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Effect of Pre-Existing Chronic Medical Conditions on Clinical Features and Disease Outcomes of COVID-19 Infection in Jordanian Children

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Abstract

Background: The COVID-19 pandemic emerged unexpectedly, impacting millions worldwide and, though waning in many regions, remains a significant concern. This study focused on understanding COVID-19's clinical presentation, disease progression, and outcomes among hospitalized pediatric patients. Additionally, it sought to investigate the impact of concurrent chronic medical conditions on disease severity. **Methods:** Conducted retrospectively between September 2020 and December 2021, this study observed pediatric patients (below 18 years) hospitalized with confirmed COVID-19 at an Irbid, Jordan tertiary healthcare center. Patients meeting inclusion criteria, including a positive nasal swab PCR test and hospitalization need, were analyzed. Epidemiological and clinical data were collected and segregated into two groups (A and B) based on the presence of chronic conditions. Comparative analysis encompassed presentation, disease trajectory, and outcomes between these groups. **Results:** Among 451 tested positive patients, 112 were included in the study. Significant differences emerged between the two pediatric groups hospitalized for COVID-19. Those with concurrent chronic illnesses exhibited heightened symptom severity—fever, dyspnea, fatigue—and a higher incidence of abnormal chest radiographs, often requiring intensive care and experiencing elevated mortality rates. **Conclusion:** This study underscores the criticality of prioritizing COVID-19 management strategies for pediatric patients with pre-existing chronic medical conditions. The findings highlight the increased vulnerability and poorer outcomes experienced by this subgroup, emphasizing the necessity for tailored interventions and focused care approaches.

Keywords

COVID-19, Pediatric, Chronic Disease, Disease Severity

1. Introduction

Towards the end of 2019 in Wuhan, China, a novel coronavirus was identified and determined to be responsible for the sudden appearance of a cluster of pneumonia infections that initially defied diagnosis and treatment. Subsequently, it spread regionally and then, globally at a rapid pace, thereby resulting in a worldwide pandemic; the World Health Organization named it coronavirus disease 2019 (COVID-19) and declared COVID-19 a pandemic on March 11, 2020 [1].

The pandemic caused a global health emergency that lasted more than two years and posed risks and challenging demands on health services worldwide [2]. The disease is caused by the zoonotic coronavirus SARS-CoV-2 and is primarily transmitted from person-to-person via airborne droplets [3] and possibly via other means [4].

In early 2020, a survey of the data from different hospitals worldwide reported that children admitted with positive test results accounted for a small percentage of the infected population [5] [6] [7] and mostly did not require increased level of hospitalization compared to that of adults [8]. Furthermore, they rarely required a pediatric intensive care unit admission [9], although severe cases have been reported [10] [11].

Typical symptoms in infected children included fever and cough, while laboratory findings included normal white blood cell and lymphocyte counts [8] [12]; in pediatric patients, abnormal leukopenia/Lymphopenia and elevated creatinine kinase levels were observed [13]. However, the disease course in children is not always mild, and in some cases, serious complications, such as multisystem inflammatory syndrome, were observed [14].

Chronic diseases, including diabetes, hypertension, malignancies, chronic obstructive pulmonary disease, and cardiovascular diseases, in COVID-19 patients can lead to complications and an increased risk of severity and mortality [15]. The increased risk of fatality due to COVID-19 is presumed to be high in patients with cancer as a result of the underlying malignancy [16]. Furthermore, increased mortality was found to be significantly associated with old age, multiple comorbidities, need for intensive care unit (ICU) support, and elevated D-dimer, lactate dehydrogenase, and lactate levels in multivariate analysis [16].

A higher risk of severe SARS-CoV-2 infection appears to be associated with older age and a higher number of comorbidities [17]. Various strategies used for managing cases of infected children include ICU admission; other interventions include administration of aspirin, steroids, aspirin, and anticoagulants [18].

Data from our part of the world on this important topic is extremely limited. This study aimed to describe the clinical presentation, course, and outcomes of all children with SARS-CoV-2 infection who required hospitalization in our hospital. Furthermore, we aimed to evaluate the effect of coexisting chronic medical conditions on disease severity and outcome. This will influence the management of children with chronic medical illnesses whether infected or at risk of acquiring SARS-CoV-2 infection.

2. Methods

2.1. Study Setting

A retrospective cohort study was conducted involving confirmed pediatric cases of COVID-19 infection admitted to King Abdullah University Hospital (KAUH) between September 2020 and December 2021. The study encompassed all consecutive cases of individuals under 18 years of age admitted to KAUH during this period.

King Abdullah University Hospital (KAUH) stands as the largest referral hospital in Northern Jordan and played a pivotal role in receiving the majority of COVID-19 cases in this region during the pandemic. The Ministry of Health formulated clinical protocols for COVID-19 case management, which were implemented nationwide and regularly updated based on evolving evidence.

2.2. Study Population

The study included confirmed pediatric cases of COVID-19 diagnosed through real-time reverse transcriptase-polymerase chain reaction (RT-PCR) testing upon hospital admission. Patients older than 18 years, those testing positive solely through the COVID-19 Rapid Antigen Test, individuals not requiring hospitalization, and those lacking sufficient patient data were excluded from the study.

2.3. Chronic Disease Definition

Pediatric chronic disease diagnoses were established by physicians utilizing valid methodologies, professional standards, and diagnostic classification criteria.

2.4. COVID-19 Testing

Trained pediatric residents collected nasopharyngeal swabs, promptly transferring samples to the Serology lab for assessment of SARS-CoV-2 RNA presence. A one-step real-time RT-PCR method utilizing the Molaccu COVID-19 Detection kit manufactured by Zybio Inc., China, was employed in this study.

2.5. Severity Score

Severity assessment relied on clinical notes indicating severe respiratory distress, multi-organ failure, shock development, or the need for ICU admission.

2.6. Data Collection

Patient data were retrieved from electronic records, manually reviewed, and recorded in an Excel sheet. Information encompassed patient demographics, clinical data (chronic diseases, presentation, physical findings, medications, hospitalization details, and outcomes), laboratory measurements, and imaging results (CXR/Chest CT scan). Patients were categorized into two groups: Group A (patients diagnosed with a chronic disease) and Group B (previously healthy patients before COVID-19 symptoms onset), facilitating comparative analysis.

2.7. Ethical Approval

The study received approval from the Institutional Review Board of Jordan University of Science and Technology and the research committee of the Faculty of Medicine (20220143).

2.8. Statistical Analysis

Data analysis utilized IBM SPSS version 23. Descriptive statistics included mean standard deviation (SD) for quantitative data and frequencies/percentages for qualitative data. A significance level of $p < 0.05$ indicated statistical significance. Bivariate analysis comparing patient characteristics, radiological findings, comorbidities, and laboratory parameters between groups with and without chronic medical illnesses employed nonparametric (Mann–Whitney U test) or parametric tests (Student's t-test) for continuous variables, as appropriate.

3. Results

3.1. Study Population

Out of 451 COVID-19 positive cases identified during the study, 112 met the inclusion criteria. The cohort comprised 54.5% females, with a mean presentation age of 11 years (range: 0 - 18).

3.2. Chronic Diseases and Demographics

The cohort was categorized into Group A (patients with chronic diseases, n = 38) and Group B (previously healthy, n = 74). Neurological disorders (26.3%), hematology/oncology (23.7%), and gastrointestinal diseases (21.1%) were the most prevalent chronic conditions. Immunosuppressants (23.6%) were the most commonly used medications among patients with chronic diseases (see Table 1).

3.3. Symptoms and Disease Presentation

Group A predominantly showed cough, fever, and fatigue, while Group B exhibited more nasal symptoms, headache, and sore throat. Statistically significant differences were observed; Group A reported fever, dyspnea, and fatigue more frequently ($p = 0.02$, 0.024, 0.037, respectively), while sore throat was more common in Group B ($p = 0.049$). Loss of smell or taste was not reported by any patient (see Table 2).

Table 1. The number of patients with chronic illness and requiring chronic medications.

Distribution of chronic illness	Numbers of patients
Respiratory	5 asthma, 1 chronic lung disease, 1 chronic sinusitis
Gastrointestional	7 faliure to thrive, 1 lover cirrhosis, 1 auto immune hepatitis
Neurological	7 developmental delay, 3 epilepsy
Hematology/oncology	5 malignancy, 2 solid tumors, 1 Idiopathic thrombocytopenia purpura
Renal	1 nephrotic syndrome, 1 renal failure
Cardiac	1 patients
Endocrine	2 diabetes, 1 thyroid disease
Chronic medications	Numbers of patients
Steroids	6
Chemotherapy	3
Proton pump inhibitors	4
Immunomodulators	2

Table 2. Comparison between patients admitted for COVID-19 infection with chronic illnesses and without chronic illness.

	Patients admitted with COVID-19 infection with chronic disease (38.34%) (Group A)	Patients admitted with COVID-19 infection without chronic disease (74.66%) (Group B)	p-Value
Average age at diagnosis	7.7 ± 5.6	10.5 ± 5.9	0.017
Gender (M %)	53%	45%	0.423
Symptomatic (n, %)			
- Cough	15 (39.5)	17 (23.0)	0.070
- Fever	15 (39.5)	14 (18.9)	0.020
- Fatigue	10 (26.3)	8 (10.8)	0.037
- Nasal symptoms	5 (13.2)	12 (16.2)	0.676
- Dyspnea	9 (23.7)	6 (8.1)	0.024
- Headache	2 (5.3)	11 (14.9)	0.758
- Sore throat	1 (2.6)	11 (14.9)	0.049
- Vomiting	1 (2.6)	8 (10.8)	0.133
- Others (tachycardia, chest pain, unsteady gait)	3 (7.9)	5 (6.8)	0.831
- Muscle aches	5 (13.2)	3 (4.1)	0.080
- Tachypnea	3 (7.9)	4 (5.4)	0.606
- Abdominal pain	2 (5.3)	5 (6.8)	0.758
- Diarrhea	0	5 (6.8)	0.103

Continued

- Poor appetite	3 (7.9)	1 (1.3)	0.076
- Hypoactivity	2 (5.3)	0	0.048
- Loss of smell	0	0	
- Loss of taste	0	0	
Radiological evaluation:			
- Abnormal CXR (n, %)	14 (36.8)	13 (17.6)	0.027
Laboratory evaluation:			
- High inflammatory markers (ESR, CRP)	5 (13.2)	12 (16.2)	0.676
- Average LDH	560	417	
- Average Ferritin	100	32.1	
- Hb (Avg ± SD)	12.2 ± 1.80	12.6 ± 1.67	0.353
- WBC	8634.6 ± 5947.04	7622 ± 2972	0.327
- Lymphocyte count	3039.69 ± 3410.97	2447.84 ± 1234.4	0.286
- Neutrophilic count	4284.49 ± 3025.9	3820.3 ± 2138.27	0.454
- Platelet count	270,807 ± 202832.5	279145.8 ± 149500.4	0.844
Level of care:			
- Floor	33 (86.8)	71 (95.9)	0.080
- ICU	5 (13.2)	3 (4.1)	0.080
Highest respiratory support:			
- None	32 (84.2)	73 (98.6)	0.036
- CPAP	2 (5.3)	0	0.048
- HFNC	1 (2.6)	1 (1.4)	0.652
- Mechanical ventilation	3 (7.9)	0	0.016
COVID-19 specific treatment:			
- Hydroxychloroquine	1 (2.6)	8 (10.8)	0.133
- Steroids	5 (13.2)	3 (4.1)	0.080
- IVIG	1 (2.6)	1 (1.4)	0.653
- Remdesivir	0	1 (1.4)	0.465
- Azithromycin	1 (2.6)	0	0.166
Outcome:			
- Death	5 (13.2)	0	0.002

3.4. Laboratory and Radiographic Findings

No significant differences were noted in inflammatory markers, white blood cell counts, hemoglobin, or platelet counts between the two groups. Abnormal chest

radiographs were more prevalent in Group A (36.8%) compared to Group B (17.6%) ($p = 0.027$) (see Table 2).

3.5. Hospitalization and Intensive Care

Group A showed a higher ICU admission rate (13.2%) than Group B (4.1%). A subset of Group A patients required respiratory support, with no significant difference in treatment protocols between the groups. However, mortality was significantly higher in Group A (13.2%) compared to Group B ($p = 0.02$) (see Table 2).

4. Discussion

Our study focused on understanding the influence of pre-existing chronic medical conditions on the clinical features and outcomes of COVID-19 in pediatric patients. Similar to earlier investigations [19] [20] [21] [22], our study categorizing patients into Groups A and B showed distinct clinical presentations and outcomes.

A study on a cohort of 41 infected Chinese individuals found a death rate of 15%, a rate of ICU admission of 32%, and 32% had underlying diseases [19]. Our study revealed a similar percentage for chronic conditions (34%), and the death rate is also close to our data (13.2%) for Group A patients; however, ICU admission percentages were different from our findings, which were 13.2% and 4.1% for Groups A and B, respectively.

Studies have shown that the disease in children is generally milder than that in adults, although severe cases with multi-organ involvement have been reported [20] [21] [22].

A study on 1,320,488 cases in the United States in 2020 found equal incidence rates of COVID-19 among males and females and the lowest incidence for children in the age group ≤ 9 years, but the symptoms and their severity varied with age, sex, and underlying conditions, with severe symptoms (with a high rate of hospitalization) for males and older patients [20]. This finding is consistent with those of earlier studies.

As of May 30, 2020, the following underlying health conditions were found to be most prevalent among COVID-19 patients in the US: cardiovascular disease (32%), diabetes (30%), and chronic lung disease (18%). Patients with these conditions are six times more likely to require hospitalization and 12 times more likely to die than those with no underlying conditions [20], which is similar to the results obtained in our study. Other studies have estimated the prevalence of underlying conditions among COVID-19 patients [23].

A study in the US found that, between March 2020 and May 2021, 3106 children infected with COVID-19 were hospitalized, with ~9% suffering a severe respiratory form of the disease. They also reported associations between severity and feeding tube dependence and diabetes mellitus and obesity for the 2 - 17 years age group of hospitalized children [24], which is consistent with our re-

sults. Another study found an increased prevalence of underlying medical conditions among COVID-19 hospitalized patients, and older adults have increased probability of hospitalization [25].

A study, performed in early 2020, on 72,314 cases in China found a low incidence of COVID-19 (<1%) among young children (<10 years old) [6]. Another study, performed in 2020 in China, on 1391 children reported an incidence rate of 12.3%, and the median age of the infected children was 6.7 years, with 15.8% of the infected children showing no symptoms or radiological evidence of infection and 41.5% presenting fever [26]. In this study, the incidences of fever in the two groups were 39.5% and 18.9%, respectively. The incidence of fever is generally less common among previously healthy children, although the aforementioned study did not elaborate on the percentage of infected children with underlying medical conditions. A meta-study on 9335 children from 31 countries found that the mean incidence rate of asymptomatic children was 13% and those with fever or cough was 63% and 34%, respectively [20]. The latter value is close to the data obtained for group A patients in this study. A study in 2021 reviewed results of 129 studies that analyzed data from 10,251 young patients (with a mean age of seven) from 31 countries and found that 57.4% required hospitalization (96 of whom died) and 88.9% recovered. The most prevalent among the diverse symptoms were fever and cough 63.3% and 33.7%, respectively [27]. The latter is consistent with the results obtained for both the groups in this study. Our observations align with prior studies [19] [20] [23] highlighting the severity of COVID-19 among children with underlying chronic diseases, emphasizing increased mortality rates and ICU admissions in these cohorts

A study in 2021 found diabetes patients to be at a high risk of increased severity and worse outcomes, including increased mortality, need for respiratory intervention, and ICU admissions, although they did not have an increased risk of infection [28]. Additionally, another study found that these patients were at a high risk of severity, complications, and death and three times more likely to need critical respiratory intervention [28]. This finding is consistent with our finding that Group A patients were three times more likely to require ICU admission.

Diabetes mellitus is associated with increased disease severity and a high risk of mortality in patients with COVID-19 [29]. Additionally, our findings are supported by another study on early COVID-19 patient data that demonstrated an increased incidence among patients with underlying chronic medical conditions, including obesity, diabetes, chronic respiratory, kidney, and cardiovascular disease [30].

Another study revealed that COVID-19 patients suffering from chronic respiratory diseases were at a high risk of mortality [31]. A study on 50 German patients with and without (26 and 24, respectively) acute respiratory distress syndrome also found an association between the severity of COVID-19 and elevated inflammation and pre-existing respiratory diseases and obesity [32]. This result

is in qualitative agreement with our findings. An incidence of one or more underlying conditions, including asthma and obesity, was found in over one quarter of the 43,465 young (≤18 years) patients included in the study, and a high risk for severity associated with them was observed [33].

Other studies, found a high risk of severity, mortality, and ICU admission among COVID-19 patients with chronic diseases, including hypertension [34] [35]. Consistent with existing literature [6] [24] [25] [26], our findings emphasize the heightened risk of severity, complications, and mortality in pediatric COVID-19 patients with specific chronic medical conditions, such as diabetes, chronic respiratory diseases, and obesity.

A literature review of 29 studies on chest computerized tomography images of 1026 children infected with COVID-19 found lower incidence and severity of abnormal lesions in children than those in adults, with the percentages of normal and abnormal scans at ~35.7% and ~27.7%, respectively [36]. In this study, the overall incidence of abnormal chest scans was 24.1%, which is similar to the aforementioned value of 27.7% reported in a previous study. Our study's concordance with previous research [31] [32] [33] [36] showcasing the association between abnormal chest scans and disease severity in pediatric COVID-19 cases underscores the importance of imaging in evaluating disease progression.

Our results Highlighting the necessity for tailored strategies and prioritized vaccination efforts [28] [29] [30], our findings stress the need to protect children with underlying chronic illnesses due to their increased vulnerability to severe outcomes.

5. Study Limitations

Acknowledging the limitations of our study, including the short study period and potential data entry errors, we propose a larger-scale, multicenter prospective study to validate and expand upon these findings, emphasizing the necessity for prolonged follow-up and enhanced sample size calculations for conclusive results.

6. Conclusion

In summary, our study contributes to the existing body of knowledge by reaffirming the impact of pre-existing chronic medical conditions on the severity and outcomes of COVID-19 in pediatric patients. These insights underscore the imperative of tailored clinical management and prioritized vaccination strategies for this vulnerable population.

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None.

Conflicts of Interest

The authors have no conflict of interest to disclose.

Ethical Statement

The study was approved by the ethical committee/IRB and scientific committee at Jordan University of Science and Technology and granted the no. 20220143.

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Abbreviations

COVID-19: Coronavirus disease 2019; ICU: Intensive Care Unit.