

*Research Article***Clinical manifestations of COVID-19 infection in infants and children during first and second waves in Minia Governorate – Egypt****Mostafa M. Asem<sup>1</sup> Mohamed A. Mohamed<sup>2</sup>, Asmaa N. Moustafa<sup>2</sup>, and Ahmed H. Kasem<sup>3</sup>,**<sup>1</sup> Department of forensic medicine and clinical toxicology, Faculty of medicine, Minia University<sup>2</sup> Department of Pediatric Medicine & Neonatology, Faculty of Medicine, Minia University<sup>3</sup> Department of Chest Disease, Faculty of Medicine, Minia University**Abstract**

**Background:** Coronaviruses causing dangerous diseases for both humans and animals. A new coronavirus was found to be the source of a cluster of pneumonia cases in Wuhan, China's Hubei province, at the end of 2019. The aim of the study is determined various clinical manifestations of COVID-19 in infant and children. **Methods:** This prospective clinical study was conducted at Minia isolation hospitals and Minia University Hospital of Pediatrics, Minia, Egypt during the period from the first of April, 2020 to 31th of august 2021. 62 children were included in this study aged from 4 months -16 years. Infants and children were diagnosed as Covid-19 positive with real time PCR, then we compare these data between the 1st wave (during 2020) and the 2<sup>nd</sup> wave (during 2021). **Results:** The second wave of 2021 showed significant difference as regarding comorbidities, respiratory symptoms and signs. **Conclusion:** Children at any age and both sexes are susceptible to COVID-19 virus infection. **Conclusion:** Children cases in the year 2020, show no or mild clinical manifestations compared with those admitted during 2021.

**Keywords:** COVID-19, Children, Infants, Co-morbidities, Waves**Introduction**

Coronaviruses causing dangerous diseases for both humans and animals. A new coronavirus was found to be the source of a cluster of pneumonia cases in Wuhan, China's Hubei province, at the end of 2019. It quickly spread throughout China, culminating in an epidemic, with a growing number of cases reported in other countries throughout the world.<sup>(1)</sup> COVID-19 infection rates in children are relatively low, and published data on COVID-19 focuses mostly on adults. On January 20, 2020, the first pediatric case was recorded in a 10-year-old kid from Shenzhen, China, whose family had visited Wuhan City.<sup>(2)</sup>

Children tend to be less likely than adults to be impacted. Children often account for 1 to 5% of laboratory-confirmed cases in

surveillance from various countries. Children under the age of 18 make up around 6% of laboratory-confirmed cases reported to the Centers for Disease Control and Prevention (CDC) in the United States. The American Academy of Pediatrics publishes data on the number of cases in children in each state. COVID-19 is available to children of all ages.<sup>(3)</sup>

COVID-19 symptoms are comparable in children and adults, although symptom frequency differs. Although severe cases have been observed, COVID-19 appears to be milder in children than in adults. Boys and girls were equally impacted among the 69,703 laboratory-confirmed COVID-19 cases in children aged 20 years reported to the United States Centers for Disease Control and Prevention (CDC) by May 30, 2020.<sup>(4)</sup>

The following symptoms were most common in children aged 0 to 9 years: 63 percent of people have a fever, cough, or shortness of breath. In smaller case series, similar clinical symptoms, including sore throat and exhaustion, have been documented. Chills or shaking chills have been recorded as additional symptoms in adults.<sup>(5)</sup>

### Patients and methods

This prospective clinical study was conducted at Minia isolation hospitals and Minia University Hospital of Pediatrics, Minia, Egypt during the period from the first of April, 2020 to 31<sup>th</sup> of August 2021. 62 children were included in this study aged from 3 months -16 years. Infants and children were diagnosed as Covid-19 positive with real time PCR. The aim of the study is determine various clinical manifestations of COVID-19 in infant and children and also compare these data between the 1<sup>st</sup> wave (during 2020) and the 2<sup>nd</sup> wave (during 2021) in Egypt.

#### Inclusion criteria

- 1- Age: from 0 up to 18 years old
- 2- Covid-19 diagnosis confirmed laboratory with real-time PCR

#### Exclusion criteria

- 1- Suspected cases (not confirmed with PCR)
- 2- Associated blood diseases
- 3- Associated autoimmune diseases

#### Data collection

All infants and children were subjected to:

##### I. Full history:

1. Age.
2. Sex.
3. History of upper or lower respiratory tract infection
4. History of medical problems
5. History of chronic diseases
6. Family history of recent COVID 19 infections
7. . Family history of any medical conditions

##### II. Thorough clinical examination to all children:

##### A. General examination:

1. Vital signs: temperature, heart rate, respiratory rate and blood pressure

2. Head and Neck. Examination of any abnormalities in head and neck, or lymph node enlargement
3. Neurological examination
4. Cardiovascular examination
5. Abdominal examination
6. Musculoskeletal examination
7. Skin.
8. Back and genitalia.

##### B. Systemic examination:

Respiratory examinations: inspection of the chest for any deformities or limitation of respiratory movements, palpation and percussion of the chest for any abnormalities, and auscultation for breath sounds, air entry, crepitation or wheezes

### Statistical Methods

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 25.

Descriptive statistics were done for parametric (normally distributed) quantitative data by mean, Standard deviation (SD) and minimum and maximum of range and for non-parametric quantitative data by median and interquartile range (IQR), while for qualitative data by frequency and percentage.

Analyses were done between the two years for parametric quantitative data using Independent Samples T test and for non-parametric quantitative data using Mann Whitney test. Analyses were done between the two groups for Qualitative data using Chi square test and Fisher's exact test. The level of significance was taken at (P value  $\leq 0.05$ )

### Results

During the period of the study 62 children were admitted to hospital and diagnosed as COVID-19 Positive, aged from 4 months - 16 years with median age of 4 years and IQR (0.5-9). 34 males and 28 females. The hospital stay was ranged from 2-19 days with median 8 days IQR (6-9). From 62 patients 48 patient discharged to their

homes and 14 patients died. Patients with chronic illness was 16 out of 62 (25.8%), most of them were suffered from cardiac diseases (8.1%), renal diseases (6.5%) and Down's syndrome (6.5%) Fig. 1.

Comparisons between the 2 pandemic waves of COVID-19 in Egypt "the 1<sup>st</sup> wave was at 2020 and the 2<sup>nd</sup> wave was at 2021" there was insignificant differences as regarding age and sex distribution of the patients. Patients admitted during 2021 year showed significant increase in the incidence of the chronic illness (48.4%) compared to (3.2%) during 2020 year. (Table 1)

As regarding frequency of most relevant clinical manifestation of COVID-19, patients admitted during 2021 years showed significant increase in the frequency of fever, cough, dyspnea, respiratory distress and diarrhea in compared with those who admitted during 2020, While the frequency of skin rash was signific-

antly increased at 2020. Abdominal pain and vomiting showed insignificant difference between the two years. (Table 2)

General examination of patients revealed that, GCS, fair general condition and SO<sub>2</sub> showed significant increase in patients admitted during 2020, while heart rate, respiratory rate, temperature, frequency of cyanosis and frequency of sluggish pupil showed significant increase in patient admitted during 2021. Blood pressure showed insignificant differences between the two years. (Table 3)

As regarding systemic examination, patients admitted during 2021 showed significant increase in the frequency of decreased air entry, wheezes, crepitations, mechanical ventilation, abnormal CNS examination and abnormal CVS examination. Abdominal examination showed insignificant difference between the two years. (Table 4)

**Table 1: Demographic data between the 2020 and 2021**

		Year		P value
		2020	2021	
		N=31	N=31	
<b>Age</b>	<i>Median</i>	6	1.5	0.094
	<i>IQR</i>	(1.5-9)	(0.3-9)	
	<i>&lt; 1 year</i>	6 (19.4%)	14 (45.2%)	0.069
	<i>1-10 years</i>	19(61.2%)	11(35.5%)	
<i>&gt;10 years</i>	6(19.4%)	6(19.4%)		
<b>Sex</b>	<i>Male</i>	18(58.1%)	16(51.6%)	0.610
	<i>Female</i>	13(41.9%)	15(48.4%)	
<b>Chronic disease</b>	<i>No</i>	30(96.8%)	16(51.6%)	<0.001*
	<i>Yes</i>	1(3.2%)	15(48.4%)	

Table 2: Clinical presentation between the 2020 and 2021

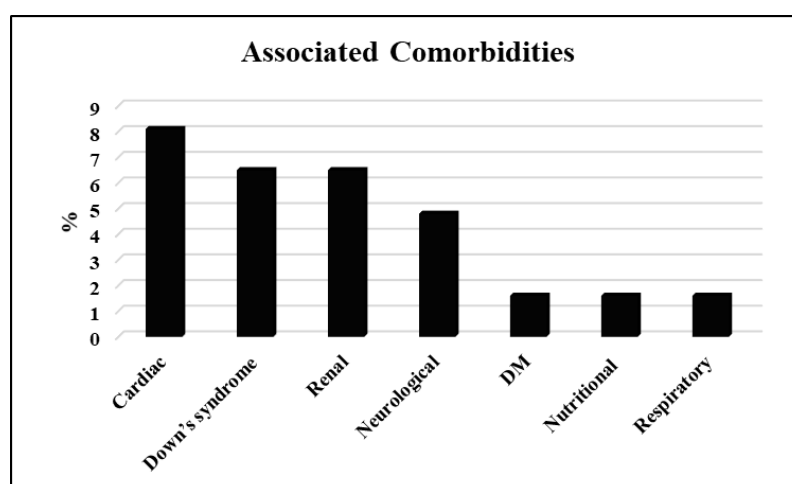
		Year		P value
		2020	2021	
		N=31	N=31	
<b>Fever</b>	No	14(45.2%)	1(3.2%)	<b>&lt;0.001*</b>
	Yes	17(54.8%)	30(96.8%)	
<b>Cough</b>	No	26(83.9%)	3(9.7%)	<b>&lt;0.001*</b>
	Yes	5(16.1%)	28(90.3%)	
<b>SOB</b>	No	30(96.8%)	0(0%)	<b>&lt;0.001*</b>
	Yes	1(3.2%)	31(100%)	
<b>RD grade</b>	No	30(96.8%)	0(0%)	<b>&lt;0.001*</b>
	I	1(3.2%)	2(6.5%)	
	II	0(0%)	19(61.3%)	
	III	0(0%)	9(29%)	
	IV	0(0%)	1(3.2%)	
<b>Vomiting</b>	No	27(87.1%)	24(77.4%)	0.319
	Yes	4(12.9%)	7(22.6%)	
<b>Diarrhea</b>	No	19(61.3%)	31(100%)	<b>&lt;0.001*</b>
	Yes	12(38.7%)	0(0%)	
<b>Abdominal pain</b>	No	28(90.3%)	26(83.9%)	0.449
	Yes	3(9.7%)	5(16.1%)	
<b>Skin rash</b>	No	24(77.4%)	31(100%)	<b>0.005*</b>
	Yes	7(22.6%)	0(0%)	

Table 3: General examination between the 2020 and 2021

		Year		P value
		2020	2021	
		N=31	N=31	
<b>GCS</b>	Range	(14-15)	(7-15)	<b>&lt;0.001*</b>
	Mean $\pm$ SD	14.5 $\pm$ 0.5	11.2 $\pm$ 2.5	
<b>General condition</b>	Fair	31(100%)	15(48.4%)	<b>&lt;0.001*</b>
	Less than fair	0(0%)	6(19.4%)	
	Bad	0(0%)	10(32.3%)	
<b>Cyanosis</b>	No	31(100%)	22(71%)	<b>0.002*</b>
	Yes	0(0%)	9(29%)	
<b>Pupil</b>	RRR	31(100%)	24(77.4%)	<b>0.011*</b>
	Sluggish	0(0%)	7(22.6%)	
<b>HR</b>	Range	(75-95)	(90-180)	<b>&lt;0.001*</b>
	Mean $\pm$ SD	85.6 $\pm$ 6.4	128.1 $\pm$ 19.1	
<b>RR</b>	Median	(15-25)	(20-60)	<b>&lt;0.001*</b>
	IQR	19.7 $\pm$ 2.5	39 $\pm$ 10.9	
<b>Temperature</b>	Range	(37-37)	(37-39)	<b>&lt;0.001*</b>
	Mean $\pm$ SD	37 $\pm$ 0	37.7 $\pm$ 0.5	
<b>SBP</b>	Range	(90-105)	(70-140)	0.321
	Mean $\pm$ SD	96.6 $\pm$ 5.1	99.4 $\pm$ 14.3	
<b>DBP</b>	Range	(60-70)	(40-100)	0.166
	Mean $\pm$ SD	64.8 $\pm$ 3.8	61.6 $\pm$ 12.1	
<b>SO2</b>	Range	(98-99)	(80-99)	<b>&lt;0.001*</b>
	Mean $\pm$ SD	98.8 $\pm$ 0.4	94.5 $\pm$ 5.5	

**Table 4: Systemic examination and mechanical ventilation between the 2020 and 2021**

		Year		P value
		2020	2021	
		N=31	N=31	
<b>Air entry</b>	<i>Fair</i>	30(96.8%)	2(6.5%)	<b>&lt;0.001*</b>
	<i>Decreased</i>	1(3.2%)	29(93.5%)	
<b>Wheezes</b>	<i>No</i>	30(96.8%)	13(41.9%)	<b>&lt;0.001*</b>
	<i>Yes</i>	1(3.2%)	18(58.1%)	
<b>Crepitation</b>	<i>No</i>	31(100%)	8(25.8%)	<b>&lt;0.001*</b>
	<i>Yes</i>	0(0%)	23(74.2%)	
<b>Abdominal</b>	<i>NAD</i>	31(100%)	28(90.3%)	0.238
	<i>Abnormal</i>	0(0%)	3(9.7%)	
<b>CNS</b>	<i>NAD</i>	31(100%)	24(77.4%)	<b>0.011*</b>
	<i>Abnormal</i>	0(0%)	7(22.6%)	
<b>CVS</b>	<i>NAD</i>	31(100%)	23(74.2%)	<b>0.005*</b>
	<i>Abnormal</i>	0(0%)	8(25.8%)	
<b>Mechanical ventilation</b>	<i>No</i>	31(100%)	21(67.7%)	<b>0.001*</b>
	<i>Yes</i>	0(0%)	10(32.3%)	



**Fig. 1: History of chronic diseases of all patients**

**Discussion**

Regarding the clinical data of the current study, our results was in accordance with Nallasamy et al., 2021<sup>(6)</sup> who found that 68% of his patients aged 1-10 years, 29% aged less than 1 year and 3% aged older than 10 years, and also disagree with Lenicek Krleza et al., 2021<sup>(7)</sup> who found that 8.8% of his patients were below one year, 53.1% of his patients from 1-10 years and 38.1% were older than 10 years, but also it showed insignificant difference between the two waves. Our results were in contrast with Dewi et al, 2021<sup>(8)</sup> who

reported no cases of Covid below one year.

COVID-19 may put babies under the age of one at a greater risk of serious illness than older children. This is likely owing to their undeveloped immune systems and narrower airways, which make them more susceptible to respiratory viral infections that cause breathing problems. Eastin, C., & Eastin, T. 2020,<sup>(9)</sup> So neonates in developing countries are more at risk to be infected than those in developed countries.

As regarding sex distribution, our result was in accordance with Polónyiová et al., 2021<sup>(10)</sup> who found that 54.8% were males and 45.2% were females, and also agree with Lenicek Krleza et al., 2021<sup>(7)</sup> who found that 52.7 % male and 47.8% females. The explanation for this is that such difference is common in countries such as India which have a preference for male gender Shukla et al., 2014.<sup>(11)</sup> Also, the females have stronger humoral and cellular immune responses to infection or antigenic stimulation which can be beneficial in protection and clearance of various pathogens Muenchhoff and Goulder 2014<sup>(12)</sup> this male predominance may be due to a gene located on the X chromosome involved with the function of the thymus or with synthesis of immunoglobulin Ghosh & Klein, 2017.<sup>(13)</sup>

Regarding chronic illness, our study match with results of Nallasamy et al., 2021<sup>(6)</sup> who found that 19% of patients suffered from comorbidities, 6% was cardiac, 6% with developmental disorders and 3% with renal disorders. In our results we found that the frequency of comorbidities was higher at the second wave, this was disagreed with Krajcar et al, 2020<sup>(14)</sup> who found that comorbidities were higher during the first wave. Sharif et al., 2021<sup>(15)</sup> decided that increasing comorbidities with other factors were associated with more severe symptoms, high fatality rates and prolonged hospital stay in patients with COVID-19. Inflammation and impaired innate immune responses are common symptoms of chronic medical problems in patients. This may make such people more susceptible to COVID-19 infection and illness consequences. Yang et al., 2020<sup>(16)</sup>

As regarding clinical manifestations of COVID 19, our study was in agreement with Chua et al., 2021<sup>(17)</sup> who found that increase the rate of respiratory symptoms during 2021 and last 2020. While Krajcar et al., 2020<sup>(14)</sup> was disagree with us as they found that increase the frequency of respiratory and GIT manifestation during the 1<sup>st</sup> wave. This difference in frequency of clinical manifestations between different wave may be due to SARS-CoV-

2 strains mutations such as the spike protein D614G mutation which is associated with increase the rate of infection of COVID-19 Korber et al., 2020<sup>(18)</sup>

Regarding general and systemic examination of our patients, those admitted during 2021 were higher affected than who admitted during 2020, as they showed more affected general condition and disturbed conscious level and also showed cyanosis, tachypnea and tachycardia. Respiratory system examination revealed that patients admitted during 2021 were highly affected, as some of them need mechanical ventilation (32.3%). This can be explained by the increase of presence of comorbidities in 2021 and mutations of the virus COVID CDC, 2020<sup>(19)</sup>

### Conclusion

Children at any age and both sexes are susceptible to COVID-19 virus infection. Children cases in the year 2020, show no or mild clinical manifestations compared with those admitted during 2021. Presence of chronic co-morbidities aggravate the clinical presentation and increase the risk for mortalities. Finally with each new wave of COVID-19 pandemic infection, the children more severely affected with the virus.

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