

## Nutritional Assessment of Critically Ill Children with COVID-19 Admitted to PICU

NAHLA A. MOHAMED, Ph.D.\* and HANAN F. MOHAMMED, M.D.\*\*

*The Department of Pediatrics, El-Galaa Teaching Hospital, General Organization of Teaching Hospitals and Institutes\* and Department of Clinical Pathology, El-Galaa Teaching Hospital, General Organization of Teaching Hospital\*\**

### Abstract

**Background:** Nutrition has important role in the regulation of optimal immune functions, as it provides proper nutrients such as minerals, and vitamins, as well as macronutrients in adequate concentrations to immune system. however, nutritional deficiencies are associated with impaired immune response and have negative impact on human resistance to infection.

**Aim of Study:** Evaluation of the nutritional status of critically ill pediatric patients diagnosed with COVID-19 admitted to PICU and study correlation between nutritional deficiency and outcome.

**Patients and Methods:** This retrospective cohort study of hospitalized patients with COVID-19 enrolled at the pediatric intensive care unit of El-Galaa Teaching Hospital. All confirmed COVID-19 patients have been screened in the period between June 1<sup>st</sup>, 2023 and may 31<sup>th</sup>, 2024. The study reviewed the demographic data, anthropometric data, nutritional and medical history, laboratory investigation, duration of hospital stays and outcome of the hospitalized patients during the period of the study.

**Results:** A total of 60 patients with COVID-19 aged 2 to 10 years were evaluated in this study. Non-survivors' patients with COVID-19 had significantly lower anthropometric measurements (Z score for weight, Z score for height and body mass index Z score) as compared to survivors. There was statistically decrease in folic acid, Vitamin D, Zinc, Selenium (38.3%, 23.3%, 65%, 36.7% respectively) in COVID-19 patients. While severe vitamin D deficiency was reported in 21.7% of patients. There was statistically significant decrease in folic acid, Vitamin D, Zinc, Selenium in non-survivors as compared with survivors' patients. Also, there was statistically significant increase in duration of hospital stay in non-survivors' patients.

**Conclusion:** Pediatric patients with COVID-19 may have nutritional deficiency in one or more micronutrients that may

affect their immune response to infection, severity of disease, complications and duration of hospitalization. They will benefit from screening and supplementation of vitamins and trace elements.

**Key Words:** COVID-19 – Selenium – Vitamin D – Zinc folic acid – Micronutrients.

### Introduction

**RESPIRATORY** tract infections (RTIs) particularly pneumonia represents major public health problems among children. It was considered as leading cause of death in under-five children especially in developing countries [1] as UNICEF reported child death every 39 s from pneumonia [2].

In 2019, World Health Organization (WHO) reported 740, 180 death in under-five children from pneumonia in USA which represent 14% of deaths in this age group [3]. On December 2019, the novel coronavirus named as SARS-CoV-2 first reported in Wuhan, China, then rapidly spreading worldwide within a few months, causing a major public health burden [4]. Then, The WHO announced COVID-19 as pandemic in March 2020 [5].

COVID-19 mainly affects the respiratory system, causing pneumonia and leads to many symptoms including fever, cough, myalgia, headache, and fatigue [6], the disease can affect multiple organ systems [7].

Most of affected patients especially young children are asymptomatic or have mild symptoms do not need hospitalization [8], but patients with severe symptoms as shortness of breath, cardiovascular, gastrointestinal or neurologic symptoms may require admission to hospital or pediatric intensive care unit (ICU) [9]. Some of them may progress to acute respiratory distress syndrome (ARDS) requiring mechanical ventilation [10].

---

**Correspondence to:** Dr. Nahla A. Mohamed, The Department of Pediatrics, El-Galaa Teaching Hospital, General Organization of Teaching Hospitals and Institutes

Viral infections including coronaviruses evoke “cytokine storm” that leads to activation of pulmonary capillary endothelial cell, infiltration of neutrophil and increased oxidative stress (reactive oxygen and nitrogen species) [11]. ARDS, usually associated by uncontrolled inflammation, oxidative injury and alveolar capillary barrier damage [12]. Impaired immunity is important risk factor for viral respiratory infection [13].

Several factors play essential role in the development and optimized the proper functions of immune system [14], most important one of them is nutrition as many vitamins, including vitamins A, B6, B12, C, D, E, and folate; and trace elements, including zinc, iron, selenium, magnesium, and copper, play important roles in supporting proper immune response to infection [15].

Infections increase deficiency of micronutrient by lowering intake of nutrient, aggravating losses, also impairing their proper utilization especially in children because they more vulnerable to nutritional deficiency [16].

Malnutrition as result of excesses, deficiencies, or imbalances in energy and nutrient intake may lead to secondary immune disturbance [17], that characterized by disruption of physical and chemical barrier, phagocytosis and cell-mediated immunity dysfunction, an impaired complement system and cytokine production [18].

### Patients and Methods

This retrospective study was carried out in the pediatric intensive care unit of El Galaa Teaching Hospital. After obtaining the approval of Ethics Committee of General Organization of Teaching Hospital and Institutes and conducted according to Helsinki declaration of the World Medical Association.

This study used the medical records of one hundred pediatric patients with confirmed COVID-19

by polymerase chain reaction (PCR) swab test in the period between June 1<sup>st</sup>, 2023 and may 31<sup>th</sup>, 2024, where 40 patients were excluded due to incomplete data or presence of chronic disease affect nutritional status of patients including cardiovascular, endocrinal, renal, hematological or gastrointestinal diseases. The study reviewed the demographic data, anthropometric data, nutritional and medical history, laboratory investigation, duration of hospital stays and outcome of the hospitalized patients during the period of the study.

### Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 27. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also, qualitative variables were presented as number and percentages. The one-sample Kolmogorov-Smirnov test can be used to test that a variable is normally distributed. The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test when the expected count in any cell found less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using Independent *t*-test while with non-parametric distribution were done by using Mann-Whitney test. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *p*-value was considered significant at level of *p*-value <0.05.

### Results

A total of 60 patients with COVID-19 aged 2 to 10 years were evaluated in this study and the mean age were 5.52±2.2 years (age range 2.1 to 10 years). The percentage value was 55% for females and 45% for males.

Table (1): Demographic data and characteristics of the studied patients.

Variable	Total No.=60	Survivors No.=39	Non-survivors No.=21	Test value	<i>p</i> -value
<i>Age:</i>					
Mean ± SD	5.52±2.2	5.04±2.23	6.41±1.88	-2.389•	0.020
Range	2.1 – 10	2.1 – 9	2.9 – 10		
<i>Sex:</i>					
Female	33 (55.0%)	25 (64.1%)	8 (38.1%)	3.730*	0.053
Male	27 (45.0%)	14 (35.9%)	13 (61.9%)		

*p*-value >0.05: Non-significant.

*p*-value <0.05: Significant.

*p*-value <0.01: Highly significant.

\*: Chi-square test.

•: Independent *t*-test.

Table (2): Comparison between survivors and non- survivors regarding anthropometric measurements of the studied patients.

Variable	Survivors No.=39	Non-survivors No.=21	Test value	p- value
Median (IQR)	0.2 (-1.1 – 0.9)	-1.02 (-1.64 – 0.17)	-2.893#	0.004
Range	-2.86 – 2.9	-3.49 – 1.47		
<i>Weight z score:</i>				
> -3 SD	0 (0%)	3 (14.3%)	7.839*	0.098
-3SD s/d <-2 SD	2 (5.1%)	0 (0%)		
-2 SD s/d 1 SD	32 (82.1%)	16 (76.2%)		
>1SD s/d 2 SD	3 (7.7%)	2 (9.5%)		
>2 SD	2 (5.1%)	0 (0%)		
Median (IQR)	0.44 (-0.9 – 1)	-1.44 (-2.1 – 0.29)	-2.645#	0.008
Range	-3.9 – 2.1	-2.4 – 1.3		
<i>Height z score:</i>				
> -3 SD	2 (5.1%)	0 (0%)	10.228*	0.037
-3SD s/d <-2 SD	2 (5.1%)	7 (33.3%)		
-2 SD s/d 1 SD	26 (66.7%)	10 (47.6%)		
>1SD s/d 2 SD	7 (17.9%)	4 (19%)		
>2 SD	2 (5.1%)	0 (0%)		
Median (IQR)	0.39 (-0.9 – 1.2)	-0.6 (-1.27 – 0.29)	-2.583#	0.010
Range	-2.98 – 2.8	-3.9 – 1		
<i>BMI z score:</i>				
> -3 SD	0 (0%)	5 (23.8%)	17.116*	0.002
-3SD s/d <-2 SD	2 (5.1%)	0 (0%)		
-2 SD s/d 1 SD	25 (64.1%)	16 (76.2%)		
>1SD s/d 2 SD	10 (25.6%)	0 (0%)		
>2 SD	2 (5.1%)	0 (0%)		
Mean ± SD	16.42±7.15	16.33±6.75	0.046•	0.964
Range	9.5 – 35	10.3 – 34		
<i>MUAC (centimeters):</i>				
Normal	25 (64.1%)	13 (61.9%)	1.307*	0.520
Moderate acute malnutrition	12 (30.8%)	8 (38.1%)		
Severe acute Malnutrition	2 (5.1%)	0 (0%)		

p-value >0.05: Non-significant.

p-value <0.05: Significant.

p-value <0.01: Highly significant.

\*: Chi-square test.

•: Independent t-test.

#: Mann-Whitney test. BMI, Body mass index.

MUAC: Mid-upper arm circumference.

Non-survivors' patients with COVID-19 had significantly lower anthropometric measurements (Z score for weight, Z score for height and body mass index Z score) as compared to survivors but no statistically significant difference as regarding mid-upper arm circumference between both groups.

Table (3) shows statistically significant decrease in the level of hemoglobin (Hb), total leucocytic count, lymphocyte, neutrophil but increase in D-dimer, neutrophil lymphocyte ratio, platelet lymphocyte ratio in non-survivors as compared with survivors and no statistically significant difference as regarding platelet count between both groups.

There was statistically decrease in folic acid, Vitamin D, Zinc, Selenium (38.3%, 23.3%, 65%, 36.7% respectively) in COVID-19 patients. While severe vitamin D deficiency was reported in 21.7% of patients with COVID-19. There was statistically significant decrease in folic acid, Vitamin D, Zinc, Selenium in non-survivors as compared with survivors' patients with COVID-19.

There was statistically significant difference as regarding need for mechanical ventilation and length of hospitalization between survivors and non-survivors 'patients with COVID-19.

Table (3): Comparison between survivors and non-survivors regarding laboratory investigations of the studied patients.

Variable	Survivors No.=39	Non-survivors No.=21	Test value	p- value
<i>HB:</i>				
Mean ± SD	9.9±1.6	8.21±1.49	3.998•	0.000
Range	6.8 – 12.5	6.6 – 11		
<i>TLC:</i>				
Median (IQR)	4.9 (4.5 – 8.1)	4.2 (3.4 – 5.7)	-2.046#	0.041
Range	3.4 – 12	2.1 – 10.2		
<i>Lymphocyte:</i>				
Median (IQR)	2.1 (0.9 – 2.7)	1.3 (1.2 – 2.9)	-0.831#	0.406
Range	0.8 – 2.4	0.6 – 1.4		
<i>Neutrophil:</i>				
Median (IQR)	2.4 (2.1 – 5.6)	2.1 (1.8 – 2.3)	-3.215#	0.001
Range	1.5 – 7.8	1.2 – 4.3		
<i>Platelet:</i>				
Mean ± SD	228.36±89.95	185.62±55.43	1.980•	0.052
Range	98 – 450	90 – 250		
<i>D-dimer:</i>				
Mean ± SD	0.92±0.86	2.41±1.17	-5.626•	0.000
Range	0.1 – 3.2	0.8 – 4.1		
<i>Neutrophil lymphocyte ratio:</i>				
Median (IQR)	2.5 (2.1 – 3.1)	7.2 (6.9 – 8.3)	-5.864#	0.000
Range	1.8 – 8.3	6.4 – 9.3		
<i>Platelet lymphocyte ratio:</i>				
Mean ± SD	160.38±27.35	329.76±47.17	-17.648•	0.000
Range	142 – 267	265 – 430		

p-value >0.05: Non-significant.

p-value <0.05: Significant.

p-value <0.01: Highly significant.

• : Independent t-test.

#: Mann-Whitney test. BMI, Body mass index.

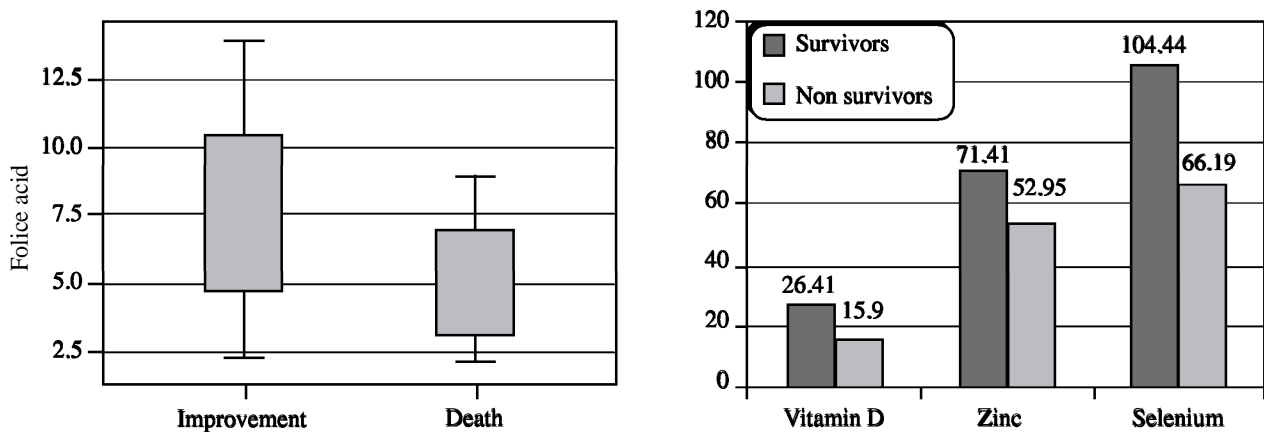


Fig. (1): Comparison between survivors and non-survivors regarding folic acid, vitamin Zinc and selenium level among the studied patients.

Table (4): Comparison between survivors and non-survivors regarding levels of folic acid, vitamin D, zinc and selenium among the studied patients.

Variable	Total No.=60	Survivors No.=39	Non-survivors No.=21	Test value	p-value
Median (IQR)	6 (4 – 10)	6.1(4.6 – 11)	4 (3.1 – 7)	-2.911#	0.004
Range	2.1 – 14	2.2 – 14	2.1 – 8.9		
<i>Folic acid:</i>					
Low	23 (38.3%)	12 (30.8%)	11 (52.4%)	2.697*	0.101
Normal	37 (61.7%)	27 (69.2%)	10 (47.6%)		
High	0 (0%)	0 (0%)	0 (0%)		
Mean ± SD	22.73±10.19	26.41±10.26	15.9±5.57	4.348•	0.000
Range	8 – 39	8 – 39	8 – 25		
<i>Vitamin D:</i>					
Sufficient ≥20	33 (55%)	27 (69.2%)	6 (28.6%)	9.150*	0.010
Deficient <20	14 (23.3%)	6 (15.4%)	8 (38.1%)		
Severe deficient ≤10	13 (21.7%)	6 (15.4%)	7 (33.3%)		
Mean ± SD	64.95±19.18	71.41±18.55	52.95±14.1	3.977•	0.000
Range	37 – 112	45 – 112	37 – 90		
<i>Zinc:</i>					
Low	39 (65%)	20 (51.3%)	19 (90.5%)	9.217*	0.002
Normal	21 (35%)	19 (48.7%)	2 (9.5%)		
High	0 (0%)	0 (0%)	0 (0%)		
Mean ± SD	91.05±39.34	104.44±42.14	66.19±13.88	4.029•	0.000
Range	34 – 191	34 – 191	45 – 89		
<i>Selenium:</i>					
Low	22 (36.7%)	10 (25.6%)	12 (57.1%)	7.949*	0.019
Normal	31 (51.7%)	22 (56.4%)	9 (42.9%)		
High	7 (11.7%)	7 (17.9%)	0 (0%)		

p-value >0.05: Non-significant.

p-value <0.05: Significant.

p-value <0.01: Highly significant.

•: Independent t-test.

#: Mann-Whitney test.

Table (5): Comparison between survivors and non-survivors regarding need for mechanical ventilation and length of hospitalization among the studied patients.

Variable	Total No.=60	Survivors No.=39	Non-survivors No.=21	Test value	p-value
<i>Mechanical ventilation:</i>					
Yes	11 (18.3%)	0 (0%)	11 (52.4%)	25.015*	0.000
No	49 (81.7%)	39 (100%)	10 (47.6%)		
<i>Length of hospitalization:</i>					
Mean ± SD	10.27±3.77	8.74±2.88	13.1±3.63	-5.087•	0.000
Range	5 – 18	5 – 16	5 – 18		

p-value >0.05: Non-significant.

p-value <0.05: Significant.

p-value <0.01: Highly significant.

\*: Chi-square test.

•: Independent t-test.

Table (6): Correlation of folic acid, vitamin D, zinc and selenium with other studied parameters among the studied patients.

Variable	Folic acid		Vitamin D		Zinc		Selenium	
	<i>r</i>	<i>p</i> -value	<i>r</i>	<i>p</i> -value	<i>r</i>	<i>p</i> -value	<i>r</i>	<i>p</i> -value
Folic acid	–	–	0.544**	0.000	0.441**	0.000	0.304*	0.018
Vitamin D	0.544**	0.000	–	–	0.724**	0.000	0.616**	0.000
Zinc	0.441**	0.000	0.724**	0.000	–	–	0.666**	0.000
Selenium	0.304*	0.018	0.616**	0.000	0.666**	0.000	–	–
Age	0.087	0.511	-0.138	0.294	-0.225	0.084	-0.083	0.526
Length of hospitalization	-0.223	0.087	-0.469**	0.000	-0.657**	0.000	-0.504**	0.000
Weight z score	0.281*	0.030	0.420**	0.001	0.437**	0.000	0.374**	0.003
Height z score	0.190	0.146	0.367**	0.004	0.479**	0.000	0.351**	0.006
BMI z score	0.300*	0.020	0.394**	0.002	0.490**	0.000	0.391**	0.002
MUAC	0.205	0.117	0.136	0.302	-0.117	0.374	0.053	0.685
HB	0.258*	0.047	0.424**	0.001	0.635**	0.000	0.594**	0.000
TLC	0.198	0.129	0.319*	0.013	0.429**	0.001	0.379**	0.003
Lymphocyte	0.173	0.185	0.213	0.102	0.259*	0.046	0.039	0.768
Neutrophil	0.104	0.428	0.158	0.228	0.336**	0.009	0.435**	0.001
Platelet	0.097	0.462	0.144	0.272	0.097	0.460	0.119	0.363
D-dimer	-0.062	0.637	-0.393**	0.002	-0.571**	0.000	-0.427**	0.001
Neutrophil lymphocyte ratio	-0.193	0.140	-0.511**	0.000	-0.534**	0.000	-0.426**	0.001
Platelet lymphocyte ratio	-0.226	0.082	-0.406**	0.001	-0.438**	0.000	-0.290*	0.025

*p*-value >0.05: Non-significant.  
*p*-value <0.05: Significant.

*p*-value <0.01: Highly significant.  
Spearman correlation coefficient.

This table shows statistically significant positive correlation between serum Vitamin D, Zinc, Selenium and anthropometric measurements including Z score for weight, Z score for height and body mass index Z score as well as hemoglobin level and negative correlation with length of hospital stay, D-dimer, neutrophil lymphocyte ratio and platelet lymphocyte ratio.

## Discussion

The immune system plays important role in protecting the host from pathogenic organisms including bacteria, viruses, fungi and parasites [19]. Proper function of immune system in fighting pathogenic organism that causing infection depend mainly on sufficient and balanced nutrition. Macronutrients, different vitamins and trace element act as essential factors for generation of energy and biosynthesis various component of immune system [20]. Good nutrition provided proper environment in which the immune system can to respond to challenge, whatever the challenge nature. While malnutrition creates an environment in which the immune system unable to respond well [21]. Our study carried out to evaluated nutritional status of pediatric patients with COVID-19 during their admission in pediatric intensive care unit and to assess the effect of their nutritional status on outcome.

In the present study, vitamin D deficiency was reported in 45% of patients with COVID-19 while severe vitamin D deficiency was 21.7% that in con-cords with study by Karakaya et al. [22]. That re-

ported vitamin D deficiency in 82% of patients with COVID-19 infection and another study by Im et al. [23]. That reported vitamin D deficiency in 78% of patients with COVID-19. Researchers suggested that vitamin D have important immunoregulatory properties and essential for the integrity and proper function of both innate and acquired immunity [24]. Vitamin D supports innate immunity by enhances the release of Cathelicidin that synthesis in epithelial cells and macrophages and consider one of important inflammatory mediators that promoting and accelerating antigen destruction [25]. Also, vitamin D play important role in both cells mediated and humoral immune responses by modulating the proliferation of T lymphocytes and regulating cytokines production and regulation of B lymphocyte proliferation, production of antibodies, and cell transformation to plasma or memory cell [26]. Vitamin D promotes differentiation of monocytes to macrophages and enhance phagocytosis, production of superoxide and killing of bacterial by innate immune cells [27]. A study by Bergman et al. [28]. suggested that prophylactic dose between 1000 IU to 4000 IU/day of vitamin D can reduce the risk of respiratory tract infections (OR, 0.64; 95% CI, 0.49 to 0.84). As well as vitamin D deficiency can affect the outcome of viral respiratory infections [28].

In the present study, zinc deficiency reported in 65% of patients with COVID-19 that in agreement with study by Jothimani et al. [29] who reported zinc deficiency in 57.4% of patients with COVID-19. Also, suggested a higher rate of complica-

tion (70.4% vs 30.0%,  $p=0.009$ ) in zinc deficient COVID-19 patients, with an OR of 5.54. As well as, patients with zinc deficiency showed an increased risk of the development of ARDS (18.5% vs 0%,  $p=0.06$ ), prolonged hospital stays (mean 7.9 vs 5.7 days,  $p=0.048$ ), were more prone to received corticosteroids (44.4% vs 10%,  $p=0.02$ ), and had higher risk of mortality [5 (18.5%) vs 0 (0%),  $p=0.06$ ] when compared with normal zinc patients with COVID-19. Another study by Ghanei et al. [30] reported low serum zinc level in patients with COVID-19. In contrast to our finding study by Karakaya et al. and Im et al., that reported [22] normal zinc level in patients with COVID-19.

Zinc is an essential trace element required for several biological processes acting as a cofactor, structural element and signaling molecule. It responsible for regulation of metabolism of many macronutrients including carbohydrate and lipid, as well as the proper functioning of the cardiovascular, nervous, and reproductive system [31]. Also, play essential role regarding proliferation, differentiation, maturation, and functioning of different component of immune system including leukocytes and lymphocytes. Zinc have a signaling role as modulator of inflammatory responses [32]. It is considered important element in nutritional immunity. So, zinc deficiency has great effect on immune response to inflammatory and infectious diseases [33].

Recent studies showed the role of zinc as immune modulator and antiviral agent in treatment SARS-CoV-2 as zinc can inhibit the RNA polymerase of coronaviruses that required for its replication, [34] other study suggest that zinc ionophore pyrrolidine dithiocarbamate may play a key role in inhibit replication of SARS-CoV-2 in vitro [35]. The zinc-binding metallothioneins required in antiviral defense [36]. Zinc deficiency has a great effect on bone marrow, by lowering the precursor of immune cells, result in decreasing production of B lymphocytes as well as may lead to thymic atrophy, reducing T lymphocytes output [37]. Therefore, zinc is important in maintaining proper T and B lymphocyte numbers [38]. Zinc deficiency interfere with normal function of innate immunity, including phagocytosis, natural killer cell activity and respiratory burst [39].

According to our result selenium found deficient in 36.7% of studied patients that in agreement with study by Im et al., that reported selenium deficiency in 42% patients with COVID-19. In contrast to our finding study by Karakaya et al., [22] that found normal serum selenium level in COVID-19 patients. Selenium by its effects on redox signaling activities can contribute to the defense against pathogens [40]. Recent study by Heller et al., suggested that selenium together with zinc can exert a protective role and may improve chance of survival in patients with COVID-19 [41]. As well as selenium administration

can enhance the response and increase antibodies titers to COVID-19 vaccine as it may act as a cofactor in immunity response that is mediated by the vaccine [42].

Selenium consider as one of immunoregulator micronutrients as it involved in the regulation of the inflammatory mediators' synthesis, it might increase the activity of phagocytic cells. Selenium administration can increase the immune response of Th1 cells, stimulation of T cells and capable to strength ened the innate immune system [43].

selenium deficiency in humans assumed to decrease natural killer cell activity, increased mycobacterial disease [44] and could result in the appearance of more pathogenicviral strains thereby increasing the risks and burdens associated with viral infection [45]. Selenium supplementation (100 to 300 $\mu$ g/day depending on the study) has been shown to enhance many aspects of immune function in humans, including in the elderly [46].

Folic acid found to be low in 38.3% of COVID-19 patients in our study but many studies found in significant decrease in folic acid level in COVID-19 patients [22,23] by 15%, 7.9% respectively.

Another study by Sheybani et al., [47] suggested folic acid can be used in prevention and treatment COVID-19 patients as it decreases the intracellular transport of the virus through inhibition of transmembrane protein called furin which is a protease enzyme required to cleave the spike protein of SARS-CoV-2 and by this way promote the virus entry into the cells. Also, Farag et al., [48] suggested folic acid supplementation may significantly decrease the risk of COVID-19 infection.

#### Conclusion:

Effective immune function and proper nutrition are double-edged weapon the current study evaluates the nutritional status of patients with COVID-19. The results showed deficiency in more than one micronutrient that affect the outcome of COVID-19 infection. We suggest that proper supplementation of vitamins and trace elements will supporting the human immune system, reducing risk of viral respiratory tract infections especially COVID-19, helps to reduce the severity of disease improving survival of critically ill patients and reducing the mortality. Further studies with larger sample size are needed to determine the effects of micronutrient supplementation on the course of infection with COVID-19.

#### References

- 1- SHI T., MCLEAN K., CAMPBELL H. and NAIR H.: Etiological role of common respiratory viruses in acute lower respiratory infections in children under five years: A systematic review and meta-analysis. *J. Glob. Health*, 5: 010408, 2015. <https://doi.org/10.7189/JOGH.05.010408>.

- 2- UNICEF. Pneumonia in children statistics–UNICEF data 2021: UNICEF; 2021. Available from: <https://data.unicef.org/topic/childhealth/pneumonia/>. Accessed 23 July 2022.
- 3- World Health Organization (WHO). Pneumonia 2021: WHO; 2021. Available from: <https://www.who.int/news-room/factsheets/detail/pneumonia>. Accessed 30 June 2022.
- 4- BUTLER M.J. and BARRIENTOS R.M.: The impact of nutrition on COVID-19 susceptibility and long-term consequences. *Brain Behav Immun*, Jul. 87: 53e4, 2020.
- 5- WHO. Coronavirus disease 2019. Events as they happen. 2020. access address, <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>. [Accessed 12 June 2020].
- 6- SKALNY A.V., RINK L., AJSUVAKOVA O.P., ASCHNER M., GRITSENKO V.A., ALEKSEENKO S.I., et al.: Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). *Int. J. Mol. Med*. Jul. 46 (1): 17e26, 2020.
- 7- GUAN W., NI Z., Y. HU, et al.: “Clinical characteristics of coronavirus disease 2019 in China,” *New England Journal of Medicine*, Vol. 382, No. 18, pp. 1708–1720, 2020.
- 8- DE SANCTIS J.B., GARCÍA A.H., MORENO D. and HAJDUCH M.: Coronavirus infection: An immunologists’ perspective. *Scand. J. Immunol.*, 93, e13043, 2021. [Cross-Ref].
- 9- AMODIO D., BUONSENSO D. and PALMA P.: Susceptibility of SARS-CoV2 infection in children. *Eur. J. Pediatr.*, 182, 4851–4857, 2023 [CrossRef].
- 10- SHARMA A., KUMAR A. and FLORA S.: “Neurological manifestations in COVID-19 patients: A meta-analysis,” *ACS Chemical Neuroscience*, Vol. 12, No. 15, pp. 2776–2797, 2021.
- 11- MENG L., ZHAO X. and ZHANG H.: HIPK1 Interference attenuates inflammation and oxidative stress of acute lung injury via autophagy. *Med. Sci. Monit*, 25: 827–35, 2019.
- 12- FOWLER III A.A., KIM C., LEPLER L., MALHOTRA R., DEBESA O., NATARAJAN R., FISHER B.J., SYED A., DE WILDE C., PRIDAY A. and KASIRAJAN V.: Intravenous vitamin C as adjunctive therapy for enterovirus/rhinovirus induced acute respiratory distress syndrome. *World J. Crit Care Med.*, 6: 85–90, 2017.
- 13- HECKER L.: Mechanisms and consequences of oxidative stress in lung disease: Therapeutic implications for an aging populace. *Am. J. Physiol. Lung Cell Mol. Physiol.*, 314: L642–53, 2018.
- 14- ELMADFA I. and MEYER A.L.: The Role of the Status of Selected Micronutrients in Shaping the Immune Function. *Endocr. Metab. Immune Disord. Drug Targets*, 19: 1100–1115, 2019. [CrossRef] [PubMed].
- 16- GOMBART A.F., PIERRE A. and MAGGINI S.: A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients*, 12: 236, 2020. [CrossRef] [PubMed].
- 17- WEI W., WU X., JIN C., MU T., GU G., MIN M., MU S. and HAN Y.: Predictive Significance of the Prognostic Nutritional Index (PNI) in Patients with Severe COVID-19, *Journal of Immunology Research*, 9917302, 2021.
- 18- BOURKE C.D., BERKLEY J.A. and PRENDERGAST A.J.: Immune Dysfunction as a Cause and Consequence of Malnutrition. *Trends Immunol.*, 37: 386–398, 2016. [CrossRef] [PubMed].
- 19- GOMBART A., PIERRE A. and MAGGINI S.: A review of micronutrients and the immune system–working in harmony to reduce the risk of infection. *Nutrients*, 12: 236, 2020. doi: 10.3390/nu12010236.
- 20- MAGGINI S., PIERRE A. and CALDER P.: Immune function and micronutrient requirements change over the life course. *Nutrients*, 10: 1531, 2018. doi: 10.3390/nu10101531.
- 21- WU D., LEWIS E., PAE M. and MEYDANI S.: Nutritional modulation of immune function: Analysis of evidence, mechanisms, and clinical relevance. *Front Immunol.*, 9: 3160, 2019. doi: 10.3389/fimmu.2018.03160.
- 22- KARAKAYA G., ÜNAL O. and KOÇ N.: Evaluation of nutritional status in pediatric patients diagnosed with Covid-19 infection. *Clinical Nutrition ESPEN*, 44: 424e428, 2021.
- 23- IM J.H., JE Y.S., BAEK J., CHUNG M.H., KWON H.Y. and LEE J.S.: Nutritional status of patients with COVID-19. *Int J Infect Dis.*, Nov. 100: 390-393, 2020. doi: 10.1016/j.ijid.2020.08.018.
- 24- LUCAS R., GORMAN S., GELDENHUYS S. and HART P.: Vitamin D and immunity. *F1000 Prime Rep.*, 6, 2014. doi:10.12703/P6-118.
- 25- MILLER J. and GALLO R.L.: Vitamin D and innate immunity. *Dermatol. Ther.*, 23 (1): 13-22, 2010. doi:10.1111/j.1529-8019.2009.01287.
- 26- CHEN S., SIMS G., XIAO C., YUE G. and LIPSKY P.: “Modulatory effects of 1,25-dihydroxy vitamin D3 on human B cell differentiation,” *The Journal of Immunology*, Vol. 179, No. 3, pp. 1634–1647, 2007.
- 27- SABETTA J.R., DEPETRILLO P., CIPRIANI R.J., SMARDIN J., BURNS L.A. and LANDRY M.L.: “Serum 25-hydroxy vitamin D and the incidence of acute viral respiratory tract infections in healthy adults,” *PLoS ONE*, Vol. 5, No. 6, Article ID e11088, 2010.
- 28- BERGMAN P., LINDH A.U., BJORKHEM-BERGMAN L., et al.: Vitamin D and respiratory tract infections: A systematic review and meta-analysis of randomized controlled trials. *PloS ONE*, 8: e65835, 2013.
- 29- JOTHIMANI D., KAILASAM E., DANIELRAJ S., NALLATHAMBI B., RAMACHANDRAN H., SEKAR P., MANOHARAN S., RAMANI V., NARASIMHAN G., KALIAMOORTHY I. and RELA M.: COVID-19: Poor outcomes in patients with zinc deficiency. *Int. J. Infect. Dis.*, Nov. 100: 343-349, 2020. doi: 10.1016/j.ijid.2020.09.014.
- 30- GHANEI E., BAGHANI M., MORAVVEJ H., et al.: Low serum levels of zinc and 25-hydroxy vitamin D as potential risk factors for COVID-19 susceptibility: A pilot case-con-



- trol study. *Eur. J. Clin. Nutr.*, 76: 1297–1302, 2022. <https://doi.org/10.1038/s41430-022-01095-5>.
- 31- READ S.A., OBEID S., AHLENSTIEL C., et al.: The role of zinc in antiviral immunity. *Adv. Nutr.*, 10: 696–710, 2019.
- 32- MAYWALD M., WESSELS I., RINK L.: Zinc signals and immunity. *Int. J. Mol. Sci.*, 18: 2222, 2017.
- 33- MAARES M. and HAASE H.: Zinc and immunity: An essential interrelation. *Arch. Biochem. Biophys.*, 611: 58–65, 2016.
- 34- KAUSHIK N., SUBRAMANI C., ANANG S., et al.: Zinc salts block hepatitis E virus replication by inhibiting the activity of viral RNA-dependent RNA polymerase. *J. Virol.*, 91i: e00754–17, 2017.
- 35- UCHIDE N., OHYAMA K., BESSHO T., et al.: Effect of antioxidants on apoptosis induced by influenza virus infection: Inhibition of viral gene replication and transcription with pyrrolidine dithiocarbamate. *Antiviral Res.*, 56: 207–17, 2002.
- 36- SUBRAMANIAN VIGNESH K. and DEEPE Jr.G.: Metallothioneins: Emerging modulators in immunity and infection. *Int. J. Mol. Sci.*, 18: 2197, 2017.
- 37- TE VELTHUIS A.J.W., VAN DEN WORM S.H.E., SIMS A.C., et al.: Zn<sup>2+</sup> inhibits coronavirus and arterivirus RNA polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. *PLoS Pathog.*, 6: e1001176, 2010.
- 38- HASAN R., RINK L. and HAASE H.: Zinc signals in neutrophil granulocytes are required for the formation of neutrophil extracellular traps. *Innate Immun.*, 19: 253–64, 2013.
- 39- HASAN R., RINK L. and HAASE H.: Chelation of free Zn<sup>2+</sup> impairs chemotaxis, phagocytosis, oxidative burst, degranulation, and cytokine production by neutrophil granulocytes. *Biol. Trace Elem Res.*, 171: 79–88, 2016.
- 40- ZHANG Y., ROH Y., HAN S., PARK I., LEE H., OK Y., et al.: Role of selenoproteins in redox regulation of signaling and the antioxidant system: A review. *Antioxidants*, 9: 383, 2020. doi: 10.3390/antiox9050383.
- 41- HELLER R., SUN Q., HACKLER J., SEELIG J., SEIBERT L., CHERKEZOV A., et al.: Prediction of survival odds in COVID-19 by zinc, age and selenoprotein P as composite biomarker. *Redox Biol.*, 38: 101764, 2021. doi: 10.1016/j.redox.2020.10.1764.
- 42- IVORY K., PRIETO E., SPINKS C., ARMAH C., GOLDSON A., DAINTY J., et al.: Selenium supplementation has beneficial and detrimental effects on immunity to influenza vaccine in older adults. *Clin. Nutr.*, 36: 407–15, 2017. doi: 10.1016/j.clnu.2015.12.003.
- 43- TOURKOCHRISTOU E., TRIANTOS C. and MOUZAKI A.: The influence of nutritional factors on immunological outcomes. *Front Immunol.*, 12: 665968, 2021. doi: 10.3389/fimmu.2021.665968.
- 44- ROY M., KIREMIDJIAN-SCHUMACHER L., WISHE H.I., et al.: Supplementation with selenium and human immune cell functions. I. Effect on lymphocyte proliferation and interleukin 2 receptor expression. *Biol. Trace Elem Res.*, 41: 103–14, 1994.
- 45- HAWKES W.C., KELLEY D.S. and TAYLOR P.C.: The effects of dietary selenium on the immune system in healthy men. *Biol. Trace Elem Res.*, 81: 189–213, 2001.
- 46- KIREMIDJIAN-SCHUMACHER L., ROY M., WISHE H.I., et al.: Supplementation with selenium and human immune cell functions. II. Effect on cytotoxic lymphocytes and natural killer cells. *Biol. Trace Elem Res.*, 41: 115–27, 1994.
- 47- SHEYBANI Z., DOKOOHAKI M.H., NEGAHDARIPOUR M., DEHDASHTI M., ZOLGHADR H., MOGHADAMI M., et al.: The role of folic acid in the management of respiratory disease caused by COVID-19. *Chem. Rxiv*, 2020.
- 48- FARAG A., HAFEZ N., DWEDAR R., BILAL D., SAID A., ELBARMELGI M., et al.: The use of folic acid as a prophylaxis against COVID-19 among healthcare workers. *Microbes and Infectious Diseases*, 4 (1): 56–62, 2023.

## تقييم الحالة الغذائية للاطفال ذوى الحالات الحرجة المصابين بكوفيد١٩ المحجوزين فى الرعاية المركزة للاطفال

خلفية الدراسة: تلعب التغذية دور اساسى فى تنظيم وظائف للجهاز المناعى حيث انها تمدد بالمواد الاساسية من فيتامينات ومعادن والعناصر الغذائية المهمة بتركيزات مناسبة تساعد على القيام بوظيفتها بالطريقة المثلى، فى حين ان سوء التغذية قد يؤثر تأثير اساليا على قدرة جهاز المناعة فى مقاومة الامراض.

الغرض من البحث: تقييم الحالة الغذائية للاطفال ذوى الحالات الحرجة المصابين بكوفيد١٩ المحجوزين فى الرعاية المركزة للاطفال.

دراسة العلاقة بين نقص التغذية وشدة العدوى بكوفيد ١٩ بين الاطفال المحجوزين فى الرعاية المركزة للاطفال.

منهج البحث: دراسة بحثية رجعية.

المرضى وطريقة العمل: تم مراجعة الملفات الطبية لستين مريض مصاب بالكوفيد١٩ من الاطفال المحجوزين فى الرعاية المركزة للاطفال فى مستشفى الجلاء التعليمى فى الفترة بين ١ يونية ٢٠٢٣ الى ٣١ مايو ٢٠٢٤ وتم بحث معدلا النمو من طول ووزن وكتلة الجسم ومحيط منتصف الذراع العلوى وتاريخ التغذوى والتاريخ المرضى والتحليل الطبية ومدة الاقامة بالمستشفى.

النتائج: تبين نقص معدلات النمو من طول ووزن وكتلة الجسم والمعادن من زنك وسيلينيوم وفيتامينات من فيتامين د وفوليك اسيد فى الاطفال المتوفين عن الاطفال الذين تم شفاهم .

التطبيقات المقترحة: الاهتمام بالتغذية الصحية السليمة والفيتامينات المهمة لتعزيز الجهاز المناعى وبالتالي القدرة على مقاومة الاصابة بعدوى كوفيد ١٩ والامراض الفيروسية التى تؤدى الى مضاعفات خطيرة قد تصل إلى الوفاة فى بعض الاحيان.