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EARLY DETERMINATION OF NUTRITIONAL PROBLEMS IN PEDIATRIC CANCER PATIENTS*

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Mild and marginal malnutrition must be identified to prevent the development of severe protein-energy malnutrition in pediatric cancer patients. We aimed to evaluate nutritional status and determine daily energy, protein and micronutrient intake to identify mild or marginal malnutrition in pediatric cancer patients. Daily energy, protein and micronutrient intake, anthropometric measurements and biochemical indices were studied in 45 patients (25 in remission, 20 newly diagnosed or relapsed) who consumed energy, protein, vitamins and minerals below the recommended guantities. According to the weight-for-height index, 23 children (51.1%) were determined to be malnourished. Absolute and relative prealbumin values were 19.4 ± 7.2 mg/dl and 74.3 ± 29.1 mg/dl in the remission group, and 14.8 ± 5.1 mg/dl and 58.1 ± 23.3 in the active disease group, respectively ($p < 0.05$). Relative prealbumin values were found to be low in 63.6 percent of nonmalnourished children, and 80 percent of children with mild malnutrition. We conclude that malnutrition is common in pediatric cancer patients, and prealbumin is a reliable and sensitive indicator of mild and marginal malnutrition. Determining prealbumin values and assessing the deficiency of micro- and macronutrients before malnutrition is detected by anthropometric measures may provide a warning that nutritional problems may occur. *Key words: pediatric oncology, prealbumin, malnutrition.*

Increased metabolic rates associated with illness, malabsorption, mechanical gastrointestinal problems and cachexia caused by elevated levels of tumor necrosis factor may cause nutritional problems in pediatric cancer patients[1-3]. Nausea and vomiting associated with aggressive multimodal chemotherapy, and side effects of radiation therapy such as stomatitis, dysphagia, diarrhea and somnolence, may produce further nutritional deficits. Behavioral and environmental factors such as poor eating habits, decreased palatability of hospital food and noncompliance with dietary regimens may also contribute to poor nutrition[4]. Cancer itself may cause poor oral energy and protein intake. Therefore, pediatric cancer patients represent a high-risk group for protein energy malnutrition[5,6]. Malnutrition occurs more frequently in patients diagnosed with Ewing's sarcoma, Wilms' tumor, head and neck tumors, advanced lymphomas and neuroblastoma[7].

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Malnutrition decreases chemotherapy tolerance, increases the tendency for infections due to deterioration in cell-mediated immunity, and is associated with poor prognosis[1-4, 6]. Therefore, determination of the nutritional status of pediatric cancer patients and early detection of their nutritional problems is as important as the regulation of chemotherapy regimens. In patients in whom assessment of nutritional status has been studied, anthropometric variables (weight, height, weight for height, triceps skinfold thickness, midarm circumference) and biochemical indices (albumin, transferrin) have been measured[2, 8, 9]. These measurements, however, are not sensitive enough to detect mild or moderate protein-energy malnutrition[5]. In pediatric cancer patients, mild and marginal malnutrition must be identified to prevent the development of severe protein-energy malnutrition.

The aim of this study was to evaluate the nutritional status and determine the consumption of nutrients (oral intake of energy, protein and micronutrients) to identify mild or marginal malnutrition in pediatric cancer patients, and to compare the nutritional status and oral intake of patients with active disease to patients in remission.

Material and Methods

Forty-five patients (27 male and 18 female) followed at Ege University's Pediatric Oncology and Hematology Department participated in this study. The patient group consisted of 20 patients with leukemias, 13 with bone tumors and 12 with other solid tumors. Twenty-five of these children were in remission (remission group), and 20 were newly diagnosed or relapsed (active disease group). The mean age of the children in remission was 10.3 ± 5.2 years, and in the active disease group 10.7 ± 5.5 years (Table I). No significant difference in sex or age was found between the two groups.

Table I: Selected Characteristics of Pediatric Cancer Patients

Characteristics	Remission Group (n = 25)	Active Disease Group (n = 20)	Total (n = 45)
Age (years)	10.3 ± 5.2*	10.7 ± 5.5*	10.5 ± 5.4*
Sex			
Male	16 (64%)	11 (55%)	27 (60%)
Female	9 (36%)	9 (45%)	18 (40%)
Tumors			
Leukemia	13 (52%)	7 (35%)	20 (44%)
Bone tumors	7 (28%)	6 (30%)	13 (28%)
Other tumors	5 (20%)	7 (35%)	12 (16%)

* Values are mean ± SD. No significant age differences were found between groups.

Dietary intake history over three consecutive days, and daily energy, protein and micronutrient intake were calculated. Patients' daily energy and nutrient intake were evaluated according to 1989 Recommended Dietary Allowances (RDAs)[10].

Because the allowances for pediatric cancer patients are 15 percent greater than the allowances for healthy children, energy and protein intake in these patients was compared to the RDAs increased by 15 percent[6]. None of the patients in the study group received enteral or parenteral nutrition. Also, the percentage of patients consuming macro- and micronutrients below the recommended levels was evaluated.

Anthropometric measurements of all patients were determined by a clinician. Children were weighed once wearing a light gown and no shoes on an electronic scale to the nearest 100 g. Height was measured with a standard stadiometer in children older than two years and in the supine position to the nearest 0.1 cm in children less than two years of age.

Percentiles for weight and height were compared with the data of the 50th percentile of the National Center for Statistics (NCHS), and the nutritional status of patients was evaluated according to the weight-for-height index[11].

The weight-for-height index was calculated by dividing the observed weight by the expected weight of a child of the same height and sex at the same percentile. A weight-for-height index of less than 0.85 signified advanced malnutrition, an index of 0.85 to 0.90 signified moderate malnutrition, and an index of 0.90 to 0.95 signified mild malnutrition. A weight-for-height index of greater than 0.95 was indicative of normal nutritional status.

Two milliliters of venous blood was obtained from the patients. Serum urea, creatinine and albumin levels were measured by an autoanalyser (A. Menarini diagnostics), and prealbumin and transferrin levels were measured by immunonephelometry (Beckman Protein Array). Serum albumin levels less than 3.5 g/dl, and serum transferrin levels less than 200 mg/dl were considered as abnormal, as proposed in the literature[12]. Since prealbumin values vary with age and sex, observed values were converted to relative values as follows: observed prealbumin/expected prealbumin x 100[13]. Relative prealbumin values below 80 percent of expected levels were considered abnormal since this level corresponds to the mean -1 SD of the referenced values for age and sex. While prealbumin levels were measured, the axillary temperature of all children was determined to be less than 37 °C; infection was not detected in any children.

For the statistical evaluation, Student's t-test and fisher exact test were used.

Results

The oral protein and energy intake of children of various ages with cancer are shown in Table II. Children in all age-groups consumed half of the energy that was recommended. There was no significant difference in energy intake between the remission and active disease groups.

Table II: Daily Energy and Protein Intake in Pediatric Cancer Patients

Age Group (Years)	Daily Energy Intake (Kcal/day)			Daily Protein Intake (g/day)		
	Remission Group	Active Disease Group	Recommended*	Remission Group	Active Disease Group	Recommended*
1-3	765 ± 166	542 ± 23	1495	26.2 ± 4.8	15.3 ± 3.4	18.4
4-6	1219 ± 469	1108 ± 463	1920	42.2 ± 16.1	36.3 ± 8.0	27.6
7-10	1476 ± 301	1097 ± 710	2300	54.9 ± 9.9	36.3 ± 28.2	32.2
11-14 (male)	1537 ± 362.5	1439 ± 150	2875	51.6 ± 12.3	48.9 ± 5.2	51.8
11-14 (female)	1821 ± 131	1779 ± 100	2530	55.0 ± 1.0	30.3 ± 3.1	52.9
15-18 (male)	1571 ± 172	1330 ± 625	3600	48.4 ± 20.8	45.6 ± 25.3	67.9
15-18 (female)	1236 ± 124	1112 ± 220	2530	47.8 ± 3.6	39.9 ± 4.3	50.6

* Values are expressed as mean ± SD.
** Patients' daily energy and nutrient intakes were evaluated according to 1989 RDAs.

We found that children with cancer accepted protein much better than energy. Children in remission except those 15-18 years old consumed protein at proper levels. However, children over age 11 in the active disease group consumed protein below recommended levels.

The vitamin and mineral intake of patients is displayed in Tables III and IV. Patients in both the active disease and remission groups consumed vitamin A and B and minerals below recommended levels. We found that all patients consumed half of the recommended amounts of calcium, iron, zinc and copper, independent of the activity of disease (Table IV).

Table III: Daily Vitamin Intake in Pediatric Cancer Patients

Vitamins	1-3 Years	4-6 Years	7-10 Years	11-14 Years (M)	11-14 Years (F)	15-18 Years (M)	15-18 Years (F)
Vitamin A (IU/day)							
Remission group	1989 (95)	2467 (117)	3142 (82)	2606 (54)	4059 (84)	4405 (88)	3662 (73)
Active disease group	862 (41)	2036 (97)	1904 (50)	1832 (38)	3888 (80)	1239 (25)	2562 (51)
Thiamin (mg/day)							
Remission group	0.3 (43)	0.4 (44)	0.6 (60)	0.6 (46)	0.7 (64)	0.7 (47)	0.6 (55)
Active disease group	0.2 (29)	0.4 (44)	0.5 (50)	0.6 (46)	0.4 (36)	0.7 (47)	0.5 (45)
Riboflavin (mg/day)							
Remission group	0.7 (88)	0.9 (82)	1.0 (83)	0.8 (62)	1.4 (108)	0.9 (50)	0.7 (54)
Active disease group	0.4 (50)	0.5 (45)	0.9 (75)	1.3 (87)	0.6 (46)	0.9 (50)	0.7 (54)
Niacin (mg/day)							
Remission group	5.0 (56)	8.1 (68)	10.9 (84)	13.4 (89)	12.7 (85)	10.2 (51)	9.1 (61)
Active disease group	2.1 (23)	5.9 (49)	5.2 (40)	9.9 (66)	7.5 (50)	10.5 (53)	8.4 (56)
Vitamin C (mg/day)							
Remission group	35.7 (88)	41.5 (92)	41.1 (91)	127.7 (255)	185.3 (231)	95.2 (159)	70.5 (118)
Active disease group	24.7 (62)	20.9 (46)	87.5 (194)	53.4 (107)	49.9 (100)	94.6 (153)	64.5 (108)

The values in parenthesis show the percentage of the vitamin consumed according to 1989 RDAs.

Table IV: Daily Minerals Intake in Pediatric Cancer Patients

Minerals	1-3 Years	4-6 Years	7-10 Years	11-14 Years (M)	11-14 Years (F)	15-18 Years (M)	15-18 Years (F)
Calcium (mg/day)							
Remission group	346 (43)	496 (62)	489 (61)	557 (46)	746 (62)	528 (44)	427 (36)
Active disease group	238 (30)	161 (20)	513 (64)	359 (30)	254 (21)	374 (31)	315 (26)
Iron (mg/day)							
Remission group	3.9 (39)	5.6 (56)	7.4 (74)	6.3 (42)	9.4 (63)	8.4 (70)	8.0 (53)
Active disease group	2.5 (25)	5.8 (58)	4.7 (47)	9.9 (66)	9.3 (62)	9.1 (76)	5.4 (36)
Zinc (mg/day)							
Remission group	3.4 (34)	4.4 (44)	6.1 (61)	4.8 (40)	4.8 (40)	4.8 (32)	4.6 (38)
Active disease group	1.8 (18)	3.1 (31)	4.0 (40)	4.4 (37)	3.3 (28)	2.8 (19)	3.8 (32)
Copper (mg/day)							
Remission group	0.3 (33)	0.6 (46)	0.9 (60)	1.1 (55)	0.9 (45)	1.1 (55)	0.7 (35)
Active disease group	0.3 (33)	0.6 (46)	0.6 (40)	0.8 (67)	0.5 (28)	0.7 (35)	0.8 (40)

The values in parenthesis show the percentage of the mineral consumed according to 1989 RDAs.

Ninety-five percent of patients consumed energy and 35.5 percent consumed protein at less than recommended levels (Fig. 1). We showed that 51.1, 84.6, 53.4, 62.1 and 36.7 percent of patients consumed vitamin A, thiamin, riboflavin, niacin, and vitamin C, respectively, at less than RDA levels. Most of the patients consumed minerals at less than RDA levels. Calcium, iron and zinc were consumed at less than recommended levels by 88.2, 75.8 and 89.1 percent of patients, respectively. There was no significant difference in the consumption of vitamins and minerals between the remission and active disease groups.

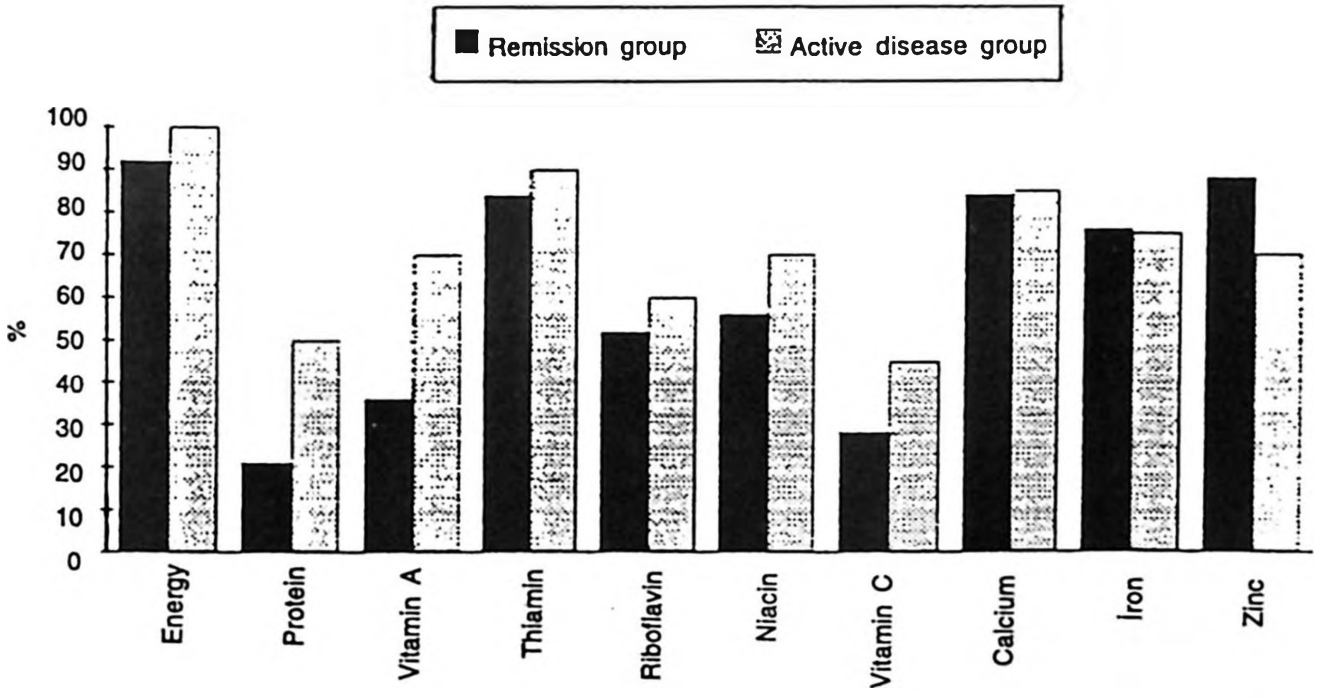

Fig. 1: The percentage of patients who consumed energy, protein, vitamins and minerals at lower than recommended levels in the remission and active disease groups.

Micro and macronutrients were consumed ineffectively by various tumor groups. No significant difference was found in the daily consumption of nutrients between groups.

The weight and height percentiles of our patients varied from the 3rd to the 97th percentile of NCHS growth charts. According to the weight-for-height index, 23 children (51.1%) were determined to be malnourished. Thirteen children (28.9%) displayed advanced malnutrition, five (11.1%) moderate malnutrition and five (11.1%) mild malnutrition. Twenty-two (48.9%) of these children had a normal nutritional status. Fifty-six percent of the children in remission were normal in nutritional status, whereas 44 percent of them had malnutrition (12% mild, 8% moderate, and 24% advanced). In the active disease group, 40 percent were normal in nutritional status, while 60 percent of them had malnutrition (10% mild, 15% moderate, and 35% advanced). The frequency of malnutrition in the active disease group was not significantly different from that of the remission group. Children with advanced malnutrition consumed 30 percent of the energy recommended, whereas children with mild malnutrition consumed 49.3 percent.

Children with malnutrition consumed significantly less energy and protein compared to children with normal nutritional status. However; the children with normal nutritional status according to anthropometric measurements consumed 52.7 percent of the energy recommended.

The biochemical measurements of pediatric cancer patients are summarized in Table V. Serum albumin levels of all children were greater than 3.5 g/dl. Serum albumin levels of patients in the active disease group were found to be significanty lower than those in the remission group ($p < 0.05$).

Table V: Biochemical Measurements in Pediatric Cancer Patients

Biochemical Measurements	Remission Group (n = 25)	Active Disease Group (n = 20)	Total (n = 45)
Creatinine (mg/dl)	0.6 ± 0.2	0.5 ± 0.1	0.5 ± 0.1
Albumin (g/dl)	4.7 ± 0.6	4.3 ± 0.6*	4.5 ± 0.6
Transferrin (mg/dl)	253 ± 87	255 ± 68	254 ± 78
Prealbumin (mg/dl)	19.4 ± 7.2*	14.8 ± 5.1*	16.8 ± 5.3
Relative prealbumin (%)	74.3 ± 29.1*	58.1 ± 23.3*	63.0 ± 19.9

Relative prealbumin = observed prealbumin/expected prealbumin x 100; excepted prealbumin values for age and sex are those of Bevegna et al.[13].

* The means of the active disease group were significantly different from those of the remission group for prealbumin and relative prealbumin according to Student's t test ($p < 0.05$).

Seventy-three percent of the patients in the study group had relative prealbumin values below 80 percent of the expected vlaues for age and sex. Relative prealbumin values were found to be low in 63.6 percent nonmalnourished children, 80 percent of those with mild malnutrition, 80 percent of those with

moderate malnutrition and 92.3 percent of patients with advanced malnutrition, according to the weight-height index (Fig. 2). Relative prealbumin values were significantly higher in patients who/had received prednisone (75.2 ± 28.1 mg/dl) compared to those who had not (65 ± 25.3 mg/dl).

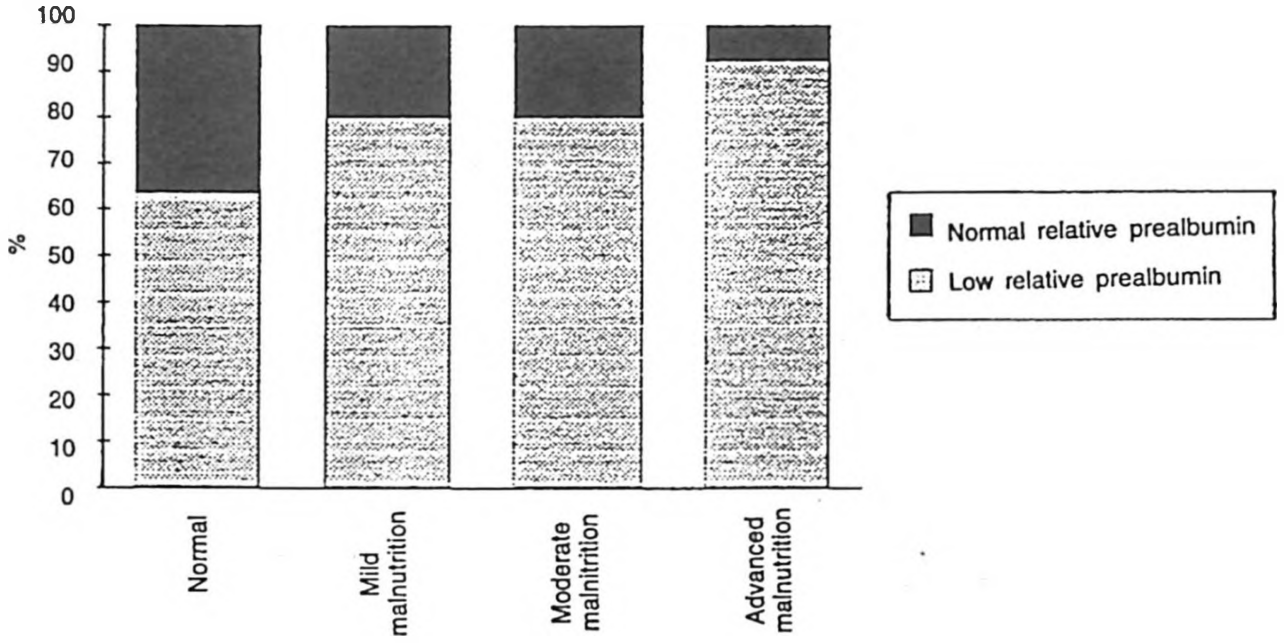

Fig. 2: The percentage of patients whose relative prealbumin values were less than 80 percent of the recommended values for age and sex.

Discussion

In developed countries it has been estimated that malnutrition is seen in eight to 32 percent of pediatric cancer patients[14]. In Turkey there are many problems related to educational status, traditional nutritional habits of families and environmental conditions. Therefore, malnutrition continues to be a major problem in Turkey, although its frequency is decreasing[15].

Especially with chronic diseases such as cancer, the risk of malnutrition is increasing. In this study, malnutrition according to the weight for height index was determined in 51.1 percent of pediatric cancer patients, a higher ratio than that in developed countries.

Malnutrition has been diagnosed by biochemical and anthropometric measurements in previous studies[2, 8, 9]. Some researchers have reported that weight-for-height ratios are the most reliable measurement of nutritional status in pediatric cancer patients, whereas others have suggested that these ratios may underestimate malnutrition[16-18]. Serum albumin levels of less than 3.2 mg/dl have also been identified as a threshold to warrant malnutritional intervention, although some studies report that low serum albumin levels may reflect an acute

metabolic response to fever and infection rather than true depletion of body mass[12]. Although in our study group malnutrition was common, as determined by weight-for-height ratios, serum albumin levels of patients were found to be normal. However, serum albumin levels were lower in the active disease group than in the remission group. These results suggested that albumin is not a reliable indicator in the early diagnosis of malnutrition in pediatric cancer patients, but may reflect acute metabolic response to active disease.

There is controversy about transferrin as an index of malnutrition. Some studies report transferrin as an index of malnutrition, while others state that it is not a reliable indicator[19,20]. Seventeen percent of our malnourished patients had low transferrin levels.

Prealbumin is considered to be a sensitive indicator of protein energy malnutrition, also reflecting short-term changes in nutritional status[19,21]. Changes in prealbumin levels are reported to occur at an earlier stage than changes in anthropometric measurements[19]. Yu et al.[5] reported that prealbumin was the most sensitive indicator of visceral protein status in leukemic patients. In our study group, 80 percent of patients with mild malnutrition had low relative prealbumin values, verifying that prealbumin is a reliable and sensitive indicator of mild and marginal malnutrition. According to anthropometric measurements, 69.6 percent of patients with normal nutritional status had low prealbumin values. This finding suggests that prealbumin may be found low before malnutrition is detected by anthropometric measurements, and low prealbumin values may indicate the need for nutritional intervention. Children in the active disease group had lower prealbumin values than children in the remission group, suggesting that the disease activity may affect the nutritional state of children with malignancy.

Prealbumin is affected by any inflammation or infection. In this study, prealbumin levels could not have been affected since infection was not observed in any of the patients.

It has been reported that prednisone increases the hepatic synthesis of prealbumin and diminishes its fractional metabolism, thus increasing prealbumin levels[22]. However, Yu et al.[5] found that serum prealbumin levels in children with leukemia receiving prednisone were higher than in patients not receiving prednisone, and suggested that increased prealbumin levels were due to better caloric and protein intake, since prednisone usually improves appetite. We also observed that prealbumin levels in children receiving prednisone were significantly higher than in those not receiving.

Nutritional support after malnutrition has occurred is often insufficient, as it is usually difficult to correct the deficiency. Therefore, it is important to prevent malnutrition before it occurs. We observed that patients with normal nutritional

status consumed only 52.7 percent of the recommended energy. This observation suggests that nutritional deficiency occurred in our patients before malnutrition was detected by anthropometric measures. Determining prealbumin values and assessing the deficiency of micro-and macronutrients before malnutrition is detected by anthropometric measures, may give a warning that nutritional problems are likely, allowing earlier nutritional intervention in pediatric cancer patients.

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