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Evaluation of Clinical Manifestations, Laboratory Findings and Outcome of Children with Covid-19

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Abstract

Background: Coronavirus, a common infectious disease in the 21st century, has not been studied enough in children. Therefore, this study aimed to investigate the clinical manifestations, laboratory findings, and outcomes of children with Covid-19 admitted to Shahid Beheshti Hospital in Kashan during 2020-2022.

Method: In this retrospective cohort study, the medical records of children with covid-19 referred to Shahid Beheshti hospital in Kashan between February 2020 and March 2022 were reviewed. The information extracted from the patient's medical records included demographic variables, clinical characteristics, laboratory findings, and the outcome of covid-19. The collected data were analyzed through SPSS 16, using descriptive statistics (frequency distribution, mean and standard deviation) and inferential statistics (chi-square test and ANOVA).

Result: The findings of 271 children (159 boys; 52% of the age group≤5 years) showed that fever (57.6%), cough (39.9%), nausea-vomiting (31.7%), and diarrhea were the most common clinical symptoms. Also, the majority of patients were in the abnormal range in terms of Monocyte (89.3%), PTT (84.7%), Lymphocyte (83.6%), Neutrophil (80.4%), and LDH (74.5%). Pulmonary involvement was present in 12.5% of children. Finally, four children (1.5%) died.

Conclusion: Severity of lung involvement and the outcome of the covid-19 disease (admission to the ICU and death) among children were at a low level, and in fact, it shows the better condition of children than adults in relation to this disease.

Key Words: Children, Clinical manifestations, Coronavirus, Covid-19, Death rate, ICU admission, Laboratory findings, Symptoms.

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1- INTRODUCTION

A novel coronavirus rapidly spread worldwide in late 2019, resulting in a global pandemic. The virus was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it caused coronavirus disease 2019 (COVID-19). Children usually account for one to eight percent of confirmed cases of Covid-19 (1-6). The clinical spectrum of COVID-19 ranges from asymptomatic infection to mild respiratory tract symptoms to severe pneumonia with acute respiratory distress syndrome and multi-organ dysfunction. COVID-19 is a pandemic infectious disease caused by SARS-CoV-2. Most cases in children result from household exposure. Children of any age can transmit covid-19 to others at home, in kindergarten, and school (7, 8). The relative transmissibility of COVID-19 by children in various age groups is uncertain (9-11).

Symptoms of COVID-19 are similar in children and adults, but the frequency of symptoms varies (6). COVID-19 appears to be milder in children than in adults, and symptoms may not be recognized before diagnosis (12), but severe cases have been reported (13, 14). The most common clinical findings in children are fever and cough. Other findings include shortness of breath, myalgia, rhinorrhea, headache, nausea/vomiting, abdominal pain, diarrhea, sore throat, fatigue, and loss of smell or taste. Although clinical deterioration may occur suddenly after approximately one week and should prompt urgent re-evaluation, most children recover within one to two weeks (12). Among children under ten years of age, 46% have been reported to have a fever, 37% a cough, and 7% shortness of breath. Other symptoms mentioned are body pain (10%), runny nose (7%), sore throat (13%), headache (15%), nausea and vomiting (10%), abdominal pain (7%), diarrhea (14%) and loss of sense of smell or taste (1%). Among children aged 10 to 19, 35% had a fever, 41% had a cough, and 16% had shortness of breath (6). Symptoms of gastrointestinal involvement may occur without signs of respiratory involvement (15-17). In studies of infants younger than twelve months, other clinical findings include poor feeding and fever of no apparent source (18-22). Respiratory symptoms may be low or absent (23). Bronchiolitis with the severe acute respiratory syndrome (SARS-CoV-2) has also been reported in infants (24). The emergence of new strains of SARS-CoV-2 has been associated with an increase in the incidence of children's infections, and the lack of complete information about the symptoms, laboratory findings, and consequences of this disease in children showed the importance of further investigating this disease in children. Thus, in this study examining the clinical manifestations and laboratory findings of the covid-19 disease in children was carried out to better manage the treatment process in children from the next pandemics and prevent the progression of the disease.

2- MATERIALS AND METHODS

In this retrospective cohort study (approved by the research ethics committee of Kashan university of medical sciences (IR.KAUMS.NUHEPM.REC.1400.001)), the medical records of children with covid-19 (diagnosed by positive PCR) referred to Shahid Beheshti hospital in Kashan between February 2020 and March 2022 were reviewed. The information extracted from the patients' medical records including demographic variables (gender, age and underlying disease), clinical symptoms (fever, dyspnea, cough, myalgia, fatigue, headache, nasopharyngitis, conjunctivitis, abdominal pain, anorexia, nausea&vomiting, diarrhea, skin lesions, febrile seizure and status epilepticus), clinical findings (Systolic

Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Temperature (T), Pulse Rate (PR), Respiratory Rate (RR) and Oxygen Saturation (SPO2), laboratory findings (Blood Suger (BS), White Blood Cell (WBC), Neutrophil, Lymphocyte, Monocyte, Eosinophil, Basophil, Red Blood Cell (RBC), Hemoglobin (Hb), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red cell Distribution Width (RDW), Platelet (PLT), International Normalized Ratio (INR), Prothrombin Time (PT), Partial Thromboplastin Time (PTT), Lactate Dehydrogenase (LDH), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Creatine Phosphokinase (CPK), Blood Urea Nitrogen (BUN), Creatinine (Cr), C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Troponin, Potassium (K), Sodium (Na), Albumin (Alb), Calcium (Ca), Phosphate (Phos), Magnesium (Mg) and D-dimer), pulmonary involvement (based on computed tomography (CT)) and the outcome (admission in Intensive care unit (ICU), hospitalization and death) of covid-19. The collected data was analyzed through SPSS 16 (SPSS Inc., Chicago, IL), using descriptive statistics (frequency distribution, mean and standard deviation) and inferential statistics (chi-square test and ANOVA).

3- RESULTS

In this study, the medical records of 301 children with covid-19 were examined. After filtering and correcting errors, the data of 271 children were valid. The results are presented below.

Table-1: Demographic, clinical, laboratory findings and outcome of patients

Variable		N (%) / Mean±SD (Min-Max)
Gender	Boy	159 (58.7)
	Girl	112 (41.3)
Age	Neonate (<1 month)	7 (19)
	Infant (<1 year)	26 (9.6)
	Toddler (1-2 years)	55 (20.3)
	Preschool (3-5 years)	41 (15.1)
	School-age (6-11 years)	71 (26.2)
	Adolescent (12-17 years)	59 (21.8)
Underlying disease	UTI	1 (0.4)
	Hypothyroid	1 (0.4)
	Migren	1 (0.4)
	Chronic hepatitis	1 (0.4)
	Acute lymphocytic leukemia (ALL)	1 (0.4)
	Epilepsy	1 (0.4)
contact with a person with symptoms of covid-19		35 (12.9)
Epidemic waves*	First (2020.2.20-2020.5.10)	4 (1.5)
	Second (2020.6.17-2020.7.20)	7 (2.6)
	Third (2020.8.22-2021.2.18)	25 (9.4)
	Fourth (2021.2.19-2021.6.11)	50 (18.8)
	Fifth (2021.6.12-2022.1.20)	128 (48.1)
	Sixth (2022.1.21-2022.3.20)	52 (19.5)

Clinical symptoms	Fever	156 (57.6)
	Dyspnea	39 (14.4)
	Cough	108 (39.9)
	Myalgia	37 (13.7)
	Fatigue	43 (15.9)
	Headache	27 (10)
	Nasopharyngitis	32 (11.8)
	Conjunctivitis	10 (3.7)
	Abdominal pain	20 (7.4)
	Anorexia	45 (16.6)
	Nausea Vomiting	86 (31.7)
	Diarrhea	60 (22.1)
	Skin lesions	10 (3.7)
	Febrile seizure	13 (4.8)
	Status epilepticus	10 (3.7)
Clinical findings (Abnormal range)	SBP	135 (49.8)
	DBP	122 (45)
	T	194 (71.6)
	PR	103 (38)
	RR	151 (55.7)
	SPO2	17 (6.3)
Laboratory findings (Abnormal range)	BS (n=168)	70 (41.7)
	WBC	97 (35.8)
	Neutrophil (n=265)	213 (80.4)
	Lymphocyte (n=269)	225 (83.6)
	Monocyte (n=28)	25 (89.3)
	Eosinophil (n=27)	12 (44.4)
	Basophil (n=28)	1 (3.6)
	RBC	168 (62)
	Hb	70 (25.8)
	HCT	60 (22.1)
	MCV	79 (29.2)
	MCH	71 (26.2)
	MCHC	77 (28.4)
	RDW (n=269)	68 (25.3)
	PLT	76 (28)
	INR (n=130)	26 (20)
	PT (n=130)	72 (55.4)
	PTT (n=131)	111 (84.7)
	LDH (n=145)	108 (74.5)
	ALT (n=175)	32 (18.3)
	AST (n=175)	42 (24)
	ALP (n=173)	87 (50.3)
	CPK (n=118)	16 (13.6)
	BUN (n=268)	19 (7.1)
	Cr (n=267)	30 (11.2)
	CRP (n=258)	61 (23.6)

	ESR (n=256)	119 (46.5)
	Troponin (n=121)	0
	K (n=255)	14 (5.5)
	Na (n=263)	35 (13.3)
	Alb (n=105)	19 (18.3)
	Ca (n=165)	37 (22.4)
	Phos (n=123)	28 (23.1)
	Mg (n=167)	58 (34.7)
	D-dimer (n=87)	13 (14.9)
Pulmonary involvement (based on CT)		34 (12.5)
Outcome	Admission in ICU	21 (7.7)
	Hospitalization (day)	5.49±3.62 (1-25)
	Death	4 (1.5)

* Five children were not hospitalized during the epidemic waves

The findings presented in **Table 1** show that 58.7% of the children were boys. The age groups of 6-11 years (26.2%) and 12-17 years (21.8%) had the highest frequency percentages, respectively. Also, most of the children (48.1%) were hospitalized in the fifth wave. The most common clinical symptom among the patients was fever (57.6%), followed by cough (39.9%), nausea-vomiting (31.7%), and diarrhea (22.1%). In relation to clinical findings, the temperature of 71.6% of children was in the abnormal range. Also, the majority of patients were in the abnormal range in terms of Monocyte (89.3%), PTT (84.7%), Lymphocyte (83.6%), Neutrophil (80.4%) and LDH (74.5%). Pulmonary involvement was present in 12.5% of children. Ultimately, four children (1.5%) died.

Table-2: The relationship between the variables related to covid-19 and children's gender

Variable		Male	Female	p-value
Clinical symptoms	Fever	94 (59.1)	62 (55.4)	0.537
	Dyspnea	21 (13.2)	18 (16.1)	0.508
	Cough	60 (37.7)	48 (42.9)	0.396
	Myalgia	16 (10.1)	21 (18.8)	0.040
	Fatigue	27 (17)	16 (14.3)	0.550
	Headache	11 (6.9)	16 (14.3)	0.046
	Nasopharyngitis	20 (12.6)	12 (10.7)	0.640
	Conjunctivitis	5 (3.1)	5 (4.5)	0.570
	Abdominal pain	10 (6.3)	10 (8.9)	0.413
	Anorexia	28 (17.6)	17 (15.2)	0.596
	Nausea & Vomiting	50 (31.4)	36 (32.1)	0.903
	Diarrhea	34 (21.4)	26 (23.2)	0.721
	Skin lesions	3 (1.9)	7 (6.2)	0.061
	Febrile seizure	8 (5)	5 (4.5)	0.830
	Status epilepticus	6 (3.8)	4 (3.6)	0.931
Clinical findings (Abnormal range)	SBP	72 (45.3)	63 (56.2)	0.075
	DBP	69 (43.4)	53 (47.3)	0.522
	T	110 (69.2)	84 (75)	0.296

	PR	57 (35.8)	46 (41.1)	0.383
	RR	91 (57.2)	60 (53.6)	0.550
	SPO2	6 (3.8)	11 (9.8)	0.043
Laboratory findings* (Abnormal range)	BS	44 (44)	26 (38.2)	0.457
	WBC	60 (37.7)	37 (33)	0.427
	Neutrophil	128 (83.1)	85 (76.6)	0.186
	Lymphocyte	132 (84.1)	93 (83)	0.820
	RBC	99 (62.3)	69 (61.6)	0.913
	Hb	42 (26.4)	28 (25)	0.793
	HCT	34 (21.4)	26 (23.2)	0.721
	MCV	47 (29.6)	32 (28.6)	0.860
	MCH	36 (22.6)	35 (31.2)	0.113
	MCHC	44 (27.7)	33 (29.5)	0.747
	RDW	39 (24.5)	29 (26.4)	0.733
	PLT	49 (30.8)	27 (24.1)	0.226
	INR	14 (20)	12 (20)	1.000
	PT	39 (55.7)	33 (55)	0.935
	PTT	58 (82.9)	53 (86.9)	0.523
	LDH	57 (73.1)	51 (76.1)	0.675
	ALT	19 (19.4)	13 (16.9)	0.670
	AST	23 (23.5)	19 (24.7)	0.853
	ALP	47 (49)	40 (51.9)	0.696
	CPK	11 (17.2)	5 (9.3)	0.210
	BUN	11 (7)	8 (7.2)	0.950
	Cr	14 (9)	16 (14.4)	0.165
	CRP	41 (27.5)	20 (18.3)	0.087
	ESR	75 (49.3)	44 (42.3)	0.268
	K	11 (7.4)	3 (2.8)	0.116
	Na	25 (16.3)	10 (9.1)	0.088
	Alb	13 (22.8)	6 (12.8)	0.187
	Ca	18 (19.4)	19 (26.4)	0.283
	Phos	13 (20.3)	15 (26.3)	0.434
	Mg	35 (36.1)	23 (32.9)	0.666
	D.dimer	9 (20.5)	4 (9.3)	0.145
Pulmonary involvement (based on CT)		21 (13.2)	13 (11.6)	0.695
Outcome	Admission in ICU	15 (9.4)	6 (5.4)	0.216
	Hospitalization	5.91±3.94	4.89±3.05	0.017
	Death	4 (2.5)	0	0.145

* Monocyte, Eosinophil and Basophil were not considered due to the small sample size.

The findings shown in **table 2** indicate that the frequency of headache and myalgia among girls was significantly higher than that among boys ($p<.05$). Also, the abnormal range of SPO2 ($p=.043$) in girls (9.8%) was significantly more than that in boys (3.8%). In addition, the mean of hospitalization among boys (5.91±3.94) was significantly higher than that among girls (4.89±3.05) ($p=.017$).

Table-3: The relationship between variables related to covid-19 and children's age

Variable		Neonate (<1 m)	Infant (<1 yr.)	Toddler (1-2 yr.)	Preschool (3-5 yr.)	School-age (6-11 yr.)	Adolescent (12-17 yr.)	p-value
Clinical symptoms	Fever	11 (57.9)	18 (69.2)	33 (60)	24 (58.5)	39 (54.9)	31 (52.5)	0.790
	Dyspnea	1 (5.3)	1 (3.8)	2 (3.6)	1 (2.4)	12 (16.9)	22 (37.3)	0.000
	Cough	5 (26.3)	10 (38.5)	16 (29.1)	14 (34.1)	28 (39.4)	35 (59.3)	0.015
	Myalgia	0	2 (7.7)	1 (1.8)	3 (7.3)	13 (18.3)	18 (30.5)	0.000
	Fatigue	6 (31.6)	3 (11.5)	8 (14.5)	7 (17.1)	6 (8.5)	13 (22)	0.126
	Headache	0	0	0	2 (4.9)	9 (12.7)	16 (27.1)	0.000
	Nasopharyngitis	3 (15.8)	4 (15.4)	6 (10.9)	4 (9.8)	9 (12.7)	6 (10.2)	0.961
	Conjunctivitis	0	0	2 (3.6)	0	8 (11.3)	0	0.010
	Abdominal pain	1 (5.3)	0	0	5 (12.2)	13 (18.3)	1 (1.7)	0.000
	Anorexia	6 (31.6)	3 (11.5)	9 (16.4)	10 (24.4)	7 (9.9)	10 (16.9)	0.174
	Nausea & Vomiting	6 (31.6)	12 (46.2)	22 (40)	9 (22)	21 (29.6)	16 (27.1)	0.238
	Diarrhea	6 (31.6)	12 (46.2)	15 (27.3)	6 (14.6)	13 (18.3)	8 (13.6)	0.010
	Skin lesions	0	1 (3.8)	3 (5.5)	1 (2.4)	5 (7)	0	0.295
	Febrile seizure	1 (5.3)	2 (7.7)	4 (7.3)	6 (14.6)	0	0	0.001
	Status epilepticus	1 (5.3)	0	1 (1.8)	3 (7.3)	4 (5.6)	1 (1.7)	0.462
Clinical findings (Abnormal range)	SBP	17 (89.5)	6 (23.1)	26 (47.3)	10 (24.4)	40 (56.3)	36 (61)	0.000
	DBP	14 (73.7)	15 (57.7)	28 (50.9)	10 (24.4)	25 (35.2)	30 (50.8)	0.002
	T	9 (47.4)	20 (76.9)	36 (65.5)	30 (73.2)	56 (78.9)	43 (72.9)	0.117
	PR	5 (26.3)	4 (15.4)	25 (45.5)	10 (24.4)	26 (36.6)	33 (55.9)	0.002
	RR	13 (68.4)	19 (73.1)	26 (47.3)	28 (68.3)	32 (45.1)	33 (55.9)	0.036
	SPO2	1 (5.3)	1 (3.8)	6 (10.9)	0	4 (5.6)	5 (8.5)	0.302
Laboratory findings (Abnormal range)	BS	7 (41.2)	8 (50)	10 (33.3)	11 (40.7)	14 (36.8)	20 (50)	0.726
	WBC	8 (42.1)	9 (34.6)	26 (47.3)	14 (34.1)	23 (32.4)	17 (28.8)	0.397
	Neutrophil	15 (88.2)	18 (78.3)	49 (89.1)	33 (80.5)	54 (76.1)	44 (75.9)	0.420
	Lymphocyte	17 (89.5)	19 (79.2)	50 (90.9)	36 (87.8)	55 (77.5)	48 (81.4)	0.339
	RBC	5 (26.3)	14 (53.8)	30 (54.5)	20 (48.8)	55 (77.5)	44 (74.6)	0.000
	Hb	15 (78.9)	13 (50)	8 (14.5)	8 (19.5)	12 (16.9)	14 (23.7)	0.000

	HCT	15 (78.9)	12 (46.2)	9 (16.4)	6 (14.6)	7 (9.9)	11 (18.6)	0.000
	MCV	19 (100)	9 (34.6)	4 (7.3)	17 (41.5)	19 (26.8)	11 (18.6)	0.000
	MCH	17 (89.5)	10 (38.5)	5 (9.1)	7 (17.1)	19 (26.8)	13 (22)	0.000
	MCHC	6 (31.6)	6 (23.1)	10 (18.2)	14 (34.1)	21 (29.6)	20 (33.9)	0.432
	RDW	6 (35.3)	10 (38.5)	11 (20)	9 (22)	17 (23.9)	15 (25.4)	0.491
	PLT	8 (42.1)	17 (65.4)	16 (29.1)	4 (9.8)	17 (23.9)	14 (23.7)	0.000
	INR	1 (50)	0	2 (13.3)	7 (38.9)	9 (24.3)	7 (14)	0.098
	PT	1 (50)	3 (37.5)	9 (60)	11 (61.1)	18 (48.6)	30 (60)	0.771
	PTT	2 (100)	7 (87.5)	12 (80)	18 (100)	28 (75.7)	44 (86.3)	0.218
	LDH	2 (66.7)	6 (85.7)	16 (76.2)	13 (65)	36 (69.2)	35 (83.3)	0.546
	ALT	2 (100)	5 (45.5)	5 (17.9)	1 (4.3)	9 (16.7)	10 (17.5)	0.010
	AST	1 (50)	4 (36.4)	7 (25.9)	4 (17.4)	11 (20.4)	15 (25.9)	0.736
	ALP	1 (50)	6 (54.5)	15 (57.7)	12 (54.5)	29 (53.7)	24 (41.4)	0.715
	CPK	2 (66.7)	0	1 (9.1)	1 (6.2)	5 (12.2)	7 (16.7)	0.215
	BUN	1 (5.3)	3 (11.5)	4 (7.3)	3 (7.3)	3 (4.3)	5 (8.6)	0.840
	Cr	8 (42.1)	1 (3.8)	3 (5.5)	2 (5)	3 (4.3)	13 (22.4)	0.000
	CRP	5 (27.8)	6 (24)	13 (24.1)	7 (17.1)	13 (19.7)	17 (31.5)	0.614
	ESR	5 (41.7)	11 (44)	34 (61.8)	18 (43.9)	27 (39.7)	24 (43.6)	0.227
	K	1 (5.6)	0	2 (3.8)	2 (5.6)	3 (4.5)	6 (10.2)	0.587
	Na	1 (5.3)	8 (30.8)	8 (15.4)	5 (13.5)	4 (5.7)	9 (15.3)	0.037
	Alb	0	0	8 (53.3)	9 (64.3)	0	2 (4.7)	0.000
	Ca	0	1 (10)	3 (13)	2 (9.5)	16 (34)	15 (27.3)	0.062
	Phos	1 (100)	1 (20)	3 (21.4)	1 (6.7)	5 (15.2)	17 (32.1)	0.106
	Mg	1 (25)	1 (10)	7 (28)	9 (39.1)	20 (37)	20 (39.2)	0.529
	D.dimer	0	1 (16.7)	4 (30.8)	4 (28.6)	1 (3.6)	3 (12.5)	0.107
Pulmonary involvement (based on CT)		0	0	4 (7.3)	5 (12.2)	8 (11.3)	17 (28.8)	0.001
Outcome	Admission in ICU	1 (5.3)	5 (19.2)	2 (3.6)	3 (7.3)	5 (7)	5 (8.5)	0.272
	Hospitalization	7.26±5.40	5.81±3.53	4.71±2.84	5.44±3.36	5.66±3.60	5.34±3.75	0.181
	Death	0	2 (7.7)	0	0	0	2 (3.4)	0.045

The findings presented in **Table 3** show that in terms of clinical symptoms, the frequency of dyspnea, cough, myalgia, and headache in the adolescent group is higher than in other age groups (p<0.05). Also, the frequency of conjunctivitis and abdominal pain in the school-age group was higher than that in other groups (p<0.05). In addition, the frequency of diarrhea in neonate and infant groups is higher than in other groups (p<0.05). Also, the frequency of febrile seizure was higher in the preschool group (p<0.05).

In terms of PR, adolescent and toddler groups were more in the abnormal range than other groups (p<0.05). In terms of RR, neonate, infant and preschool groups were more in the abnormal range than other groups (p<0.05). Also, in terms of systolic and diastolic blood pressure, the neonate group was more in the normal range than the other groups (p<0.05).

In terms of RBC, preschool and adolescent groups were in the abnormal range more than other groups (p<0.05). Also, in terms of Hb, HCT, MCV, MCH and Cr, the neonate group was more in the abnormal range than the other groups (p<0.05). In relation to PLT and Na, the infant group was more in the abnormal range than the other groups (p<0.05). The ALT in the preschool group had the lowest frequency in the abnormal range compared to other groups (p<0.05).

In terms of pulmonary involvement, the adolescent group had a higher frequency than other groups (p<0.05). Finally, four deaths occurred between the infant and adolescent groups (p<0.05).

Table-4: The relationship between variables related to covid-19 and the epidemic waves

Variable		First-Third	Fourth	Fifth	Sixth	p-value
Clinical symptoms	Fever	23 (63.9)	28 (56)	67 (52.3)	34 (65.4)	0.342
	Dyspnea	8 (22.2)	7 (14)	20 (15.6)	2 (3.8)	0.079
	Cough	11 (30.6)	14 (28)	67 (52.3)	12 (23.1)	0.000
	Myalgia	10 (27.8)	4 (8)	16 (12.5)	5 (9.6)	0.036
	Fatigue	4 (11.1)	12 (24)	24 (18.8)	2 (3.8)	0.023
	Headache	6 (16.7)	7 (14)	12 (9.4)	1 (1.9)	0.085
	Nasopharyngitis	5 (13.9)	6 (12)	15 (11.7)	5 (9.6)	0.942
	Conjunctivitis	6 (16.7)	0	0	2 (3.8)	0.000
	Abdominal pain	8 (22.2)	4 (8)	4 (3.1)	2 (3.8)	0.001
	Anorexia	3 (8.3)	4 (8)	31 (24.2)	5 (9.6)	0.008
	Nausea & Vomiting	12 (33.3)	26 (52)	32 (25)	15 (28.8)	0.006
	Diarrhea	8 (22.2)	20 (40)	18 (14.1)	14 (26.9)	0.002
	Skin lesions	1 (2.8)	1 (2)	6 (4.7)	2 (3.8)	0.962
	Febrile seizure	0	2 (4)	7 (5.5)	4 (7.7)	0.448
	Status epilepticus	0	0	4 (3.1)	6 (11.5)	0.015
Clinical findings (Abnormal range)	SBP	15 (41.7)	26 (52)	71 (55.5)	22 (42.3)	0.281
	DBP	10 (27.8)	28 (56)	60 (46.9)	24 (46.2)	0.076
	T	27 (75)	33 (66)	90 (70.3)	39 (75)	0.724
	PR	12 (33.3)	16 (32)	57 (44.5)	17 (32.7)	0.261
	RR	13 (36.1)	25 (50)	80 (62.5)	32 (61.5)	0.025
	SPO2	3 (8.3)	2 (4)	9 (7)	3 (5.8)	0.843
Laboratory findings (Abnormal	BS	8 (44.4)	14 (51.9)	34 (40.5)	12 (33.3)	0.516
	WBC	16 (44.4)	18 (36)	47 (36.7)	15 (28.8)	0.514
	Neutrophil	30 (83.3)	40 (80)	96 (77.4)	43 (86)	0.595

range)	Lymphocyte	32 (88.9)	43 (86)	103 (81.7)	44 (84.6)	0.733
	RBC	24 (66.7)	33 (66)	82 (64.1)	25 (48.1)	0.161
	Hb	8 (22.2)	14 (28)	21 (16.4)	25 (48.1)	0.000
	HCT	7 (19.4)	12 (24)	22 (17.2)	19 (36.5)	0.042
	MCV	9 (25)	15 (30)	39 (30.5)	15 (28.8)	0.936
	MCH	9 (25)	10 (20)	32 (25)	19 (36.5)	0.264
	MCHC	6 (16.7)	14 (28)	39 (30.5)	14 (26.9)	0.440
	RDW	10 (27.8)	15 (30)	27 (21.1)	16 (32)	0.388
	PLT	6 (16.7)	21 (42)	35 (27.3)	13 (25)	0.061
	INR	3 (27.3)	4 (22.2)	18 (19.8)	1 (11.1)	0.835
	PT	6 (54.5)	12 (66.7)	49 (53.8)	4 (44.4)	0.695
	PTT	8 (72.7)	18 (94.7)	76 (83.5)	8 (88.9)	0.407
	LDH	15 (68.2)	11 (73.3)	75 (78.9)	7 (70)	0.694
	ALT	7 (25.9)	1 (4.5)	20 (19.4)	4 (20)	0.273
	AST	6 (22.2)	5 (23.8)	25 (24)	6 (30)	0.936
	ALP	15 (55.6)	10 (50)	49 (47.6)	11 (55)	0.855
	CPK	2 (18.2)	3 (23.1)	11 (12.6)	0	0.603
	BUN	3 (8.3)	2 (4)	5 (4)	8 (15.7)	0.034
	Cr	1 (2.8)	7 (14)	13 (10.4)	9 (17.6)	0.168
	CRP	13 (43.3)	18 (36)	16 (13.2)	13 (25)	0.000
	ESR	16 (45.7)	31 (63.3)	47 (39.2)	25 (53.2)	0.031
	K	1 (2.9)	3 (6.7)	7 (5.8)	3 (6)	0.891
	Na	4 (11.1)	6 (12.8)	18 (14.6)	7 (13.5)	0.954
	Alb	2 (12.5)	1 (9.1)	15 (23.1)	1 (11.1)	0.528
	Ca	8 (30.8)	1 (4.8)	23 (24.5)	3 (14.3)	0.115
	Phos	3 (20)	7 (43.8)	13 (17.1)	5 (41.7)	0.053
	Mg	7 (24.1)	6 (30)	44 (45.4)	1 (5.9)	0.006
	D.dimer	0	2 (20)	11 (15.9)	0	0.717
Pulmonary involvement (based on CT)		1 (2.8)	4 (8)	29 (22.7)	0	0.000
Outcome	Admission in ICU	2 (5.6)	6 (12)	6 (4.7)	7 (13.5)	0.141
	Hospitalization	6.08±4.73	5.40±3.23	5.81±3.42	4.42±3.61	0.110
	Death	1 (2.8)	0	2 (1.6)	1 (1.9)	0.726

- Considering that the sample size was small in the first to third waves, it was decided to merge them.

The findings demonstrated in **Table 4** show that the frequency of cough and anorexia in the fifth wave is higher than in the other waves ($p<0.05$). Also, the frequency of myalgia, conjunctivitis and abdominal pain in the first-third wave was higher than in the other waves ($p<0.05$). In addition, in the sixth wave, the frequency of fatigue was the lowest and status epilepticus was the highest compared to other waves ($p<0.05$). Also, the frequency of nausea-vomiting and diarrhea was higher in the fourth wave ($p<0.05$).

In terms of RR, the children who were hospitalized in the first-third waves were less in the abnormal range than the other waves ($p<0.05$). In the sixth wave, in terms of Hb, HCT and BUN, the highest values and the lowest values in term of Mg were in the abnormal range compared to the other groups ($p<0.05$); while, in the fifth wave, in terms of CRP and ESR, the

lowest values were in the abnormal range compared to other groups ($p<0.05$). In addition, in terms of pulmonary involvement, children who were hospitalized in the fifth wave had a higher frequency than other waves ($p<0.05$).

4- DISCUSSION

Due to the covid-19 pandemic and the constant introduction of novel virus strains, the world today needs a continual research of the epidemiological and diagnostic features and the outcomes of patients in order to improve evaluation, prognosis, and diagnosis. Regarding the clinical presentation, laboratory and imaging findings, complications, mortality, and severity of the illness in pediatrics, there are several unanswered concerns. In the studies by Du et al. (25) and Dong et al. (15), more than half of the children infected with Covid-19 were males, and they were hospitalized during the outbreak of the Delta strain. Moreover, the majority of hospitalized patients in this study (60%) were males, which was consistent with previous research. According to the findings, the most prevalent clinical symptoms among the individuals evaluated were fever, cough, nausea/vomiting, and diarrhea. In addition, we observed that the respiratory rate and body temperature of a significant number of children were outside the normal limits. Likewise, in the research by Chang et al., the most prevalent clinical signs were fever and cough (26). Compared to the studies by Chang et al. (26) and Han et al. (27), the prevalence of diarrhea, vomiting, and other gastrointestinal symptoms was higher in our study, which may be a result of the varied study periods and the prevalence of different virus strains.

The study by Tezer et al. showed that 23% of hospitalized children had underlying diseases, of cardiovascular disease, chronic lung disease (asthma), and most prevalently immunosuppression (induced by cancer, chemotherapy, etc.) (28). However, in the present study, underlying diseases were found in less than 3% of the hospitalized children. Additionally, among 43,465 COVID-19 patients in the study conducted by Kompaniyets et al., 28.7% had underlying disorders including asthma, neurodevelopmental disorders, anxiety-related disorders, depressive disorders, and obesity (29). In the meantime, we realized that the explanation for this discrepancy in the results might be related to the different sampling, controlling the effect of confounders, various inclusion and exclusion criteria, and different sample sizes of the studies.

In this study, a high percentage of participants had abnormalities in their monocyte, lymphocyte, and neutrophil counts, as well as their PTT and LDH levels. According to similar studies, the majority of children with COVID-19 have normal WBC, with leukopenia being the most prevalent abnormality (30, 31). In Henry et al. study, the number of leukocytes was normal in most children, and there was lymphopenia in 3% of cases (32). More than 80 percent of patients in our research had lymphocyte count abnormalities, and the frequency of leukocytosis and leukopenia was 35.8 percent.

In addition, lymphocytosis was found more frequently in children than in adults in the study by Du et al (25). According to Kosmeri et al., the most prevalent finding in children and infants with COVID-19 was lymphocytosis (33). In our study, an imbalance in the number of lymphocytes was recognized as one of the most prevalent laboratory disorders among children; based on data, more than 25 percent of patients had anemia, and 28 percent had thrombocytopenia. According to a research by Du et al., Fifty percent of children with COVID-19 had abnormal LDH levels, and positive LDH levels were much greater in children than in adults (25). More than 74% of the evaluated

population in our population had a high LDH level, which was attributed to differences in the study population and confounders impacting the LDH level, particularly differences in underlying diseases. Lung involvement was found in the imaging of all COVID-19 patients (34). In addition, 12.5 percent of children had lung involvement based on CT scan findings. The right and left lower lobes were the most involved lobes (35).

The most frequent radiographic finding in the study by Chang et al. was ground glass opacities (48%) (26). However, in another study by Samy et al., there were only nine patients with lung opacities, five with consolidation and two with GGO, and two with consolidation with GGO (35). In the study conducted in Wuhan, 8% of the hospitalized pediatric patients were admitted to the ICU (36) which is consistent with the results of the present study. Hoang et al. reported 0.09 percent death rate among children with COVID-19 (37) but our study revealed 1.5 percent mortality rate. Due to the lower sample size compared to the linked study, the prevalence of death increased significantly in our investigation.

In a review by Ludvigsson et al., it was reported that, overall, the symptoms are milder, the prognosis was better, and the death rate was lower in children than in adult patients, due to a lower prevalence of comorbidities in children (38). In a retrospective cohort study conducted in Wuhan, 26% of the adult patients needed ICU and 28.3% died during hospitalization (39) while in our study 8% of patients needed ICU and 1.5% of patients died.

5- CONCLUSION

The results showed that the severity of lung involvement and the outcome of the covid-19 disease (admission to the ICU and death) among children are at a low level, and in fact, it shows the better condition of children than adults in relation to this disease.

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