Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Nutrition ESPEN 44 (2021) 424–428

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Evaluation of nutritional status in pediatric patients diagnosed with Covid-19 infection

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ARTICLE INFO

Article history:
Received 31 October 2020
Accepted 22 April 2021

Keywords:
Nutritition status
Covid-19 ınfection
Pediatric patients

SUMMARY

Aim: The aim of this study was to evaluate the nutritional status, the nutritional effect on the risk of infection and the severity of the disease, and the contribution of nutrition to the course of the infection in pediatric patients diagnosed with coronavirus disease who required additional nutritional support after hospitalization.

Methods: The body weight, height, body mass index, upper arm circumference, and triceps skinfold thickness of 49 patients aged 1 month to 18 years and diagnosed with Covid-19 and then hospitalized at the Ankara City Hospital, Pediatric Health and Diseases Hospital, Pediatric Infection ward between 15 May and 15 June 2020 were measured. Total protein, albumin, prealbumin, selenium, zinc, ferritin, folate, and selenium, C, D, E, and B12 levels were studied from blood drawn simultaneously from the patients.

Results: A total of 49 patients aged 8–18 years were evaluated. The median age was 13 years (age range 8–18). The females made up 53% and the males 47% of the group. No patient needed intensive care admission. Only 3 patients received antibiotic treatment and the others were followed up without treatment. The weight was normal in 75% and the height was normal in 90%. Mid-arm circumference and triceps thickness were normal in 72% of the patients. Vitamin D deficiency was present in 82%, vitamin B12 deficiency in 18%, vitamin C deficiency in 17%, ferritin deficiency in 16%, folate deficiency in 15%, vitamin A deficiency in 13%, and vitamin E deficiency in 7%.

Conclusion: No patient required intensive care admission. Only 3 patients received antibiotic treatment and the others were followed up without treatment. Malnourishment was present in 3% of the patients while 9% were obese. Vitamin D deficiency was the most common vitamin deficiency while vitamin B12, vitamin C, Ferritin, vitamin A, vitamin E, and Folate deficiency were less common. Selenium and zinc levels were normal in all patients. There was no correlation between anthropometric values and susceptibility to childhood COVID-19 infection or the clinical course. It is possible that vitamin D deficiency increases susceptibility to the infection.

1. Introduction

COVID-19 is a respiratory system disease caused by the new type coronavirus called SARS-CoV-2 [1]. It was first reported at the end of 2019 and quickly spread around the world within a few months. The WHO declared COVID-19 a pandemic in March 2020 [2]. COVID-19 predominantly affects the respiratory system, causing pneumonia and conditions resulting in acute respiratory distress syndrome requiring mechanical ventilation [3]. While COVID-19 affects all groups in the population, it is more severe with higher mortality rates in those with poor immunity and underlying comorbidities such as diabetes, cardiovascular diseases and obesity [4]. Effective, preventive or curative treatments for COVID-19 have not yet been found, so it is believed that a strong immune system could be protective [5]. Treatment of COVID-19 essentially depends on the patient's own immune system. The immune system protects

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https://doi.org/10.1016/j.clnesp.2021.04.022

the patient against pathogens such as viruses, bacteria, and fungi [6]. Many factors are effective in the development and protection of immunity, and one of these factors is the person's nutritional status [7]. A sufficient amount and correct ratio of macro and micronutrients are necessary for the maintenance of vital functions. Recently, the role that micronutrients play in the immune function has been emphasized more strongly [8]. There is a large number of clinical studies revealing that vitamins, including A, B12, C, D, E and folate, and trace elements such as zinc, iron, and selenium play important and supplementary roles in supporting the immune system [8]. Nutrition is one of the most important factors in the preservation and development of immunity. It is part of the treatment regimen, especially for acute and chronic diseases for which an etiological treatment has not yet been found.

It is well known that nutrition is a very important factor in regulating immunological homeostasis. Insufficient protein and energy intake and subclinical deficiencies of some micronutrients can impair the immune response [9]. Nutrition is important for growth and development and their deficiencies are more common in children. Since our hospital is a tertiary hospital, we followed a large number of children Covid 19 patients and thought that we could obtain important data about the disease.

We aimed to evaluate the nutritional status of pediatric patients diagnosed with COVID-19 disease and investigate the effect of nutritional status on the risk of transmission and the severity of the disease in addition to the contribution of nutrition to the course of infection in patients who require additional nutritional support after hospitalization.

2. Methods

This study was conducted in patients diagnosed with Covid-19 and hospitalized in Ankara City Hospital Pediatric Health and Diseases Hospital's pediatric infection ward between 15 May and 15 June 2020. Body weight, height, body mass index, upper arm circumference, and triceps skinfold thickness was measured in 49 patients aged 1 month to 18 years. Total protein, albumin, prealbumin, selenium, zinc, ferritin, folate, and the vitamin A, C, D, E, and B12 levels were studied from blood taken simultaneously from the patients. The data analysis was conducted by using the SPSS statistics software version 26.

3. Results

A total of 49 subjects aged 8–18 years were evaluated in this study and the mean age were 13 years (age range 8–18 years). The percentage value was 53% for females and 47% for males. The age and gender distributions of our patients are shown in Table 1. The weight was normal in 76% and the height was normal in 90% while 3% were malnourished and 9% were obese. Mid-arm circumference and triceps thickness were normal in 72% of the patients. The median and mean values of the body weight, height, mid-arm circumference, and triceps thickness are shown in Tables 1 and 2. Total protein, albumin, and prealbumin were within normal range in all patients. According to the data, Vitamin D deficiency was most common, with a deficiency (less than 20 ng/mL) found in 54% of patients, and severe deficiency (less than 10 ng/mL) in 28%. Regarding the other nutrients, vitamin B12 deficiency was present in 18%, vitamin C deficiency in 17%, ferritin deficiency in 16%, folate deficiency in 15%, vitamin A deficiency in 13%, and vitamin E deficiency in 7%. None of the patients had selenium or zinc deficiency. At least one nutrient deficiency was found in 91% of the patients. The median value and deficiency percentages of each nutrient are shown in Table 3. No patient needed intensive care. Only 3 patients received antibiotic treatment and the others were followed up without treatment.

Table 1
The median and mean values of the body weight, height, mid-arm circumference, and triceps thickness of COVID-19 patients.

Demographic characteristics	Parameters	Min – Max	Median	Mean ± sd %
Age		8 – 18	13	13 ± 3
Sex	Female			26 53%
	Male			23 47%
Weight (kilograms)		21 – 100	52	50 ± 15
Weight	Low			3 7%
	Normal			37 75%
	High			9 18%
Height (centimeters)		124 – 182	159	156 ± 14
Height	Low			1 2%
	Normal			44 90%
	High			4 8%
Mid-arm circumference (centimeters)		15 – 44	24	24 ± 5
Mid-arm circumference	Low			9 18%
	Normal			35 72%
	High			5 10%
Triceps thickness (centimeters)		15 – 54	22	24 ± 7
Triceps thickness	Low			9 18%
	Normal			35 72%
	High			5 10%

Sd: Standart deviation, Min: Minimum, Max: Maximum.

4. Discussion

Most COVID-19 patients were found to be deficient in at least one nutrient with vitamin D deficiency being the most common in this study. Nutrition is known to be a very important factor in the regulation of the immune system. Effective, preventive or curative treatments for COVID-19 are not clearly defined yet but it is thought that a strong immune system may be protective [5]. As it becomes increasingly clear that hyperinflammation is an important component of COVID-19 disease, there is greater emphasis on vitamin D deficiency [10].

Vitamin D plays a role in the production of antimicrobial peptides in the respiratory epithelium, provides protection from viral infections, and decreases the severity of symptoms [11]. It has been shown to have a protective effect against respiratory tract infections [12]. It also has useful effects such as inhibiting renin activity and down regulating the renin-angiotensin system. Besides, 25(OH)D has been shown to suppress angiotensin and regulate its expression. A relationship has been reported between the 25(OH)D level and COVID-19 mortality [13]. 25(OH)D strengthens cellular immunity by suppressing the production of biochemical molecules such as interleukin-6, interferon gamma, and tumor necrosis factor-α secreted from Th1 cells in the immune system [14]. These mechanisms suggest that patients with vitamin D deficiency may be more prone to becoming infected with COVID-19 and then developing severe symptoms. Vitamin D deficiency was the most common nutrient deficiency in children with COVID-19 infection in our study, and 25(OH)D administration and protecting against its deficiency in childhood may be important factors in enhancing protection from COVID-19 infection.

Vitamin D deficiency is a major health problem in all age groups. Early treatment of vitamin D deficiency is important in pediatric

Table 2
Percentile values of body weight and height of COVID19 patients.

Parametres	Percentile	Number of patient	%
Percentile (weight)	<5.p	2	4
	5.p	1	2
	5-15.p	5	10
	15-50.p	16	33
	50-85.p	16	33
	85-95.p	4	8
	>95.p	5	10
Percentile (height)	<5.p	1	2
	5-15.p	8	17
	15-25.p	5	10
	15-50.p	11	23
	25-50.p	5	10
	50-75.p	6	12
	50-85.p	5	10
	75-85.p	3	6
	75.p	1	2
	85-95.p	3	6
	97-99.p	1	2
Weight-SDS	-1SD	1	2
	-1SD- medyan	12	24
	-2SD- -1SD	9	19
	<-2SD	1	2
	>2SD	2	4
	1SD – 2SD	8	16
	Median – 1SD	16	33
Height-SDS	-1SD- medyan	20	41
	-2SD- -1SD	9	18
	1SD	1	2
	1SD – 2SD	3	6
	2SD – 3SD	1	2
	Median – 1SD	15	31
Percentile (MAC)	<5.p	9	19
	>95.p	3	6
	10.p	1	2
	15-25.p	3	6
	15.p	1	2
	25-50.p	13	26
	5-10.p	1	2
	50-75.p	12	25
	75-85.p	3	6
	85-90.p	1	2
	90-95.p	2	4
Percentile (TT)	<5.p	9	19
	>95.p	3	6
	10.p	1	2
	15-25.p	3	6
	15.p	1	2
	25-50.p	13	26
	5-10.p	1	2
	50-75.p	12	25
	75-85.p	3	6
	85-90.p	1	2
	90-95.p	2	4

SDS: Standart deviation, MAC: Mid-arm circumference TT: Triceps thickness, p: Percentile.

patients with covid 19 infection [15]. 25(OH)D is known to have direct effects on innate immunity. 25(OH)D receptors (VDR) are present in lymphocytes, monocytes and macrophages. When serum 25(OH)D levels fall below 20 ng/mL, monocytes and macrophages cannot initiate the innate immune response [16]. Beyond the first year of life, vitamin D requirements increase to 600 IU/day. Multiple professional societies strongly recommend that all healthy children beyond 12 months achieve this nutritional intake either through diet or supplementation. Children with malabsorption or other chronic conditions that may alter 25(OH)D absorption/metabolism, children from high-risk groups, and those living in high latitudes may have vitamin D requirements beyond 600 IU/day. For the maximization of bone health in children, adequate calcium intake, weight-bearing exercise, and maintenance of healthy body weight are essential through puberty [17].

Table 3
The median value and deficiency percentages of each nutrient of COVID-19 patients.

Biochemical and laboratory analysis	Outcomes	Min – Max	Median	Mean ± s d/%
Total protein (g/L)		64 – 82	70	71 ± 3
Albumin (g/L)		40 – 53	47	47 ± 2
Prealbumin (g/L)		0,1 – 0,3	0,2	0,2 ± 0,05
Ferritin (μg/L)		7 – 94	28	34 ± 23
Ferritin	Normal			41 84%
	Low			8 16%
Vitamin B12 (ng/L)		141 – 442	278	281 ± 74
Vitamin B12	Normal			40 82%
	Low			9 18%
Folate (ng/mL)		4 – 17	7,5	8 ± 3
Folate	Normal			39 85%
	Low			7 15%
Vitamin D (ng/mL)		4 – 43	11,5	13 ± 7
Vit D	Normal			8 18%
	Low			38 82%
Vitamin C (mg/L)		2 – 24	8,9	10 ± 5
Vit C	Normal			38 83%
	Low			8 17%
Vitamin A (μg/L)		228 – 805	482,4	498 ± 167
Vit A	Normal			26 87%
	Low			4 13%
Vitamin E (mg/L)		6 – 19	10,4	11 ± 3
Vit E	Normal			28 93%
	Low			2 7%
Selenium (μg/L)		46 – 98	66,4	68 ± 14
Selenium	Normal			32 100%
	Low			0 0%
Zinc (μg/dL)		70 – 125	100	96 ± 15
Zinc	Normal			30 100%
	Low			0 0%

Sd: Standart deviation, Min: Minimum, Max: Maximum.

The effect of vitamin A on COVID-19 infection has not been clearly explained but it is known to be effective in viral respiratory tract diseases through the immune response [18]. In addition, some believe that isotretinoin, which is a derivative of vitamin A, is involved in the regulation of angiotensin converting enzyme 2, a critical protein for SARS-COV-2 entry into the body [19]. We found vitamin A deficiency in only 13% of children with COVID-19 infection in our study and the effect of the vitamin on COVID-10 was again not clear.

Vitamin C is concentrated in phagocytic cells such as neutrophils and increases the germicidal effect by affecting processes such as chemotaxis and phagocytosis [20]. IV glucocorticoid treatment together with high-dose vitamin C has been recommended in the early period of the disease to alleviate the inflammatory complications that may occur in patients with COVID-19 who are hospitalized with respiratory distress [21]. Vitamin C deficiency was found in 17% of the children who had COVID-19 infection in this study, and comprehensive studies are therefore required to show the effectiveness of vitamin C in this infection.

Vitamin E may possibly play a protective role against COVID-19 [8]. Zinc given in addition to chloroquine and hydroxychloroquine has been seen to provide rapid improvement in the course of the disease in patients diagnosed with COVID-19 in some studies [22]. A positive correlation was found between the amount of selenium detected in the hair samples and the COVID-19 recovery rates in an epidemiologic study conducted in 17 Chinese cities [12]. Vitamin

B12 and Folate are important for antibody production and metabolism [23]. Vitamin E deficiency was present in 6% of the children with COVID-19 infection in the current study, vitamin B12 deficiency in 18%, and folate deficiency in 15%. Zinc or selenium deficiency was not detected in any of our patients.

Adequate and healthy nutrition is important to stay healthy before or during an infectious disorder. The body's energy and nutrient requirement increases in case of an infection and especially when there is accompanying fever. It is therefore important to maintain a healthy diet during the Covid-19 pandemic for a strong immune system [24]. Determining the nutritional status of all patients who present to the hospital with a Covid-19 infection and providing early nutritional support for patients at nutritional risk are vital [25]. Although a state of inadequate nutrition that can be encountered in other infectious disorders is not seen with Covid-19, it is still important to make sure that the patients receive an adequate amount of daily protein and energy [26]. The increased mortality and morbidity risk due to inadequate nutrition is a result of increased infection rates and delayed recovery. Infections also themselves increase the demand for various nutrients. It is well known that nutrition is a very important factor in the regulation of immunological homeostasis. Inadequate intake of protein and energy and the subclinical deficiencies of some micronutrients can disturb the immune response. Considering the antioxidant, anti-inflammatory, immunomodulatory and neuroprotective effects of various macro and micronutrients ingested with the diet, it is clear that dietary interventions can be beneficial in preventing infections and/or improving treatment results [9]. There is a very complex and strong relationship between nutrition and immunity [27]. Epidemiological and experimental studies have emphasized the importance of diet in the triangle of nutrition, the immune system, and infection. The correct nutritional interventions can potentially be effective in improving the general health of the population and the immune system through the ingestion of macro and micronutrients [28]. Providing optimal nutritional support to individuals should be evaluated in three levels as regard the development and support of strong immunity. First of all, the main principle is to provide all the important macro and micronutrients required to maintain the immune cells and their functions. At the second level, one finds modulation of the immune system during the inflammatory processes of the host, and the third level consists of nutritional interventions specific to the subject to ensure personal immunity. Preventive and individualized nutritional interventions for this purpose play an important role in maintaining the immune system [29].

This study is one of the first to evaluate the nutritional status of children with COVID-19. It was a cross-sectional study conducted in a single center with relatively few patients. A control group was not included. The aim was to investigate the frequency of nutrient deficiencies in these patients. Future studies comparing children with and without COVID-19 infection in the long term and conducted on larger populations with more children and centers involved are required.

5. Conclusıon

Vitamin D deficiency was present in a significant percentage of pediatric patients with COVID-19 infection in this study. It is therefore possible that vitamin D deficiency creates susceptibility to this infection. There is currently no drug or therapeutic substance shown to have a definite effect on COVID-19 disease and methods that can decrease the severity of and susceptibility to the disease are therefore vital.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

This research received no external funding.

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