Türk Pediatri Arşivi
Turkish Archives of Pediatrics

Original Article / Özgün Araştırma

Nutritional assessment of children with Wilson's disease: single center experience

Wilson hastalıklı çocukların nütrisyonel değerlendirmesi: tek merkez deneyimi

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Cite this article as: Güngör Ş, Selimoğlu MA, Varol Fİ. Nutritional assessment of children with Wilson's disease: single center experience. Turk Pediatri Ars 2019; 54(4): 246–55.

Abstract

Aim: Nutritional status was accepted as a prognostic marker in children with chronic liver disease. In the literature, we aimed to retrospectively investigate 94 Wilson patients followed in our center due to the lack of studies investigating the frequency and prognostic effects of malnutrition and micronutrient deficiency in Wilson's patient.

Material and Methods: Our studies included 94 Wilson's disease children in the Department of Child Gastroenterology, Hepatology and Nutrition of Inonu University Medicine between 2006–2017. Presentation patterns, anthropometric measurements, laboratory findings and prognostic factors of these patients were analyzed retrospectively.

Results: The mean age of the patients was 9.11±3.2 (3.5–17) and the female/male ratio was 40/54. Mean age was lower in asymptomatic patients (p=0.000). According to all parameters, malnutrition was detected in 43 patients (45.7%). Fulminant Wilson's disease had higher height and weight z scores than nerowilson patients (p=0.045, p=0.019, respectively). Hypocalcemia, hypophosphatemia, hypouricemia, hypoalbuminemia and anemia were more common than cholestasis patients (p<0.001). Vitamin A and E are lower in patients cholestasis than non-cholestasis patients (p<0.05). Hypocalcemia, hypophosphatemia and hypo-uricemia were found higher in the fulminant group (p<0.001). According to mortality scores (Dhawan, Model for end-stage liver disease and Child-Pugh). In patients with high mortality, height Z score was found to be high (p<0.05).

Conclusion: In Wilson's disease assessment of growth, detailed anthropometric measurements as well as vitamin, trace elements and electrolytes should be closely monitored.

Keywords: Child, nutrition, Wilson's disease

Öz

Amaç: Beslenme durumu, kronik karaciğer hastalığı olan çocuklarda prognostik bir belirteç olarak kabul edilmiştir. Dizinde, Wilson hastalarında yetersiz beslenme ve mikro besin eksikliğinin sıklığı ve prognostik etkilerini araştıran çalışmaların eksikliği nedeniyle merkezimizde izlenen 94 Wilson hastasını geriye dönük olarak incelemeyi amaçladık.

Gereç ve Yöntemler: Çalışmamıza 2006–2017 yılları arasında İnönü Üniversitesi Tıp Fakültesi Çocuk Gastroenteroloji, Hepatoloji ve Beslenme bölümünde 94 Wilson hastalıklı çocuk alındı. Bu hastaların nutrisyonel durumunu değerlendirebilmek için, başvuru şekilleri, antropometrik ölçümleri, laboratuvar bulguları, prognostik etmenleri geriye dönük olarak incelendi.

Bulgular: Hastalar demografik özelliklerine göre değerlendirildiğinde yaş ortalaması: 9,11±3,2 (3,5–17) ve kız/erkek oranı 40/54 idi. Yaş ortalaması asemptomatik hastalarda semptomatik olanlardan anlamlı olarak düşük bulundu (p<0,001). Hastalarda tüm değişkenler birlikte değerlendirildiğinde 43 hastada (%45,7) malnütrisyon saptandı. Fulminan Wilson hastalarında nörowilson hastalarına göre boy ve kilo Z skorlarında istatiksel olarak anlamlı yükseklik vardı. (sırasıyla, p=0,045, p=0,019) Hipokalsemi, hipofosfatemi, hipoürisemi, hipoalbuminemi ve anemi kolestazlı hastalarda kolestazı olmayanlara oranla istatiksel olarak daha sık görüldü (p=<0,001). Vitamin A, E kolestazı olanlarda olmayanlara kıyasla daha düşüktü (p<0,05). Hipokalsemi, hipofosfatemi ve hipoürisemi fulminan grupta daha yüksek oranda saptandı (p<0,001). Mortalite skorlarına göre bakıldığında (Dhawan, model for end-stage liver disease ve Child-Pugh); Mortalitesi yüksek olan hastalarda, boy Z skoru yüksek bulundu (p<0.05).

Çıkarımlar: Wilson hastalığında büyümenin değerlendirilmesinde ayrıntılı antropometrik ölçümlerin yanında vitamin, eser elementler ve elektrolitlerin de yakından izlenmesi gerekmektedir..

Anahtar sözcükler: Beslenme, çocuk, Wilson's hastalığı

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Received / Geliş Tarihi: 08.09.2018 **Accepted / Kabul Tarihi:** 03.07.2019

DOI: 10.14744/TurkPediatriArs.2019.42402

Introduction

Nutritional status is considered a prognostic marker in children with chronic liver disease and one of the variables of the Pediatric End-stage Liver Disease (PELD) scoring system. The influence of chronic liver disease (CLD) on nutritional status depends on the age of onset, cause, and severity of liver disease. There is a two-way interaction between nutritional status and CLD. Chronic liver disease frequently causes malnutrition, and malnutrition influences the prognosis of liver disease negatively (1). In these children, nutritional support increases quality of life and posttransplant survival, and prevents serious complications including rachitis, severe muscle loss, and hemorrhagic disease. The evaluation of nutritional status and intervention is required even in children who do not have end-stage liver disease in order to prevent complications such as osteopenia and micronutrient deficiency (1–3).

Wilson's disease (WD) has very different findings ranging from the asymptomatic form, which is detected by screening, to a picture of end-stage-liver disease, and variable prognosis. Although the literature contains studies that examined nutritional status in children with CLD, to the best of our knowledge, no studies have investigated the frequency of malnutrition and its prognostic impact in WD, which is one of the metabolic causes of CLD. Therefore, we aimed to examine nutritional status and the effect of malnutrition on prognosis in 94 children with WD who were being followed up in our center.

Material and Methods

Ninety-four children with WD who were diagnosed with a score of four or above according to the Leipzig (2001) diagnostic scoring system in Inönü University Turgut Özal Medical Center Division of Pediatric Gastroenterology, Hepatology and Nutrition between 2006 and 2017, were included in our study. Genetic analysis for WD could not be performed between 2006 and 2017 in our hospital; therefore, the patients were diagnosed considering other findings (decreased serum ceruloplasmin level (0.1–0.2 g/L or <0.1 g/L), increased 24-hour urine copper (≥2-fold the upper limit of normal or >5-fold the upper limit of normal following D-penicillamine), presence of Kayser-Fleischer ring, increased hepatic dry copper weight (>250 mg (>4 mmol)/g dry weight), neurologic symptoms, presence of Coombs-negative hemolytic anemia) (4). The patients were classified in four different groups according to their signs and symptoms at presentation (4–7).

Asymptomatic WD: The patients in this group were asymptomatic. They were detected as a result of family screening or investigated because of asymptomatic transaminasemia and subsequently diagnosed as having WD.

Chronic WD: The patients in this group were being followed up because of WD and had findings of chronic liver failure [decreased albumin, increased international normalized ratio (INR), ascites, esophageal varices, advanced stage fibrosis and cirrhotic changes on liver biopsy)].

Fulminant WD: The children in this group were defined according to the Acute Liver Failure Study Group (8–10) criteria: (1) Children who did not have findings of CLD; (2) Biochemical evidence of acute liver injury; (3) Coagulopathy originating from liver disease (prothrombin time (PT) ≥15 s or INR ≥1.5 in the presence of clinical encephalopathy that was unresponsive to vitamin K, or PT ≥20 s or INR ≥2 that was unresponsive to vitamin K in the presence or absence of clinical encephalopathy).

Neurologic Wilson's disease: The WD group that is manifested by neurologic symptoms and signs.

Body weight and height measurements of the patients were screened from patient files in order to evaluate nutritional status. The body weight Z score, height Z score, weight for height (WFH) Z score, and body mass index (BMI) Z score were calculated using the World Health Organization (WHO) data. Patients who had a weight Z score, height Z score, and weight for height (WFH)-BMI Z score below -2 were considered to have low weight, chronic malnutrition (short stature), and acute malnutrition, respectively. Patients whose Z scores were below -2 for any of the following variables were considered to have malnutrition: body weight, height, WFH, and BMI. Patients who had a BMI Z score of >2 were considered overweight/obese.

Patients whose weight for age values were below 90% and who had no edema were considered to have malnutrition. Patients with a weight for age value between 89% and 75% were considered to have mild malnutrition, patients with a weight for age value between 74% and 60% were considered to have moderate malnutrition, and those with a weight for age value of <60% were considered to have severe malnutrition.

Among biochemical variables, albumin, vitamin A, vitamin E, vitamin D, calcium (Ca) and phosphorus (P) values were screened.

A corrected serum total calcium level of <9 mg/dL or <2.12 mmol/L was considered as hypokalemia, a P level of <2.5 mg/dL (0.8 mmol/L) was considered as hypophos-

phatemia, a serum magnesium concentration of <0.66 mmol/L (1.6 mg/dL) was considered as hypomagnesemia, a serum uric acid concentration of <2.0 mg/dL was considered as hypouricemia, a serum albumin level of <35 g/L or 3.5 mg/dL was considered as hypoalbuminemia, a serum retinol concentration of <0.70 μmol/L was considered as vitamin A deficiency, a serum 25-hydroxyvitamin D (25 (OH) D) level below 20 ng/mL (50 nmol/L) was considered as vitamin D deficiency, a plasma vitamin E (α-tocopherol) level of <5 μg/mL (11 μmol/L) was considered as vitamin E deficiency, and a folic acid level of <4 ng/mL was considered folic acid deficiency (11–19).

Prognostic evaluation was made according to the pediatric end-stage liver disease (PELD) model for end-stage liver disease (MELD), Child-Pugh (CHILD), and Dhawan scores. However, PELD scores were calculated for all patients aged ≤12 years, whereas MELD scores was calculated for patients aged >12 years (20–22). Our study was designed in accordance with the principles of the Declaration of Helsinki. Institutional ethics committee approval was obtained for our study (2017 Ethics committee number: 22-2).

Informed consent was not obtained from the patients because our study was a retrospective file screening study.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago) 16.0 package program. For the comparison of continuous variables, the data are expressed as mean±standard deviation because we used parametric tests. Categorical variables are expressed as median (n) and percentage (%). The Kolmogorov- Smirnov test was used to examine if the numerical variables showed normal distribution. Student's t-test or analysis of variance (ANOVA) was used for parameters that showed normal distribution. The Mann-Whitney U test or Kruskal-Wallis test was used for parameters that did not show normal distribution. The Chi-square test, Student's t-test or Mann-Whitney U test were used as a statistical significance test. A p value of <0.05 was considered statistically significant.

Results

When the patients were evaluated by demographic properties, it was found that the mean age was 9.11±3.2 (range, 3.5–17) years, and the female/male ratio was 40/54. The mean age was found to be significantly lower among patients who were asymptomatic compared with the other types of presentation (p<0.001). Fourteen (41.1%) of these patients were detected during family screening (Table 1). Jaundice (51%) was the most common symptom, and hepatomegaly (57%) and splenomegaly (52%) were the most common physical examination findings. The rates of jaundice, hepatomegaly, splenomegaly, and ascites were found to be significantly higher in patients who had fulminant and chronic WD compared with the other types of presentation (p<0.001). Four (6.7%) patients had a body weight Z score below -2 standard deviations (SDS), four patients (4.4%) had a body weight Z score above 2 SDS, and 80 (88.9%) patients had a normal body weight Z score. Seven (7.9%) patients had a height Z score below -2 SDS, three (3.4%) patients had a height Z score above 2 SDS, and 79 (88.8%) patients had a normal height SDS. Ten (11.2%) patients had a BMI Z score below -2 SDS, eight (9%) patients had a BMI Z score above 2SDS, and 71 (79.8%) patients had a normal BMI Z score. When the patients were evaluated by WFH Z scores, it was found that three (3.2%) patients had a WFZ Z score below -2 SDS, three (3.2%) patients had a WFH Z score above 2 SDS, and 83 (88.3%) patients had a normal WFH Z score. When the patients were evaluated by weight for age percentages, it was found that 22 (23.4%) patients had nutritional deficiency, 33 (35.3%) patients had mild malnutrition, and nine (9.6%) patients had moderate malnutrition. None of the patients had severe malnutrition. When all variables were evaluated together, 43 (45.7%) patients were found to have malnutrition (Table 1).

Sixty-two (66%) patients had at least one factor (hepatomegaly, splenomegaly, hepatosplenomegaly, ascites) that could influence the parameter of body weight. When the body weight, height, WFH, and BMI Z scores were compared between patients who did and did not have at least one of these factors, no statistically significant difference was found (p=0.144, p=0.146, p=0.353, p=0.173, respectively).

No statistically significant difference was found between the groups in terms of mean BMI and WFH Z scores by presentation type (p=0.34, p=0.159, respectively). The height and weight Z scores were statistically significantly higher in the fulminant WD group compared with patients with neurologic WD (p=0.045, p=0.019, respectively) (Table 2). When the patients were evaluated by presentation type and presence of malnutrition, it was found that severe malnutrition was not present in any patients. Thirty-three (35.1%) patients had mild and moderate malnutrition. Fifty-two (55.3%) patients did not have malnutrition. When these values were evaluated using the Chi-square test, it was found to be statistically significant (p=0.014). When the patients who did and did not have malnutrition were evaluated after treatment by presentation type, no

Table 1. Evaluation of nutritional parameters as laboratory tests according to presentation type

	Asymptomatic (34)	Acute-fulminant (24)	Chronic (25)	Neurologic WD (11)	Total (94)	p
	Median±SDS	Median±SDS	Median±SDS	Median±SDS	Median±SDS	
Age (mean)	7.66±3.24α	8.64±2.70	10.58±3.13β	11.27±1.55β	9.11±3.20	<0.001
Serum copper level	24.12±20.31y	126.75±80.68x	45.28±32.99y	38.25±22.60y	62.11±63.77	0.002
24-hour copper level	380.72±403.20y	1691.58±1589.98x	800±1000.89y	562.36±334.78y	854.35±1114.24	<0.001
	n–%	n–%	n–%	n–%	n–%	
Sex (F/M)	12–35.3 22–64.7	13–54.2 11–45.8	10–40 15–60	5–45.5 6–54.5	40–42.5 54–57.5	0.540
Low weight	1–3	1–4.1	3–12	1–9	6–6.4	0.646
Normal weight	31–91.1	21–87.5	19–76	9–81	80–85	0.646
Overweight	1–3	1–4.1	2–8	0	4–4.2	0.676
Short stature	3–9	1–4.1	1–4	2–18	7–7.4	0.770
Normal height	29–85.2	20–83	22–88	8–72.7	79–84	0.787
Tall	1–3	1–4.1	1–4	0	3–3.2	0.810
Malnutrition	12–35.3	9–37.5	13–52	8–72.7	42–44.7	0.168
Mild malnutrition	12–35.3	8–33.3	9–36	4–36.4	33–35.1	0.039
Moderate malnutrition	0	1–4.2	4–16	4–36.4	9–9.6	0.039
Nutritional deficiency	4–11.8α	3–12.5α	8–32	7–63.6β	22–23.4	0.002
Vit A deficiency	4/14–28.6	1/2–50	5/9–55.6	0	10/25–40	0.180
Vit E deficiency	0/14–0	1/2–50	2/9–22.2	0/5–0	3/10–30	0.067
Vit D deficiency	7/22–31.8	1/5–20	6/13–46.2	3/9–33.3	17/49–34.7	0.725
Folate deficiency	1/19–5.3	1/2–50	0/11–0	0/8–0	2/41–4.9	0.102
Hypocalcemia	0β	16/24–66.7α	9/25–36α	1/11–9.β	26/94–27.7	<0.001
Hypophosphatemia	1/34–2.9β	15/24–62.5α	7/25–28α	0β	23/94–24.5	<0.001
Hypomagnesemia	0/15–0	3/24–12.5	1/25–4	1/2–50	5/66–7.6	0.104
Hypomagnasemia	6/28–21.4β	24/24–100α	19/25–76β	5/9–55.6β	54/86–62.8	<0.001
Hypoalbuminemia	6/32–18.8β	22/23–95.7α	17/25–68α	2/10–20β	47/90–52.2	<0.001
Low BUN	3/32–9.4	5/24–20.8	8/25–32	1/10–10	17/91–18.7	0.150

There is statistically significant difference between α and β values (Crosstab-Chi-square test= P:<0.05). There is statistically significant difference between x and y values (ANOVA-post hoc test-Turkey test). WD: Wilson's disease; SDS: Standard deviation score; F: Female; M: Male; BUN: Blood urea nitrogen

statistically significant difference was found between the groups (p=0.605) (Table 2).

Forty-six (48.9%) patients had cholestasis and 48 (51.1%) patients did not have cholestasis. The body weight, height, and BMI Z scores were found to be significantly higher in patients with cholestasis compared with those without cholestasis (p=0.006, p=0.005, p=0.020, respectively). In conjunction with this condition, organomegaly and ascites were found with a statistically significant higher rate in the patients with cholestasis compared with those without cholestasis, as expected (p<0.001). The levels of vitamin A and vitamin D were lower in patients with cholestasis compared with those without cholestasis (p=0.028, p=0.030, respectively). No significant difference was found between the two groups in terms of vitamin D and folic acid levels (p=0.894, p=0.628, respectively). Hypocalcemia, hypophosphatemia, hypouricemia, hypoalbuminemia, and anemia were observed with a statistically significantly higher frequency in patients with cholestasis compared with those without cholestasis (p<0.001) (Table 3).

When we evaluated the relationship between the patients' anthropometric values and prognostic scores, we found that 58 (61.7%) patients had a PELD score of >10 and 36 (48.3%) patients had a PELD score of <10. There was no statistically significant difference between patients who had PELD scores of >10 and patients who had PELD scores of >10 in terms of anthropometric measurements (Table 4).

Table 2. Evaluation of nutritional status before and after treatment by presentation type

	Asymptomatic (34)	Acute-fulminant (24)	Chronic (25)	Neurologic WD (11)	Total (94)	p
	Median±SDS	Median±SDS	Median±SDS	Median±SDS	Median±SDS	
Before treatment						
Weight Z score	-0.205±1.09	0.200±1.24α	-0.176±1.42	-1.259±0.64β	-0.211±1.24	0.019
Height Z score	-0.233±1.16	0.330±1.08α	-0.241±1.48	-0.988±0.93β	-0.181±1.25	0.045
BMI Z score	-0.137±1.40	0.348±1.31	0.091±1.61	-0.572±1.08	-0.004±1.41	0.340
WFH Z score	0.055±1.09	-0.026±0.92	0.192±1.10	-0.672±0.66	-0.009±1.03	0.159
	n–%	n–%	n–%	n–%	n–%	
No malnutrition	22–64.7	15–62.5	12–48	3–27.3	52–55.3	
Mild malnutrition	12–35.3	8–33.3	9–36	4–36.4	33–35.1	0.014*
Moderate malnutrition	0	1–4.2	4–16	4–36.4	9–9.6	
	Asymptomatic (22)	Acute-fulminant (9)	Chronic (17)	Neurologic WD (9)	Total (57)	p
	Median±SDS	Median±SDS	Median±SDS	Median±SDS	Median±SDS	
One year after treatment						
Weight Z score	-0.441±0.88	0.300±1.11	-0.292±1.14	-0.789±0.84	-0.429±0.98	0.551
Height Z score	-0.811±1.12	-0.600±1.30	-0.423±1.13	-0.955±1.28	-0.685±1.16	0.525
BMI Z score	-0.007±1.01	-0.104±1.47	0.278±1.19	-0.866±1.19	0.200±1.18	0.267
WFH Z score	0.189±0.59	0.155±1.05	0.121±0.72	0.476±0.81	0.058±0.77	0.871
	n–%	n–%	n–%	n–%	n–%	
No malnutrition	14–63.6	6–66.7	8–47.1	4–44.4	32–56.1	
Mild malnutrition	6–27.3	1–11.1	6–35.3	2–22.2	15–26.3	0.605*
Moderate malnutrition	2–9	2–22.2	3–17.6	3–33.3	10–17.5	

The difference between α and β values is statistically significant (p<0.05 (one-way ANOVA). *Crosstab-Chi-square test was used. A p value of <0.05 was considered significant. WD: Wilson's disease; SDS: Standard deviation score; BMI: Body mass index; WFH: Weight for height

When the patients were evaluated by Dhawan mortality scores, it was found that 42 (44.7%) patients had a Dhawan score of >10 and 52 (55.3%) patients had a Dhawan score of <10. The body weight, height, and BMI Z scores were found to be statistically significantly higher in patients who had a score of >10 (p=0.001, p=0.004, p=0.025, respectively). There was no significant difference in terms of weight for height Z score (p=0.603) (Table 4).

When the patients were evaluated by MELD scores, it was found the 48 (51%) patients had a MELD score of >19 and 46 (49%) patients had a MELD score of <19. The height Z score was found to be statistically significantly higher in patients who had MELD scores of >19 compared with those who had lower scores (p=0.009). There was no significant difference in terms of weight, MI, and WFH Z scores between the groups (p=0.053, p=0.504, p=0.980, respectively) (Table 4).

When the patients were evaluated by Child-Pugh scores (CHILD), it was found that 42 (44.7%) patients were in the CHILD A group, 13 (13.8%) patients were in the CHILD B group, and 39 (41.5%) patients were in the CHILD C group. The height, weight, and BMI Z scores were significantly higher in the CHILD C group compared with the CHILD A group (p=0.041, p=0.036, p=0.041, respectively). There was no statistically significant difference between the CHILD groups in terms of WFH Z scores (Table 4).

In all mortality scores, we observed that the rates of the factors including organomegaly and ascites, which influence measurements of body weight, also increased as the score increased (p<0.001) (Table 4).

When the patients were evaluated by laboratory measurements, it was found that the levels of Ca, P, and albumin were significantly lower in patients who presented with fulminant WD compared with patients with other types of presentation (p<0.001) (Table 2).

Table 3. Evaluation of nutritional status in patients with Wilson's disease who had cholestasis

	Cholestasis absent	Cholestasis present	Total	p
	Median±SDS	Median±SDS	Median±SDS	
Weight Z score	-0.589±1.00	0.119±1.35	-0.211±1.24	0.006
Height Z score	-0.538±1.06	0.200±1.34	-0.181±1.25	0.005
BMI Z score	-0.341±1.31	0.355±1.45	-0.009±1.03	0.020
WFH Z score	-0.065±1.11	0.050±0.95	-0.004±1.41	0.599
	n–%	n–%	n–%	
Malnutrition	24–52.2	17–38.6	41–45.6	0.197
Mild malnutrition	19–41.3	12–27.9	31–34.8	0.563
Moderate malnutrition	4–8.7	4–9.3	8–9	0.694
Nutritional deficiency	11–23.9	8–18.2	19–21.1	0.505
Hepatomegaly	15–31.3	39–84.8	54 –57.4	<0.001
Splenomegaly	10–20.8	39–84.8	49–52.1	<0.001
Hepatosplenomegaly	6–12.5	36–78.3	42–44.7	<0.001
Ascites	2–4.2	32–69.6	34–36.2	<0.001
Vit A deficiency	4–20	6–60	10/30–33.3	0.028
Vit E deficiency	0	3–30	3/30–10	0.030
Vit D deficiency	12–35.3	5–33.3	17/49–34.7	0.894
Folate deficiency	1–3.7	1–7.1	2/41–4.9	0.628
Anemia	11–24.4	32–69.6	43–47.3	<0.001
Hypocalcemia	1–2.1	26–56.5	27/94–28.8	<0.001
Hypophosphatemia	1–2.1	22–47.8	23/94–24.5	<0.001
Hypomagnesemia	1–5	4–8.7	5/66–6	0.602
Hypouricemia	11–26.8	43–95.6	54/86–62.8	<0.001
Hypoalbuminemia	7–15.6	40–88.9	47/90–52.2	<0.001
Low BUN	5–11	12–26	17/91–18.7	0.067

SDS: Standard deviation score; BMI: Body mass index; WFH: Weight for height; BUN: Blood urea nitrogen

The level of vitamin A was measured in 25 of patients. Vitamin A level was low in 10 (40%) of these patients and there was no significant difference by presentation type (p=0.180). The level of vitamin E was measured in 10 patients and it was found to be low in three (30%). The level of vitamin D was found to be low in 17 of 40 patients (34.7%), but there was no significant difference between the different presentation types (p=0.725). The level of folic acid was found to be low in 2 of 41 patients (4.9%) (Table 1).

When vitamin levels were evaluated in patients who did and did not have malnutrition, no significant difference was found between the two groups in terms of vitamin A, vitamin E, vitamin D, and folic acid levels (p=0.496, p=0.475, p=0.946, p=0.707, respectively). There was no significant difference between the groups that did and did not have malnutrition in terms of aspartate transaminase (AST), alanine transaminase (ALT), and serum albumin levels (p=0.533, p=0.545, p=0.244, respectively). Hypocalcemia, hypophosphatemia, hypouricemia, and hypoalbuminemia were found with a significantly higher rate in patients who had cholestasis and in the fulminant group compared with the other presentation types (p<0.001) (Table 1, 3).

The anthropometric measurements before treatment and one year after treatment were compared in 57 patients; it was found that the weight, WFH, and BMI Z scores did not change statistically significantly over time (p=0.336, p=0.669, p=0.387, respectively). However, the mean height Z score before treatment was found to be statistically significantly higher compared with the mean height Z score after treatment (p=0.016) (Table 2).

Discussion

The cause of malnutrition is multifactorial in patients with CLD. In children, insufficient energy intake is present in more than 70% of patients. In addition, vomiting, loss of

Table 4. Effect of growth on mortality in patients with Wilson's disease

	Dhawan		
	<10	>10	
	Median±SDS	Median±SDS	p
Weight Z score	-0.605±1.085	0.226±1.290	0.001
Height Z score	-0.512±1.127	0.268±1.303	0.004
BMI Z score	-0.302±1.362	0.384±1.419	0.025
WFH Z score	-0.098±1.153	0.116±0.859	0.318
	PELD		
	<10	>10	
	Median±SDS	Median±SDS	P
Weight Z score	-0.570±0.979	-0.123±1.223	0.090
Height Z score	-0.405±1.189	-0.122±1.294	0.333
BMI Z score	-0.074±1.488	-0.060±1.291	0.965
WFH Z score	-0.109±0.703	-0.016±1.015	0.656
	MELD		
	<19	>19	
	Median±SDS	Median±SDS	P
Weight Z score	-0.474±1.049	0.0663±1.4178	0.053
Height Z score	-0.554±1.129	0.2±1.34008	0.009
BMI Z score	-0.019±1.388	0.1954±1.45601	0.504
WFH Z score	0.048±1.117	0.043±0.95677	0.980
	Child Score		
	Class A	Class B	Class C	
	Median±SDS	Median±SDS	Median±SDS	P
Weight Z score	-0.604±1.054β	0.002±1.025	0.09±1.400α	0.036
Height Z score	-0.536±1.115β	-0.008±1.252	0.167±1.342α	0.041
BMI Z score	-0.371±1.327β	0.807±1.419α	0.220±1.455	0.041
WFH Z score	-0.046±1.162	-0.122±1.181	0.116±0.818	0.723

The difference between α and β vaues is statistically significant (p:<0.05 (İndependent samples T test and One-Way ANOVA). SDS: Standard deviation score; WFH: Weight for height; BMI: Body mass index; Child: Child-Pugh score; MELD: Model for end-stage liver disease score; PELD: Pediatric end-stage liver disease score

appetite, mucosal congestion, decreased intestinal motility, and early satiety due to ascites and organomegaly are observed. Dieting because of various causes also decreases intake (23). Absorption of long-chain fatty acids is disrupted because of impairment in excretion of bile acids (24).

In a study conducted by Da Silva et al. (25) that included patients with cholestasis, it was shown that WFA and WFH Z scores were below -2 SDS in one-third of the patients. When WFH was considered, only 12.1% of the patients had a Z score below -2 SDS. When evaluated by BMI, 16.5% of the patients had a Z score below -2 SDS. It was shown that malnutrition was present in 43.9% and 46.2% of the patients according to mid-upper arm circumference and triceps skinfold thickness, respectively, and the rate was higher with these methods (8). In our study, the rates of low weight and short stature were found as 6.7% and 7.9%, respectively. Ten (11.2%) patients had a BMI Z score below -2 SDS and three (3.2%) patents had a WFH Z score below -2 SDS. When the parameters of body weight, height, WFH, and BMI Z scores were evaluated together, it was found that 42 (44.7%) patients had malnutrition (positivity of one of these parameters was considered in favor of malnutrition). When evaluated by presentation type, it was found that the weight and height Z scores were significantly lower in patients with neurologic WD compared with fulminant WD (p=0.019, p=0.045, respectively). The weight, height, and WFH Z scores were higher in patients who had organomegaly or ascites compared

with those without organomegaly or ascites. Although the influence of weight could be easily interpreted, the fact that the mean height was also high was interpreted such that height was not influenced as much in WD.

In children with CLD, organomegaly, ascites, and peripheral edema limit the reliability of body weight, which is the most important indicators for the evaluation of nutrition. Therefore, data including triceps skinfold thickness and mid-upper arm circumference, which are not influenced by the above-mentioned factors, are required in addition to a meticulous physical examination and classic anthropometric measurements (25, 26). The most important limitation and deficient aspect of our study was the fact that these parameters, which are more reliable, could not be obtained because it was a retrospective study. There was at least one factor that could influence body weight measurement in 62 (66%) of 94 subjects.

In a study conducted in Brazil with 22 children and adolescents with cholestasis, it was shown that malnutrition was present in 23.8% and 33.3%, respectively, according to WFA and HFA criteria, but the WFH value was not below -2 Z score in any patients (27). In our study, there were 44 children with cholestasis and the weight Z score was below -2 SDS in four (9%) of these patients, the height Z score was below -2 SDS in two (4.5%), the BMI Z score was below -2 SDS in three (6.8%), and the WFH Z score was below -2 SDS in only one (2.2%) patient.

In a study that evaluated protein energy malnutrition, the nature of biochemical abnormalities related with this and the relationship of these with each other using the body composition and laboratory data of 27 children who had end-stage liver failure (10), the height, weight, and head circumference values were unsurprisingly found to be significantly lower compared with their peers. However, no correlation was found between the severity of malnutrition and the degree of cholestasis, synthetic function of the liver, hepatic injury, and vitamin or mineral deficiencies. In our study, the rates of organomegaly and ascites were high in patients with cholestasis, as expected ($p<0.001$) because a small portion of these patients had fulminant liver disease and most had decompensated liver disease. Therefore, their weight, height, and BMI Z scores were higher compared with patients without cholestasis (Table 3). In contrast, the levels of vitamin A and E were lower in patients who had cholestasis compared with those without cholestasis ($p=0.028$, $p=0.030$, respectively). Hypocalcemia, hypophosphatemia, hypouricemia, hypoalbuminemia, and anemia were observed with a statistically significantly higher frequency in patients who had cholestasis compared with those without cholestasis ($p<0.001$). This shows that laboratory measurements indicating nutritional deficiency will support malnutrition, though the height and weight Z scores are influenced by the picture of organomegaly and ascites.

When the patients were evaluated by presentation type, the levels of P, Ca, and albumin were found to be significantly lower in fulminant WD compared with the other presentation types. Again, Widodo et al. (2) found that the AST, ALT, and interestingly, serum albumin levels were statistically significantly higher in patients who had malnutrition compared with those without malnutrition in a study conducted with 21 patients who had CLF. In our study, no significant difference was found between the groups who did and did not have malnutrition in terms of AST, ALT, and serum albumin levels ($p=0.533$, $p=0.545$, and $p=0.244$, respectively). These observations may suggest that there is no full correlation between hepatic dysfunction and the degree of malnutrition, and it may be possible to eliminate deficiencies by increasing body stores and micronutrient intake despite hepatic dysfunction. On the other hand, the fact that more sensitive measurements were not used in the diagnosis of malnutrition may be the reason for the results obtained both in our study and in the above-mentioned study.

It is thought that nutritional deficiency increases mortality following liver transplantation (1, 28). However, Zemberlan et al. (29) showed that there was no correlation between nutritional status and mortality following transplantation in 60 children and adolescents. Figueiredo et al. (30) investigated the effects of nutritional status on outcomes following liver transplantation and concluded that none of the nutritional measurements (BMI, anthropometry, subjective global evaluation) was correlated with increased mortality risk. In our study, no significant correlation was found between malnutrition and mortality according to PELD mortality scores, whereas mortality scores were observed to increase significantly as the body weight, height, and BMI Z scores increased according to the Dhawan score, as the height Z score increased according to the MELD Z scores, and as the height and BMI Z scores increased according to the CHILD classification (Table 4). This arises from the fact that the patients who had high mortality scores carried a least one of the risk factors influencing weight measurement including organomegaly and ascites with a higher frequency. However, the relationship of mortality score with height could not be interpreted.

In conclusion, vitamins, trace elements, and electrolytes should be monitored closely in addition to detailed anthropometric measurements in the assessment of growth in WD. Nutritional risk should be emphasized in patients

with neurologic WD specifically, in addition to the negative nutritional effects of CLD in those with WD.

Ethics Committee Approval: Ethics committee approval was obtained before starting the study. Date of Ethics Committee: 2017 Number of Ethics Committee: 22-2

Informed Consent: Since our study was a retrospective file scan, informed consent was not obtained from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.A.S., Ş.G.; Design - Ş.G., F.İ.V.; Supervision - M.A.S, Ş.G.; Materials - Ş.G., F.İ.V.; Data Collection and/or Processing - Ş.G, F.İ.V.; Analysis and/or Interpretation - Ş.G., M.A.S.; Literature Review - Ş.G., F.İ.V.; Writing - Ş.G., M.A.S.; Critical Review - Ş.G., M.A.S.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Kurul Onayı: Etik kurul onayı çalışmaya başlamadan önce alındı. Etik Kurul Tarihi: 2017 Etik Kurul Sayısı: 22-2.

Hasta Onamı: Çalışmamız geriye dönük dosya taraması olduğundan hastalardan bilgilendirilmiş onam formu alınmadı.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - M.A.S., Ş.G.; Tasarım - Ş.G., F.İ.V.; Denetleme - M.A.S, Ş.G.; Veri Toplanması ve/veya İşlemesi Ş.G, F.İ.V.; Analiz ve/veya Yorum - Ş.G., M.A.S.; Literatür Taraması - Ş.G., F.İ.V.; Yazıyı Yazan - Ş.G., M.A.S.; Eleştirel İnceleme - Ş.G., M.A.S.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

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