression in males may explain why females are less susceptible to the illness.

Our investigation found no prior interaction patterns among the patients, as only 11.11% of the studied patients had positive family history. The findings of this study contradict prior studies, which found that 90% of children contract COVID-19 from family members (**Qiu et al., 2020 and Fang et al., 2020**).

Our study found that COVID-19 in children most typically causes fever, dyspnea, and dry cough. Rhinorrhea, vomiting, diarrhea, and abdominal pain ensue. Dyspnea and dry cough were more likely in people with heart disease or genetic susceptibility. **Soltani et al. (2020) and Shahbaznejad et al. (2021)** found that fever and cough are the main symptoms of COVID-19 in children. These studies support our findings and show these symptoms. After these symptoms, 29% of patients felt dyspnea, 26% fatigue and weakness, and 23% vomiting. Our findings matched this. Gastrointestinal symptoms as anorexia, nausea, vomiting, and diarrhea in pediatric patients were linked to worse outcomes. **Esmaeeli et al. (2021)** found that cough was the most common symptom in cardiac patients with COVID-19. After the occurrence, the patient developed pyrexia,

respiratory distress, cyanosis, agitation, anorexia, and peripheral edema.

Our study found that patients were hospitalized for 17.5 days, with an interquartile range of 14-21 days. Our research also found no statistically significant differences in hospitalization length across groups. **Al-Khlaifat et al. (2023)** found no connection between comorbidities and hospitalization duration. In contrast to **Sharif et al. (2021)**, COVID-19 patients with more comorbidities and other parameters had higher mortality rates, longer hospital stays, and worse symptomatology.

Our analysis found that most trial participants had grade II respiratory distress (RD) and pneumonia. Respiratory failure, heart failure, hepatomegaly, and splenomegaly were rarer. Only a small percentage of patients need mechanical ventilation (MV). RD symptoms were found in cardiac, genetic, and rheumatological patients, but barely half of neurological and none of renal patients had them. Not all renal disease patients have renal impairment. **Kainth et al. (2020)** examined the clinical characteristics, socio-demographic variables, hospital course, and illness severity of 65 US COVID-19 patients. Fever was detected in 86% of individuals. Additionally, 60% of individuals had lower respiratory tract symptoms. In addition, 62% of patients had gastrointestinal issues. 35% of patients required critical care.

Lymphocytes have an essential role in defense against viruses. Our study showed that normal lymphocyte/total WBC count was the commonest finding (predominant in the cardiac and the renal groups) followed by lymphopenia (predominant in the rheumatological group) and finally lymphocytosis (predominant in the neurological and the cardiac group). In contrast to our study, many studies on adults showed that lymphopenia was the most common parameter in full blood count (**Huang et al., 2020**). Also, some previous studies reported that lymphopenia developed at an early stage of COVID-19 in severely diseased and critically ill patients (**Klein and Flanagan, 2016 ; Chen et al., 2020**), suggesting that lymphopenia was related to apoptosis and cell death during the cytokine release and that is why SARS-CoV-2 infection causes lymphopenia, depending on disease severity (**Suratannon et al., 2020 and Cavallo et al., 2020**).

While in children, lymphopenia may not occur due to relatively immature immune systems and differences in immune responses compared to adults. Children with mild disease had normal or increased lymphocyte counts (**Klein and Flanagan, 2016 ; Chen et**

al., 2020). Also, our results were not in agreement with a previous study in children by **Qiu et al. (2020)** which showed that the prevalence of leucopenia, and lymphopenia was similar to that in adults.

Patients with severe COVID-19 had higher peripheral blood neutrophil levels than those with mild cases and most other viral illnesses. The numerical values indicate elevated status, but not as much as in patients with bacterial pneumonia. Severe COVID-19 poses higher risks than most viral infections. For example, neutrophils contribute to thrombosis, acute respiratory distress syndrome, and multisystem inflammatory syndrome in pediatric COVID-19 patients (**Huang et al., 2020 and Ma et al., 2021**). In genetic and rheumatological cohorts, the increase was striking. The results resembled **Soltani et al. (2020), Shahbaznejad et al. (2021), Chen et al. (2020), and Sarkesh et al. (2020)**. These findings contradicted **Elghoudi et al. (2020)**, who found low levels of neutrophils and platelets among the studied patients.

COVID-19 has been recently recognized as a systemic disorder that induces a pro-inflammatory and pro-thrombotic state via hyper-activation of the inflammatory and hemostatic pathways (**Franchini et al., 2020**). While thrombotic complications in adults with COVID-19 have been widely recognized and extensively studied (**Malas et al., 2020**) together with their associated therapeutic implications, little is known about the burden of COVID-19-associated hypercoagulable state in children. Thrombotic or thromboembolic events are rare in children with COVID-19 infection or MIS-C. However, a high index of suspicion should be maintained in children with COVID-19 infection, especially in those with comorbidities predisposing to a thrombotic event (**Zaffanello et al., 2021**).

The current study showed whatever the degree of disease severity and kind of chronic disease, the pro-coagulatory and pro-inflammatory markers (CRP, Ferritin, LDH, and troponin I) were elevated in the majority of patients. This was evident in all groups except renal which showed normal results and only LDH was elevated. The mean PT was ( $12.8 \pm 1.7$  seconds), the mean PC was ( $88.3 \pm 14.2$  %), and the mean  $\pm$ SD INR was ( $1.1 \pm 0.11$ ). Our study results were in contrast to **Qiu et al. (2020)** which suggested that children had mild immunological responses and less immune damage. According to **Morello et al. (2022)**, steroid treatment in nephrotic syndrome is safe and effective. This may explain why the renal group showed normal AFR (Acute Phase Reactant). Regarding the serum level of D-dimmer, it was normal to decrease in all groups except

all rheumatological and half of genetic and a small percent of cardiac patients where it was elevated. Previous studies reported high levels of CRP and D-dimer in the early phase of COVID-19 (**Tang et al., 2020 and Cui et al., 2020**) that COVID-19 was associated with hemostatic abnormalities, and markedly elevated D-dimer levels were observed in those non-survivors (**Tang et al., 2020**). D-dimer elevations were seen in 3.75–68.0% of the COVID-19 patients (**Wu et al., 2020 and Zhou et al., 2020**). Anticoagulation therapy was associated with lower mortality in COVID-19 and this was especially true for patients with high D-dimers (**Tang et al., 2020**). False data about D-dimer caused more deaths in Egypt (**Yameny, 2021**). This may explain the lower D-dimmer levels in our study.

A considerable percentage of those tested had normal AST and ALT values, according to our findings. In contrast, higher enzyme levels were linked to cardiovascular disease, neurological disorders, and familial risk. All tested groups showed that most patients had decreasing albumin levels. **Esmaili et al. (2020) and Liu et al. (2020)** agreed with our results as their patients had low blood albumin levels. Increasing evidence suggests that juvenile COVID-19 patients have liver issues, according to **Yun et al. (2023)**. COVID-19 causes liver injury in three ways: (1) SARS-COV-2 binds to ACE-2 in the liver or bile duct, causing direct toxicity; (2) An inflammatory immune response and hypoxia; and (3) COVID-19 treatments like mechanical ventilation and antivirals affect the liver. In contrast to the findings obtained from our investigation, previous meta-analyses conducted by **Alkan et al. (2022)** found that liver injury is common in young people, despite being missed. Several additional studies have confirmed our findings that a small percentage of COVID-19-infected children had abnormal liver tests.

Serum creatinine values showed that most patients had normal renal function, except a limited number of people in both the renal and the neurological groups, according to our study. In agreement to our study, **Safadi. (2020)** found few incidences of COVID-19-related renal problems in newborns. **Cheng et al. (2020) and Melgosa et al. (2020)** noted that children are less susceptible to severe COVID-19 symptoms than older cohorts and their investigations also found that COVID-19-severe cases primarily had kidney impairment.

Our study showed that the serum Angiotensin-converting enzyme 2 (ACE2) was within the lower limit of the normal range and showed no statistical significance among the studied groups. ACE2, a counterregulator

of the renin-angiotensin system, protects against many chronic diseases. Besides chronic diseases, ACE2 is the host receptor for SARS-CoV or SARS-CoV-2 and mediates the first step of virus infection. The negative relation between ACE2 level and COVID-19 severity is not paradoxical but it is consistent with a mathematical model that predicts that the higher viral receptor does not necessarily favor the virus propagation and it can even slow it down (**Bastolla et al., 2022**). Most importantly, low ACE2 levels expose the lungs to acute inflammation (**Imai et al., 2005**), and ACE2 level is low in the most common chronic diseases including hypertension, type 2 diabetes, chronic renal failure, pulmonary diseases, and liver diseases (**Li et al., 2020; Pagliaro and Penna, 2020**). For these reasons, many authors proposed that the severity of COVID-19 is exacerbated by the degradation of ACE2 by the virus (**Annweiler et al., 2020; Sun et al., 2020; Ciaglia et al., 2020; Gurwitz, 2020; Offringa et al., 2020 and Vervoort et al., 2020**). Lower severity of COVID-19 in children despite lower ACE2 expression may be consistent with their higher expression of the alternative angiotensin II receptor and in general due to the anti-inflammatory role of the RAS at young age (**Bastolla et al., 2022**).

Our study found that all participants had lower serum TNF-alpha levels. This biomarker was lowest in cardiac, renal, and genetic cohorts. In their study of proinflammatory cytokines and chemokines in SARS-CoV-2 infection in children, **Qian et al. (2021)** used the enzyme-linked immunosorbent assay (ELISA) to measure plasma levels of IL-2, IL-4, IL-6, TNF-alpha, and IFN-gamma. This study examined the relationship between proinflammatory cytokines and chemokines. Interestingly, the levels were mostly modest, and no statistically significant associations were found between condition severity and any of the analyzed parameters. After careful analysis, some people with co-existing diseases may have had immunoparesis due to the underlying pathology. This conclusion was based on its accomplishment likelihood. Recent discoveries in COVID-19 pathophysiology have shown that cytokine release syndrome (CRS) is closely linked to disease severity. TNF-, IL-6, IL-2, IL-7, and IL-10 levels above normal indicate disease severity. Due to these circumstances, regulating the CRS in severe COVID-19 patients is proposed (**Guo et al., 2022**).

In the early stages of the COVID-19 pandemic, the wide range of symptoms and imaging results together with the severity of the illness upon initial medical presentation,

hampered disease identification (**Guan et al., 2020**). This made recognizing the condition difficult. Although the RT-PCR reverse transcription polymerase chain reaction test is the preferred method for diagnosing COVID-19, a negative result may be misinterpreted (**CDC, 2019**). Researchers found only 5.56 % of the population positive for COVID-19 by (RT-PCR). These results match **Eldin et al. (2022)**, who found 16.1% of pediatric patients had positive COVID-19 RT-PCR results. False-negative rates for RT-PCR may reach 30% (**Fang et al., 2020**). Despite their negative RT-PCR results for COVID-19, the children in our study had no conclusive explanation for their symptoms, supporting the possibility that they were infected. The fact that 11.1% of these children had documented contact with COVID-19 patients supported this observation. These children also showed COVID-19-like symptoms. Researchers found that a negative RT-PCR test result may be linked to factors like patient viral load, virus shedding, and primary viral replication site (e.g., nasopharyngeal vs. lower respiratory tract) (**Fang et al., 2020; Wolfel et al., 2020; Yang et al., 2020**). The technical expertise of sample collectors and handlers may also cause false-negative results. SARS-CoV-2 infection detection and isolation are crucial to COVID-19 control so rapid diagnostic methods like antigen detection assays or antibody testing are needed to detect SARS-CoV-2 infections. Despite a negative RT-PCR test, some people had positive results in the COVID-19 antigen and/or immunoglobulin M (IgM) antibody tests. Laboratory-based RT-PCR is still the standard SARS-CoV-2 detection method. However, it requires time and specialized equipment. Antibody and antigen tests may be rapid diagnostic tools but RT-PCR must be used to confirm negative results in cases of strong clinical suspicion of COVID-19. These tests could also be used for screening (**Chen et al., 2023**). **Hou et al. (2020)** found that IgM antibodies indicate recent SARS-CoV-2 exposure and a person with IgG antibody but no IgM antibody has been exposed to the virus. Our study found that 16.67% of patients had positive COVID-19 Ag tests. Also, 33.33% and 72.22% of patients had positive IgG and IgM antibodies, respectively.

The typical COVID-19 CT results were seen in less than 50% of our patients. **Guoqing et al. (2021)** found pneumonia-related CT anomalies only in 68 of 127 patients while all candidates had pneumonia. **Gabr et al. (2023)** found that over 70% of patients had comorbidities. However, these comorbidities did not affect chest CT results. We found no statistically significant difference between groups in COVID-19

detection and severity by computed tomography (CT) scans.

**Bhopal et al. (2021)** found that children had a much lower mortality rate than adults, ranging from 0 to 0.37 % per thousand. This discovery supports the claim that children have a lower mortality rate than adults. Hospitalized children have a higher mortality rate. Clinically diagnosed chronic medical conditions often cause inflammation and decreased immunological responses. **Yang et al. (2020)** found that these traits may increase the risk of COVID-19 infection and health issues. **Remuzzi and Remuzzi. (2020); Richardson et al. (2020)** found that COVID-19 patients with comorbidities had a higher risk of severe morbidity and death. The US study "Demographic predictors of hospitalization and mortality in US children with COVID-19 infection" by **Moreira et al. (2021)** found that 0.19% of hospitalized children died during medical treatment. Our research showed that a significant percentage of those tested recovered from COVID-19 infection without any adverse effects from the virus or pre-existing medical conditions. So that previous studies supported our conclusion. Only a few patients were complicated with respiratory failure (4 patients) and heart failure (4 patients) from the cardiac (6 patients) and neurological (2 patients) groups. The two patients who were complicated in the neurological group finally died of respiratory failure. This was consistent with **Vervoort et al. (2020)** who mentioned that cardiovascular diseases are one of the most, if not the most, severe risk factors for a complicated COVID-19 course but **Götzinger et al. (2020)** and **Simpson et al. (2020)** mentioned that limited reports of small case series or cohort studies suggested that children with congenital heart disease might be at increased risk of severe COVID-19 illness. **Cabezudo-García et al. (2020)** mentioned that children with neurological disorders were at higher risk of hospitalization and severe COVID-19 illness when hospitalized. Our results did not agree with **Meguid et al. (2022)** which found that comparison between the groups regarding the age of the children, comorbidities, complication, and SARS-COV-2 infection frequency did not show significant statistical difference.

### Conclusion

We have been able to conclude from this study that COVID-19 affects children with chronic disease in the same way as any other age group and comorbidity is still the main risk factor for death. Ultramost care of pediatric patients having underlying medical conditions with recent COVID-19 including

the early diagnosis and detection of the characteristic clinical, laboratory, and radiological findings in those patients was achieved to some extent by this study so that we can avoid the development of unwanted outcomes. The findings of this study may have potentially exaggerated the rates of patient mortality and morbidity. This is primarily attributed to the inclusion of only hospitalized cases and the limited number of patients included in the analysis. Hence, more research pertaining to pediatric COVID-19 is necessary to enhance our understanding of the factors contributing to the development of a severe clinical trajectory in children, as well as to identify the specific subgroups that may be at higher risk. This intervention has the potential to serve as a preventive measure and improve the provision of COVID-19 care and treatment for those who are most susceptible to experiencing severe illness and death.

### Study limitation

The ongoing research is presently susceptible to a range of unique defects and constraints. One crucial determinant that leads to the diminished statistical estimates of connection with the measured outcomes is the limited sample size of people included in the study. The generalizability of the study results to pediatric patients residing in different regions of the nation is hindered by the exclusive treatment of all subjects at Qena University Hospital (QUH). Hence, it is essential to do more studies on a broader scope and across diverse locations, including a larger cohort of symptomatic and asymptomatic children and adolescents afflicted with a chronic illness. This group should consist of individuals who are children and adolescents and who have the disorder. Another possible restriction is the absence of a second PCR test to confirm the absence of the illness in the other pediatric patients who initially tested negative. There is a possibility of a misclassification bias occurring between pediatric patients suspected of having COVID-19 based on clinical assessment and those who have received confirmation by PCR testing. Nevertheless, the absence of a viable explanation for the occurrence of COVID-like symptoms, along with positive antigen and antibody tests, in the children we examined, despite their negative reverse transcription polymerase chain reaction (RT-PCR) results for COVID-19, lends credence to the notion that these children were indeed affected by COVID-19. In summary, it can be determined that the sample size is insufficient in all cases, however it is notably significant in the context of juvenile patients afflicted with COVID-19, particularly those who concurrently present with other comorbidities.

Nevertheless, the majority of our findings exhibited consistency during the whole duration of the inquiry. When considering these data in conjunction with other case reports documenting the diagnosis of COVID-19 in children, it can be confidently said that our conclusions are indeed precise. We conducted a research study on the impact of COVID-19 among pediatric individuals residing in our local community who have been diagnosed with various commonly

occurring chronic diseases. This investigation facilitated the prediction of the characteristics and consequences of COVID-19 in patients, and we expect that the incorporation of more data will augment our findings. Furthermore, the global transmission of the COVID-19 virus persists, including an increasing number of countries, and is widely acknowledged as a significant menace to the well-being of the general population.

#### List of abbreviations

| Abbreviation  | Full term                                       |
|---------------|---|
| ACE-2         | Angiotensin Converting Enzyme-2                 |
| ALT           | Alanine Transaminase                            |
| AST           | Aspartate Transaminase                          |
| CBC           | Complete Blood Count                            |
| CHD           | Congenital Heart Disease                        |
| COVID-19      | Coronavirus Disease Of 2019                     |
| CRP           | C-Reactive Protein                              |
| CT            | Computed Tomography                             |
| DBP           | Diastolic Blood Pressure                        |
| Hb            | Hemoglobin                                      |
| Hct           | Hematocrit                                      |
| IgG           | Immunoglobulin G                                |
| IgM           | Immunoglobulin M                                |
| IL-1 $\beta$  | Interleukin-1 $\beta$                           |
| IL-6          | Interleukin-6                                   |
| INR           | International Normalised Ratio                  |
| IP-10         | Interferon -Induced Protein-10                  |
| IQR           | Interquartile Range                             |
| JRA           | Juvenile Rheumatoid Arthritis                   |
| LDH           | Lactate Dehydrogenase                           |
| LOS           | Length of stay                                  |
| MCH           | Mean Corpuscular Hemoglobin                     |
| MCV           | Mean Corpuscular Volume                         |
| MERS-CoV      | Middle East Respiratory Syndrome Coronavirus    |
| MIP           | Macrophage Inflammatory Protein                 |
| MV            | Mechanical Ventilation                          |
| PC            | Prothrombin concentration                       |
| PCR           | Polymerase Chain Reaction                       |
| PT            | Prothrombin Time                                |
| RBCs          | Red Blood Cells                                 |
| RBD           | Receptor Binding Domain                         |
| RDW           | Red Blood Cell Distribution Width               |
| RR            | Respiratory Rate                                |
| RT-PCR        | Reverse Transcription Polymerase Chain Reaction |
| SARS          | Severe Acute Respiratory Syndrome               |
| SARS-CoV-2    | Severe Acute Respiratory Syndrome Coronavirus-2 |
| SBP           | Systolic Blood Pressure                         |
| SPSS          | Statistics Package For The Social Sciences      |
| TMPRSS2       | Transmembrane Serine Protease 2                 |
| TNF- $\alpha$ | Tumor Necrosis Factor-Alpha                     |
| VEGF          | Vascular Endothelial Growth Factor              |
| WBCs          | White Blood Cells                               |
| WHO           | World Health Organization                       |

#### References

- Alkan G, Emiroğlu M, Tüter Öz SK, Emiroğlu HH, Türk Dağı H, and Körez MK (2022): Gastrointestinal and Liver Manifestations in Children with COVID-19 and Their Relationship to Clinical Course. *Turk Arch Pediatr.*, 57:413–420.
- Al-Khlaifat AM, Al Quraan AM, Nimri AF, Khaled NE, Ramadina N, Ayyash FF, et al. (2023): Factors Influencing the



- Length of Hospital Stay Among Pediatric COVID-19 Patients at Queen Rania Al Abdullah Hospital for Children: A Cross-Sectional Study 2023 Feb 14;15(2):e35000.
- **Ahmed A E-A, Rizk SG, Rashwan NI, Hassan MH. (2023).** COVID-19 in pediatric patients: Clinical presentations, diagnosis, and treatment. *International Journal of Chemical and Biochemical Sciences (IJCBS)*, 24(6) : 25-44.
  - **Annweiler C, Cao Z, Wu Y, Faucon E, Mouhat S, Kovacic H, et al. (2020):** Counter-regulatory 'Renin-Angiotensin' System-Based Candidate Drugs to Treat COVID-19 Diseases in SARS-CoV-2-Infected Patients. *Iddt* 20, 407–408.
  - **Bastolla U, Chambers P, Abia D, Garcia-Bermejo M, and Fresno M (2022):** Is Covid-19 Severity Associated With ACE2 Degradation? *Front. Drug Discov. , Sec. In silico Methods and Artificial Intelligence for Drug Discovery Volume 1 – 2021.*
  - **Bhopal SS, Bagaria J, Olabi B, and Bhopal R (2021):** Children and young people remain at low risk of COVID-19 mortality. *The Lancet Child & Adolescent Health*, 1; 5 (5):e12-3.
  - **Brodin P. (2021):** Immune determinants of COVID-19 disease presentation and severity. *Nat Med.*, 27:28–33.
  - **Cabezudo-García P, Ciano-Petersen NL, Mena-Vázquez N, Pons-Pons G, Castro-Sánchez MV, and Serrano-Castro PJ (2020):** Incidence and case fatality rate of COVID-19 in patients with active epilepsy. *Neurology*, 95(10):e1417-e1425.
  - **Cavallo F, Rossi N, and Chiarelli F (2020):** Novel coronavirus infection and children. *Acta Biomed*, 91(2):172–176.10.23750/abm.v91i2.9586).
  - **Centers for Disease Control Prevention (CDC).** CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel. Available at: <https://www.fda.gov/media/134922>.
  - **Chen C, Chen S, Fang S, Lu S, Bai C, and Wang Y (2023):** Diagnostic accuracy of SARS-CoV-2 antigen test in the pediatric population: *Pediatr Neonatol*, 64(3): 247–255.
  - **Chen F, Liu ZS, Zhang FR, Xiong RH, Chen Y, Cheng XF, et al. (2020):** First case of severe childhood novel coronavirus pneumonia in China. [Article in Chinese]. *Zhonghua Er Ke Za Zhi.*, 58:179–82.
  - **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. *Lancet*, 395:507–13.
  - **Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. (2020):** Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int.*, 97:829–838.
  - **Ciaglia E, Vecchione C, and Puca AA (2020):** COVID-19 Infection and Circulating ACE2 Levels: Protective Role in Women and Children. *Front. Pediatr.* 8, 206.
  - **Cui S, Chen S, Li X, Liu S, and Wang F. (2020):** Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost.* 2020; 18(6):1421–1424.
  - **Eldin NMB, Saleh M, Labib B, Othman M, Chacko L, Mae D, et al. (2022):** Clinical and Laboratory Features of PCR-Confirmed and Clinically Suspected COVID-19 Pediatric Patients: A Single Hospital-Based Experience During the First COVID-19 Wave in the United Arab Emirates. *Front.Pediatr.*, Sec. Pediatric Infectious Diseases Volume 10 – 2022.
  - **Elghoudi A, Aldhanhani H, Ghatasheh G, Sharif E, and Narchi H. (2020):** COVID-19 in children and young adolescents in Al Ain, United Arab Emirates—a retrospective cross-sectional study. *Front Pediatr.* (2020) 8:603741. 10.3389/fped.2020.603741
  - **Esmaeeli H, Ghaderian M, Zanjani KS, Ghalibafan SF, Mahdizadeh M, and Aelami MH (2021):** COVID-19 in Children with Congenital Heart Diseases: A Multicenter Case Series from Iran. *Case Rep Pediatr.*, 6690695. Published online 2021 Apr17.
  - **Esmaeili DM, Mehrabani S, Sorkhi H, Nikpour M, Tabatabaie M, Mohammadi M, and Kiani M (2020):** COVID-19 and Digestive System in Children: A Retrospective Study. *Arch Iran Med.*, 23:782–786.
  - **Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. (2020):** Sensitivity of chest CT for COVID-19: comparison to RT-PCR. *Radiolog*, 296:E115–7.
  - **Franchini M, Marano G, Cruciani M, Mengoli C, Pati I, Masiello F, et al. (2020):** COVID-19-associated coagulopathy. *Diagnosis*, 7:357–363.
  - **Gabr AE, Abdelhameed AM, Mohammad SA, Fouda EM, Maher SM, Fathallah SK, et al. (2023):** Chest CT features of coronavirus disease 2019 (COVID-19) in pediatric patients and its correlation with the clinical condition. *Egyptian Journal of Radiology and Nuclear Medicine* volume 54.

- **Garcia MA, Rucci JM, Thai KK, Lu Y, Kipnis P, Go AS et al. (2021):** Association between troponin I levels during sepsis and postsepsis cardiovascular complications. *American Journal of Respiratory and Critical Care Medicine*, 204(5): 557-565.
- **Gotzinger F, Santiago-García B, Noguera-Julían A, Lanaspá M, Lancella L, Carducci FIC, et al. (2020):** ptnet COVID-19 Study Group. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. *Lancet Child Adolesc Health*, 4(9):653-661.
- **Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. (2020):** Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.*, 382:1708–20.
- **Guo Y, Hu K, Li Y, Lu C, Ling K, Cai C, et al. (2022):** Targeting TNF- $\alpha$  for COVID-19: Recent Advanced and Controversies *Front Public Health*, 10: 833967. Published online 2022 Feb 11.
- **Gurwitz, D. (2020).** Angiotensin Receptor Blockers as Tentative SARS-CoV-2 Therapeutics. *Drug Dev. Res.* 81, 537–540.
- **Hassany M, Abdel-Razek W, Asem N, AbdAllah M and Zaid H (2020):** Estimation of COVID-19 burden in Egypt. *Lancet Infect Dis.*, 20(08):896–897.
- **Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrler T, et al. (2020):** SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*, 16;181(2):271-280.e8.
- **Hoste L, Prytula A, Dehoorne J, Bruyne RD, Biervliet SV, Waele KD et al. (2023):** Comparison of SARS-CoV-2 seroconversion in children with chronic diseases with healthy children and adults during the first waves of the COVID-19 pandemic. *Front Pediatr.*, 11: 1210181.
- **Hou H, Wang T, Zhang B, Luo Y, Mao L, Wang F, Wu S, and Sun Z (2020):** Detection of IgM and IgG antibodies in patients with coronavirus disease 2019 *Clin Transl Immunology*, 9(5): e1136.
- **Hu B, Wang D, Hu C, Hu M, Zhu F, Xiang H et al. (2020):** Clinical Features and Predictors for Outcome in Critically Ill Patients with COVID-19 Infection from Wuhan, China. *Journal of Translational Critical Care Medicine* | Volume. Jan; 2(1).
- **Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. (2020):** Clinical Features of Patients Infected With 2019 Novel Coronavirus in Wuhan, China. *Lancet*, 395:497–506.
- **Imai Y, Kuba K, Rao S, Huan Y, Guo F, Guan B, et al. (2005):** Angiotensin-converting Enzyme 2 Protects from Severe Acute Lung Failure. *Nature* 436, 112–116.
- **Kainth MK, Goenka PK, Williamson KA, Fishbein JS, Subramony A, Barone S, et al. (2020):** Early experience of COVID-19 in a US Children's Hospital. *Pediatrics*, 146:e2020003186.
- **Klein SL and Flanagan KL. (2016):** Sex differences in immune responses. *Nat Rev Immunol.* 2016; 16:626–38.
- **Kumar A and Kaistha S (2023):** Abdominal Crunch Syndrome Creates a Diagnostic Challenge in Treating a Pilot with Acute Upper Abdominal Pain. *Aerospace Medicine and Human Performance*, 94(2): 86-89.
- **Li Y, Zhou W, Yang L, and You R (2020):** Physiological and Pathological Regulation of ACE2, the SARS-CoV-2 Receptor. *Pharmacol. Res.* 157, 104833.
- **Liu X, Tang J, Xie R, Li W, Chen J, Guo Y, et al. (2020):** Clinical and Epidemiological Features of 46 Children <1 Year Old With Coronavirus Disease 2019 in Wuhan, China: A Descriptive Study. *J Infect Dis.*, 222:1293–1297.
- **Livingston E and Bucher K (2020):** Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA*, 323(14):1335.
- **Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. (2020):** SARS-CoV-2 Infection in Children. *N Engl J Med.*, 382:1663–5.
- **Ma A, Zhang L, Ye X, Chen J, Yu J, Zhuang L, et al. (2021):** High Levels of Circulating IL-8 and Soluble IL-2r Are Associated With Prolonged Illness in Patients With Severe COVID-19. *Front Immunol*, 12:626235.
- **Malas MB, Naazie IN, Elsayed N, Mathlouthi A, Marmor R, Clary B (2020):** Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: a systematic review and meta-analysis. *E.Clinical Medicine*, 29-30.
- **Maryam N, Fatemeh C, Bahman A, Abdolhalim R, Leila B, Hamed N et al. (2021):** COVID-19 in Pediatrics: Demographic, Clinical, Laboratory, and Radiological Characteristics of Infected Patients With SARS-CoV-2 *Front Pediatr.*, 9: 808187. Published online 2022 Jan 13.
- **Meguid NA, Nashaat NH, Abdallah HR, Hemimi M, Elnahry A, El-Hariri HM, et al. (2022):** Influence of COVID-19 pandemic lockdown on a sample of Egyptian children with Down syndrome. *Egyptian Journal of Medical Human Genetics*, 23.1: 68.
- **Melgosa M, Madrid A, Álvarez O, Lumbreras J, Nieto F, Parada E, et al.**

- (2020): Pediatric Nephrology Association (2020) SARS-CoV-2 infection in Spanish children with chronic kidney pathologies. *Pediatr Nephrol.* 10.1007/s00467-020-04597-1.
- **Merad M and Martin JC (2020):** Pathological inflammation in patients with COVID-19. A key role for monocytes and macrophages. *Nat. Rev. Immunol.*, 20, 355–362, Erratum in 2020, 20, 448.
  - **Moreira A, Chorath K, Rajasekaran K, Burmeister F, Ahmed M, and Moreira A (2021):** Demographic predictors of hospitalization and mortality in US children with COVID-19. *European Journal of Pediatrics*, 180:1659-63.
  - **Morello W, Vianello FA, Proverbio E, Peruzzi L, Pasini A, and Montini G (2022):** COVID-19 and idiopathic nephrotic syndrome in children: systematic review of the literature and recommendations from a highly affected area. *Pediatr Nephrol.*, 37(4): 757–764.
  - **Mostafa AS, Abdalbaky A, Fouda EM, Shaaban HH, Elnady HG, Hassab-Allah M, et al. (2020):** Practical approach to COVID-19: an Egyptian pediatric consensus. *Egyptian Pediatric Association Gazette*, Dec; 68(1):1-8.
  - **Neumann J, Prezzemolo T, Vanderbeke L, Roca CP, Gerbaux M, et al. (2020):** Increased IL-10-producing regulatory T cells are characteristic of severe cases of COVID-19. *Clin. Transl. Immunol.*, 9, e1204, PMID: PMC7662088.
  - **Offringa A, Montijn R, Singh S, Paul M, Pinto YM, and Pinto-Sietsma SJ (2020):** The Mechanistic Overview of SARS-CoV-2 Using Angiotensin-Converting Enzyme 2 to Enter the Cell for Replication: Possible Treatment Options Related to the Renin-Angiotensin System. *Eur. Heart J. Cardiovasc. Pharmacother.* 6, 317–325.
  - **Pagliaro P and Penna C (2020):** ACE/ACE2 Ratio: A Key Also in 2019 Coronavirus Disease (Covid-19)? *Front. Med.* 7, 335.
  - **Penha D, Pinto EG, Matos F, Hochegger B, Monaghan C, Taborda-Barata L et al. (2021):** CO-RADS: coronavirus classification review. *Journal of Clinical Imaging Science*, 11(9).
  - **Qian G, Zhang Y, Xu Y, Hu W, Hall I, Yue J, et al. (2021):** Reduced inflammatory responses to SARS-CoV-2 infection in children presenting to hospital with COVID-19 in China. *E Clinical Medicine*. Volume 34, 100831
  - **Qiu H, Wu J, Hong L, Luo Y, Song Q and Chen D (2020):** Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis.*, 20(06):689–696.
  - **Rahmati M and Moosavi M (2020):** Cytokine-targeted therapy in severely ill COVID-19 patients: Options and cautions. *EJMO*, 4, 179–181.
  - **Remuzzi A and Remuzzi G (2020):** COVID-19 and Italy: what next? *Lancet.*, 395:1225–8.
  - **Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. (2020):** Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA.*, 22;323(20):2052–9.
  - **Safadi MAP (2020):** The intriguing features of COVID-19 in children and its impact on the pandemic. *J Pediatr.*, 96:265–268.
  - **Sarkesh A, Daei Sorkhabi A, Sheykhsaran E, Alinezhad F, Mohammadzadeh N, Hemmat N, et al. (2020):** Extrapulmonary clinical manifestations in COVID-19 patients. *Am J Trop Med Hyg.*, 103:1783–96.
  - **Schafer K, Goldschmidt E, Oostra D, Fish J, Russell T, Lurie F (2022):** The clinical significance of ultra-high D-dimer levels. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, 10(1): 8-13.
  - **Shahbaznejad L, Rouhanizadeh H, Navaeifar MR, Hosseinzadeh F, Movahedi FS and Rezai MS (2021):** Clinical characteristics and outcomes of COVID-19 in children in northern Iran. *Int J Pediatrics*, 5558287.
  - **Sharif N, Opu RR, Ahmed SN, Sarkar MK, Jaheen R, Daullah MU et al. (2021):** "Prevalence and impact of comorbidities on disease prognosis among patients with COVID-19 in Bangladesh: A nationwide study amid the second wave." *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 15(4): 102148.
  - **Simpson M, Collins C, Nash DB, Panesar LE, and Oster ME (2020):** Coronavirus disease 2019 infection in children with pre-existing heart disease. *J Pediatr.*, 227:302-307.e2.
  - **Singh S, Darnal SK, and Chand AB (2021):** Serum Ferritin Concentration in Corona Virus Disease 19. *Nepal J Health Sci.* 2021 Jul-Dec, 1 (2): 34, 7.
  - **Soltani J, Sedighi I, Shalchi Z, Sami G, Moradveisi B, and Nahidi S (2020):** Pediatric coronavirus disease 2019 (COVID-19): An insight from west of Iran. *North Clin Istanbul*, 7:284.

- **Soriano LDH, Sterling A, Edgin J, Hamilton DR, Berry-Kravis E, Nunnally AD et al. (2022):** Associations Among Sex, Cognitive Ability, and Autism Symptoms in Individuals with Down Syndrome. Original Paper, Open Access, Published: 31 October 2022.
- **Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, et al. (2020):** The different clinical characteristics of corona virus disease cases between children and their families in China - the character of children with COVID-19. *Emerg Microbes Infect.*, 9 (01):707–713.
- **Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang F, et al. (2020):** Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. *World J Pediatr.*, Mar 19.
- **Sun ML, Yang JM, Sun YP, and Su GH (2020):** Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia. *Zhonghua Jie He He Hu Xi Za Zhi* 43, 219–222.
- **Suratannon N, Dik WA, Chatchatee P, and Hagen PM (2020):** COVID-19 in children: heterogeneity within the disease and hypothetical pathogenesis. *Asian Pac J Allergy Immunol*, 38:170–177.
- **Tang N, Bai H, Chen X, Gong J, Dengju LD, and Sun Z (2020):** Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost.*, 18:1094– 1099.
- **Tang N, Li D, Wang X, and Sun Z (2020):** Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.*, 18(4):844–847.
- **Vervoort D, Luc JGY, and Percy E (2020):** Assessing the collateral damage of the novel coronavirus: a call to action for the Post-COVID-19 era. *Ann Thorac Surg.*, 110:75760.
- **Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. (2020):** Virological assessment of hospitalized patients with COVID-2019. *Nature*, 581:465–9.
- **Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, et al. (2020):** Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*, 367, 1260–1263.
- **Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, et al. (2020):** Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study. *Clin Infect Dis.*, 29:ciaa199.
- **Wu P, Hao X, Lau EHY, Wong JY, Leung KSM, Wu JT, et al. (2020):** Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China. *Euro Surveill*, 25(03).
- **Yameny AA (2021):** D-dimer levels in COVID-19 out-hospitalized patients in Egypt Ahmed Abdelhalim Yameny Society of Pathological Biochemistry and Hematology, Egypt. *Journal of Medical and Life Science* www. jmals. journals.ekb.eg.
- **Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. (2020):** "Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis.*, 94:91-95.
- **Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. (2020):** Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med.*, 8:475–81.
- **Yang Y, Yang M, Yuan J, Wang F, Wang Z, Li J, et al. (2020):** Laboratory diagnosis and monitoring the viral shedding of SARS-CoV-2 infection. *Innovation (N Y)*, 1:100061. doi: 10.1016/j.xinn.2020.100061.
- **Yun Y, Feng Z, and Zhang J (2023):** COVID-19 and liver dysfunction in children: Current views and new hypotheses *World J Hepatol*, 27; 15(3): 353–363. Published online 2023 Mar 27.
- **Zaffanello M, Piacentini G, Nosetti L, Ganzarolli S, and Franchini M (2021):** Thrombotic risk in children with COVID-19 infection: A systematic review of the literature. *Thromb Res.*, 205: 92–98.
- **Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD and Fouchier RA (2012):** Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N. Engl. J. Med.*, 367, 1814–1820.
- **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. *Lancet*, 395(10229):1054-62.
- **Zimmermann P and Curtis N. (2021):** Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Arch Dis Child*, 106:429–39.