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Original article

The impact of phenylketonuria on PKU patients' quality of life: Using of the phenylketonuria-quality of life (PKU-QOL) questionnaires

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SUMMARY

Background & aims: Phenylketonuria (PKU) has a very high prevalence throughout the world. Nowadays, number of studies about impact of this metabolic disease on patients increasing. The aim of our study is to examine PKU patients' quality of life according to PKU-QOL questionnaires.
Methods: Patients (n = 63) diagnosed with PKU were included this study; child (9–11 years (n = 20)), adolescent (12–15 years (n = 22)) and adult (18–35 years (n = 21)). PKU-QOL questionnaires (include 4 modules) developed for PKU patients were used. In accordance with purpose, data were analysed by nonparametric tests (Kruskal Wallis One-Way Analysis of Variance Test and Mann–Whitney U Test), according to results of normality tests.
Results: Most of the individuals were female (65,1%) and mean age was 15,7 ± 6,4 years. Symptoms; there were statistically significant differences in all domains excluding tiredness. Especially, median score of slow thinking was very frequent symptom in children as 100,0. PKU in general; there were found that median scores were higher in children. Phe-free amino acid supplement administration: as the age increased, scores were lower. Dietary protein restriction: Overall difficulty following dietary protein restriction and Food enjoyment were found similar in groups (p > 0,05).
Conclusions: It was concluded that PKU affects younger people more negatively.

1. Introduction

Among the first hereditary metabolic diseases, Phenylketonuria (PKU), which has a globally high prevalence, was first described by Asbjorn Folling in 1934 as hereditary metabolic disease characterized by severe mental impairment, motor problems and skin abnormalities [1,2]. In the 1950s, low-phenylalanine diet was developed by Horst Bickel for PKU treatment [3]. In the same years, the deficiency in Phenylalanine Hydroxylase (PAH) activity in PKU has been identified. When it came to the 1960s, Robert Guthrie developed a diagnostic test (Guthrie test) for the diagnosis of hyperphenylalanine, which is now widely used worldwide [4]. Over the years 1980, research on the human PAH gene has been increased and this genetic map has been created. Since the 1990s, special products have been developed for individuals with PKU, and the problems faced by individuals with PKU in social life have begun to be addressed.

Elevated Phe levels, a condition commonly observed in individuals with PKU, reduce the entry of other large neutral amino acids into the brain [5]. Due to inability in conversion of phenylalanine to tyrosine, phenyl ketones is formed which causes a damage in the brain. Therefore, PKU patients must follow the lifelong protein restricted diet. It is possible that PKU affects PKU patients' quality of life negatively. The aim of present study is to examine PKU patients' quality of life according to PKU-QOL questionnaires which are specifically developed for PKU patients.

2. Materials and methods

2.1. Study design

This descriptive qualitative research was conducted with child, adolescent and adults diagnosed with PKU. It were reached to patients by PKU Family Assosiation in Turkey. Study data were

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collected between January 2016 and May 2017. The sample group of the study consisted of a total of 63 individuals consisting of 20 children, 22 adolescents and 21 adults with PKU. In accordance with the scale used, the participants were divided into 3 groups; children (9–11 years), adolescents (12–17 years) and adults (>18 years). Participation in study was based on volunteerism and the study was completed with individuals diagnosed with PKU, without regard to any criteria. It was taken an ethics committee approval (report number 2016–004) from ethics committee of Ankara Hematology Oncology Children's Training and Research Hospital. An informed consent form in which the details of research and the contact information has been signed to individuals participating in study.

2.2. Evaluation of PKU-QOL scales and scores

In this prospective and non-interventional study, PKU-QOL questionnaires developed by Regnault et al. were used [6]. Validity and reliability of Turkish had done by Regnault et al. [6]. Questionnaires were taken from Mapi Research Trust, Lyon, France.

PKU-QOLs comprises four modules: i; PKU Symptoms, ii; PKU in General, iii; Administration of Phe-free Protein Supplements, iv; Dietary Protein Restriction. These modules includes some domains; PKU Symptoms: Self-health rated status (not for child), Headaches, Stomach aches, Tiredness, Lack of concentration, Slow thinking, Trembling hands (only for adults), Irritability, Aggressiveness, Moodiness, Sadness, Anxiety.

PKU in General: Emotional impact of PKU, Practical impact of PKU, Social impact of PKU, Overall impact of PKU, Anxiety-blood test, Anxiety-blood Phe levels, Anxiety-blood Phe levels during pregnancy (only for female adults), Financial impact of PKU (only for adults), Information on PKU (only for adults).

Administration of Phe-free Protein Supplements: Adherence to supplements, Practical impact of supplements, Guilt if poor adherence to supplements, Impact of supplements on family, Taste-supplements.

Dietary Protein Restriction: Food temptations, Adherence to dietary protein restriction, Social impact of dietary protein restriction, Practical impact of dietary protein restriction (not for child), Overall impact of dietary protein restriction (not for child), Taste – specialty low protein food, Guilt if dietary protein restriction not followed, Overall difficulty following dietary protein restriction, Food enjoyment.

The recall period focused on the past one week for all sections except for 'patient's general feeling' where the recall period was 'in general'. The following interpretation rules were applied for all domain scores in a range from 0 to 100: for symptom scores, a higher score is associated with more frequent symptoms, for adherence scores, a higher score is associated with a poorer adherence, for other scores, a higher score is associated with a greater impact.

Once items are scored, a domain score is calculated for each domain with more than 70% of the items completed using the formula below;

$$\text{Domain score} = \frac{\text{Sum of item scores within the domain}}{\text{Number of non missing item scores within the domain}} \times 25$$

2.3. Statistical analysis

Normality of data was tested by the Shapiro–Wilk test and $p < 0.05$ was accepted as a normal distribution (nonparametric). Group differences in PKU-QOL datas were assessed by Kruskal Wallis One-Way Analysis of Variance Test or the Mann–Whitney U Test, since the data were nonparametric. Scores were expressed as Median and Interquartiles 1–3 (Q1-Q3) to take into account some extreme values. The data were analyzed by using the SPSS 15.0 statistical software (IBM SPSS Statistics 15.0) and statistical significance was used at $p < 0.05$.

3. Results

3.1. Study samples

Majority of participants was female (65,1%) and mean age was 15,7 ± 6,4 years. Average number of individuals in the family was 3,9 ± 1,0, which is normal levels for Turkey. Most of individuals were normal weight (63,5%), but 55,0% of children was under weight. All PKU patients consume protein-Phe free supplements. Also, protein restriction diet and pharmacological (BH4) treatment percents were 17,4% and 95,3% respectively (Table 1).

3.2. PKU-QOL scores according to age groups

All PKU-QOL scores are shown in Tables 2–5 as four modules.

In Table 2, there is PKU symptoms module. Median scores of self-rated health status were 50,0 in adolescents and adults ($p > 0,05$). There were statistically significant differences in all domains excluding tiredness ($p < 0,05$). The most frequent symptom in children was slow thinking (100,0). Median scores of sadness and aggressiveness were 0,0 in adolescents. The most frequent symptoms in general were tiredness and lack of concentration. It was concluded that children had higher scores, which means negative, in this module.

Scores of PKU in general module are shown in Table 3. The lowest median score as positively for children was social impact of PKU (37,5), for adolescent and adults were anxiety – blood test (0,0). The highest median score observed in all age groups was anxiety – blood Phe levels. There are statistical differences between groups in social impact of PKU, overall impact of PKU and anxiety – blood test ($p < 0,05$). Moreover, anxiety – blood Phe levels during pregnancy, financial impact of PKU and information on PKU, just for adults, median scores were 62,5, 25,0 and 75,0, respectively. Also, children had higher median scores in all domains that means negative.

Phe-free amino acid supplement administration module, there were significant differences excluding taste – supplements ($p < 0,05$). Highest median scores in all domains, which means negative outcome, were observed in children. Adults were more adherence to supplements with 8,3 median score (Table 4).

Table 5 shows median scores of dietary protein restriction module. In this module, children have median scores higher than

Table 1
Characteristics of individuals in the study.

		Child (n = 20)		Adolescent (n = 22)		Adult (n = 21)		Overall (n = 63)	
		n	%	n	%	n	%	n	%
Gender	Female	11	55,0	12	54,5	18	85,7	41	65,1
	Male	9	45,0	10	45,5	3	14,3	22	34,9
BMI (kg/m^2)	Under weight	11	55,0	4	18,2	1	4,8	16	25,4
	Normal weight	6	30,0	18	61,8	16	76,2	40	63,5
	Over weight	3	15,0	–	–	4	19,0	7	11,1
PKU treatment	Protein restriction diet	18	90,0	22	100,0	20	95,2	60	95,3
	Pharmacological treatment (BH4)	4	20,0	3	13,6	4	19,1	11	17,4
	Protein-Phe free supplements	20	100,0	22	100,0	21	100,0	63	100,0
Age (year)	X ± S	10,2 ± 0,6		13,3 ± 1,1		23,5 ± 5,1		15,7 ± 6,4	
	Median	10		13		22		13	
	Min–Max	9–11		12–15		18–35		9–35	
Number of individual in the family	X ± S	3,9 ± 0,7		3,9 ± 1,1		3,9 ± 1,2		3,9 ± 1,0	

Table 2
Scores of PKU symptoms module.

	Domains		Child (n = 20)	Adolescent (n = 22)	Adult (n = 21)	2/z	p
Symptoms	Self-rated health status	**X ± S**	–	56,8 ± 17,5	59,5 ± 21,6	0,4	0,642**
		(Min–Max)		(25,0–100,0)	(25,0–100,0)		
		Median		50,0	50,0		
		(Q1–Q3)		(50,0–75,0)	(50,0–75,0)		
	Headaches	**X ± S**	42,5 ± 21,6	20,4 ± 19,9	25,0 ± 22,4	9,8	**0,007**[a,*]
		(Min–Max)	(25,0–100,0)	(0,0–50,0)	(0,0–75,0)		
		Median	37,5	25,0	25,0		
		(Q1–Q3)	(25,0–50,0)	(0,0–31,2)	(0,0–50,0)		
	Stomach aches	**X ± S**	65,0 ± 17,1	20,4 ± 22,6	20,2 ± 20,3	32,2	**0,000**[a,b,*]
		(Min–Max)	(50,0–100,0)	(0,0–75,0)	(0,0–75,0)		
		Median	62,5	25,0	25,0		
		(Q1–Q3)	(50,0–75,0)	(0,0–31,2)	(0,0–25,0)		
	Tiredness	**X ± S**	46,2 ± 20,3	35,2 ± 25,2	41,6 ± 30,9	2,4	0,301*
		(Min–Max)	(25,0–75,0)	(0,0–100,0)	(0,0–100,0)		
		Median	50,0	25,0	50,0		
		(Q1–Q3)	(25,0–68,7)	(25–50,0)	(12,5–75,0)		
	Lack of concentration	**X ± S**	65,0 ± 28,5	31,8 ± 26,9	25,0 ± 17,6	18,4	**0,000**[a,b,*]
		(Min–Max)	(25,0–100,0)	(0,0–75,0)	(0,0–50,0)		
		Median	75,0	25,0	25,0		
		(Q1–Q3)	(25,0–75,0)	(25,0–50,0)	(12,5–75,0)		
	Slow thinking	**X ± S**	77,5 ± 32,3	22,7 ± 30,7	17,8 ± 26,4	26,3	**0,000**[a,b,*]
		(Min–Max)	(25,0–100,0)	(0,0–100,0)	(0,0–100,0)		
		Median	100,0	25,0	0,0		
		(Q1–Q3)	(37,5–100,0)	(0,0–25,0)	(0,0–25,0)		
	Trembling hands	**X ± S**	–	–	16,6 ± 19,9		
		(Min–Max)			(0,0–50,0)		
		Median			0,0		
		(Q1–Q3)			(0,0–25,0)		
	Irritability	**X ± S**	68,7 ± 22,7	21,6 ± 17,7	20,3 ± 18,7	33,1	**0,000**[a,b,*]
		(Min–Max)	(25,0–100,0)	(0,0–50,0)	(0,0–75,0)		
		Median	75,0	25,0	25,0		
		(Q1–Q3)	(50,0–75,0)	(0,0–25,0)	(0,0–25,0)		
	Aggressiveness	**X ± S**	32,5 ± 11,7	14,7 ± 22,7	5,9 ± 13,4	24,1	**0,000**[a,b,*]
		(Min–Max)	(25,0–50,0)	(0,0–75,0)	(0,0–50,0)		
		Median	25,0	0,0	0,0		
		(Q1–Q3)	(25,0–50,0)	(0,0–25,0)	(0,0–0,0)		
	Moodiness	**X ± S**	43,7 ± 17,9	12,5 ± 12,8	41,6 ± 22,8	27,1	**0,000**[a,c,*]
		(Min–Max)	(25,0–75,0)	(0,0–25,0)	(0,0–100,0)		
		Median	50,0	12,5	50,0		
		(Q1–Q3)	(25,0–50,0)	(0,0–25,0)	(25,0–50,0)		
	Sadness	**X ± S**	50,0 ± 21,4	17,1 ± 22,3	34,5 ± 23,1	17,4	**0,000**[a,*]
		(Min–Max)	(25,0–100,0)	(0,0–75,0)	(0,0–75,0)		
		Median	50,0	0,0	25,0		
		(Q1–Q3)	(25,0–68,7)	(0,0–25,0)	(25,0–50,0)		
	Anxiety	**X ± S**	55,0 ± 26,4	15,9 ± 14,5	28,5 ± 25,3	22,1	**0,000**[a,b,*]
		(Min–Max)	(25,0–100,0)	(0,0–50,0)	(0,0–75,0)		
		Median	50,0	25,0	25,0		
		(Q1–Q3)	(31,2–68,7)	(0,0–25,0)	(0,0–50,0)		

* Kruskal Wallis One-Way Analysis of Variance Test, ** Mann–Whitney U Test. a; 9–11/12–17 age groups, b; 9–11/18–35 age groups, c; 12–17/18–35 age groups. 0 (no impact/no symptom), 100 (extremely severe impact/very frequent symptom).

Table 3
Scores of PKU in general module.

	Domains		Child (n = 20)	Adolescent (n = 22)	Adult (n = 21)	2/z	p**
PKU in general	Emotional impact of PKU	**X ± S**	50 ± 15,5	37,7 ± 18,0	39,5 ± 15,6	3,8	0,150
		(Min–Max)	(33,3–83,3)	(12,5–68,7)	(18,7–56,2)		
		Median	50,0	46,8	37,5		
		(Q1–Q3)	(35,4–62,5)	(18,7–50,0)	(21,8–56,2)		
	Practical impact of PKU	**X ± S**	58,1 ± 27,2	34,8 ± 29,7	39,06 ± 33,6	5,9	0,052
		(Min–Max)	(25,0–87,5)	(0,0–91,6)	(6,2–81,2)		
		Median	50,0	33,3	34,3		
		(Q1–Q3)	(28,1–87,5)	(0,0–41,6)	(9,3–73,4)		
	Social impact of PKU	**X ± S**	51,2 ± 27,2	21,96 ± 19,5	17,8 ± 14,5	20,1	**0,000**[a,b]
		(Min–Max)	(25,0–100,0)	(0,0–58,3)	(0,0–50,0)		
		Median	37,5	8,3	16,6		
		(Q1–Q3)	(33,3–83,3)	(8,3–41,6)	(8,3–25,0)		
	Overall impact of PKU	**X ± S**	52,9 ± 25,5	36,7 ± 11,9	25,3 ± 8,6	31,5	**0,000**[a,b,c]
		(Min–Max)	(31,2–78,1)	(20,4–56,8)	(10,0–43,3)		
		Median	50,0	36,3	22,9		
		(Q1–Q3)	(39,1–68,7)	(25,0–48,3)	(19,3–34,5)		
	Anxiety – blood test	**X ± S**	53,1 ± 17,1	23,8 ± 34,0	6,5 ± 15,1	27,4	**0,000**[a,b]
		(Min–Max)	(25,0–100,0)	(0,0–100,0)	(0,0–50,0)		
		Median	50,0	0,0	0,0		
		(Q1–Q3)	(50,0–50,0)	(0,0–43,7)	(0,0–6,2)		
	Anxiety – blood Phe levels	**X ± S**	67,5 ± 35,4	52,2 ± 38,5	51,1 ± 31,1)	2,7	0,260
		(Min–Max)	(25,0–100,0)	(0,0–100,0)	(0,0–100,0)		
		Median	87,5	50,0	50,0		
		(Q1–Q3)	(25,0–100,0)	(25,0–100,0)	(25,0–75,0)		
	Anxiety – blood Phe levels during pregnancy*	**X ± S**	–	–	59,7 ± 33,3		
		(Min–Max)			(0,0–100,0)		
		Median			62,5		
		(Q1–Q3)			(25,0–100,0)		
	Financial impact of PKU	**X ± S**	–	–	29,7 ± 31,2		
		(Min–Max)			(0,0–100,0)		
		Median			25,0		
		(Q1–Q3)			(0,0–50,0)		
	Information on PKU	**X ± S**	–	–	77,3 ± 24,8		
		(Min–Max)			(25,0–100,0)		
		Median			75,0		
		(Q1–Q3)			(62,5–100,0)		

Phe; Phenylalanine. **Kruskal Wallis One-Way Analysis of Variance Test, *Female patients only (n = 18), a; 9–11/12–17 age groups, b; 9–11/18–35 age groups, c; 12–17/18–35 age groups. Lower scores represent more positive outcome.

50,0 excluding overall difficulty following dietary protein restriction. In all three groups, median scores of guilt if dietary protein restriction not followed (75,0/50,0/75,0), overall difficulty following dietary protein restriction (25,0/21,8/50,0) and food enjoyment (62,5/50,0/75,0) were similar (p > 0,05).

4. Discussion

PKU, previously a common cause of severe intellectual disability, is a metabolic disorder now promptly diagnosed and effectively treated thanks to newborn screening programs [7]. Newborn

Table 4
Scores of Phe-free amino acid supplement administration module.

	Domains		Child (n = 20)	Adolescent (n = 22)	Adult (n = 21)	2/z	p
Phe-free amino acid supplement administration	Adherence to supplements	**X ± S**	43,1 ± 14,3	48,8 ± 13,3	27,7 ± 20,9	32,8	**0,000**[b,c]
		(Min–Max)	(25,0–62,5)	(18,7–75,0)	(8,3–50,0)		
		Median	50,0	43,7	(8,3)		
		(Q1–Q3)	(25,0–50,0)	(43,7–54,6)	–		
	Practical impact of supplements	**X ± S**	62,5 ± 35,8	38,9 ± 28,4	36,6 ± 21,3	6,3	**0,041**[a,b]
		(Min–Max)	(25,0–100,0)	(0,0–100,0)	(12,5–75,0)		
		Median	50,0	31,2	37,5		
		(Q1–Q3)	(25,0–100,0)	(18,7–56,2)	(18,7–56,2)		
	Guilt if poor adherence to supplements	**X ± S**	71,2 ± 18,6	53,4 ± 33,0	40,4 ± 33,9	10,9	**0,004**[a,b]
		(Min–Max)	(50,0–100,0)	(0,0–100,0)	(0,0–100,0)		
		Median	75,0	50,0	25,0		
		(Q1–Q3)	(50,0–75,0)	(25,0–100,0)	(25,0–50,0)		
	Relationships within family because of supplements	**X ± S**	53,7 ± 24,7	20,4 ± 23,9	11,9 ± 21,8	24,9	**0,000**[a,b]
		(Min–Max)	(25,0–75,0)	(0,0–100,0)	(0,0–75,0)		
		Median	75,0	25,0	0,0		
		(Q1–Q3)	(25,0–75,0)	(0,0–25,0)	(0,0–25,0)		
	Taste – supplements	**X ± S**	55,0 ± 23,7	44,3 ± 34,4	44,1 ± 26,1	2,2	0,324
		(Min–Max)	(25,0–75,0)	(0,0–100,0)	(0,0–75,0)		
		Median	75,0	50,0	50,0		
		(Q1–Q3)	(25,0–75,0)	(18,7–56,2)	(25,0–62,5)		

Phe; Phenylalanine. Kruskal Wallis One-Way Analysis of Variance Test, a; 9–11/12–17 age groups, b; 9–11/18–35 age groups, c; 12–17/18–35 age groups. Lower scores represent more positive outcome.

Table 5
Scores of dietary protein restriction module.

	Domains		Child (n = 20)	Adolescent (n = 22)	Adult (n = 21)	2/z	p
Dietary protein restriction	Food temptations	**X ± S**	58,1 ± 25,0	26,7 ± 25,9	30,9 ± 35,1	12,4	**0,002**[a,b,*]
		(Min–Max)	(25,0–87,5)	(0,0–75,0)	(0,0–100,0)		
		Median	62,5	12,5	12,5		
		(Q1–Q3)	(28,1–84,3)	(0,0–50,0)	(0,0–50,0)		
	Adherence to dietary protein restriction	**X ± S**		40,9 ± 8,1	42,1 ± 13,1	31,5	**0,000**[a,b,*]
		(Min–Max)		(25,0–50,0)	(25,0–66,6)		
		Median		41,6	41,6		
		(Q1–Q3)		(33,3–50,0)	(32,3–50,0)		
	Social impact of dietary protein restriction	**X ± S**	55,0 ± 24,5	25,2 ± 29,1	17,9 ± 20,4	18,5	**0,000**[a,b,*]
		(Min–Max)	(25,0–85,0)	(0,0–95,0)	(0,0–87,5)		
		Median	52,5	7,5	10,0		
		(Q1–Q3)	(27,5–80,0)	(5,0–45,0)	(4,5–29,1)		
	Practical impact of dietary protein restriction	**X ± S**	–	39,1 ± 16,7	49,3 ± 10,9	3,2	**0,012**[c,**]
		(Min–Max)		(21,4–78,5)	(28,5–71,4)		
		Median		35,7	50,0		
		(Q1–Q3)		(21,4–47,3)	(41,1–58,9)		
	Overall impact of dietary protein restriction	**X ± S**	–	30,6 ± 33,5	35,4 ± 12,7	−1,7	**0,022**[c,**]
		(Min–Max)		(0,0–100,0)	(15,3–78,8)		
		Median		25,0	32,7		
		(Q1–Q3)		(0,0–100,0)	(27,0–43,2)		
	Taste – specialty low protein food	**X ± S**	66,2 ± 18,6	28,4 ± 24,7	29,7 ± 25,7	22,6	**0,000**[a,b,*]
		(Min–Max)	(25,0–100,0)	(0,0–75,0)	(0–75)		
		Median	75,0	25,0	25,0		
		(Q1–Q3)	(50,0–75,0)	(0,0–50,0)	(0,0–50,0)		
	Guilt if dietary protein restriction not followed	**X ± S**	68,7 ± 22,7	54,5 ± 35,1	58,3 ± 33,8	1,6	0,435
		(Min–Max)	(25–100)	(0,0–100,0)	(0,0–100,0)		
		Median	75,0	50,0	75,0		
		(Q1–Q3)	(50,0–75,0)	(25,0–100,0)	(25,0–75,0)		
	Overall difficulty following dietary protein restriction	**X ± S**	41,2 ± 23,3	30,6 ± 33,5	38,1 ± 35,1	2,3	0,312
		(Min–Max)	(25–75)	(0–100)	(0–100)		
		Median	25,0	21,8	50,0		
		(Q1–Q3)	(25,0–75,0)	(14,5–41,6)	(0,0–50,0)		
	Food enjoyment	**X ± S**	72,5 ± 24,1	53,4 ± 23,5	61,9 ± 34,1	5,4	0,067
		(Min–Max)	(50,0–100,0)	(0,0–100,0)	(0,0–100,0)		
		Median	62,5	50,0	75,0		
		(Q1–Q3)	(50,0–100,0)	(50,0–75,0)	(50,0–75,0)		

[a]Kruskal Wallis One-Way Analysis of Variance Test, **Mann–Whitney U Test, a; 9–11/12–17 age groups, b; 9–11/18–35 age groups, c; 12–17/18–35 age groups. Lower scores represent more positive outcome.

screening programs are extremely beneficial for preventing late diagnosis of PKU. Despite the fact that there are beautiful developments, there is limited study for PKU patients in terms of quality of life. This is the first study to investigate the quality of life in patients with PKU in Turkey.

In 2001, PKU prevalance in Turkey was 1.4200 [8] which is higher than other countries. Also in 2012, estimated PKU prevalance in Europe was 1.10000 [9]. The aim of present study was to evaluate patients with PKU in terms of quality of life, as PKU have the highestprevalance in Turkey among other countries. Questionnaires specially developed for PKU patients by Regnault et al. [6] were used. A total of 63 patients with PKU between 9 and 35 years participated in study. In summary we hypothesised that PKU negatively affects PKU patients' life.

Obesity/malnutrition status in PKU patients also should be take into account. In our study, majority of children were under weight. As age increase, it closed to normal weight. Indeed, adults with PKU, unlike children, are free to make their own decisions relating to dietary and activity choices and often lose contact with healthcare professionals, leading to reduced opportunity for advice on a healthy lifestyle [10]. However, There are not enough studies on the development of obesity in individuals with PKU [11].

PKU symptoms module; PKU, an autosomal recessive and congenital disorder of phenylalanine amino acid metabolism, has some neurophysiological symptoms [12,13]. These symptoms can negatively affect the life of individuals with PKU [14]. In our study, since the median scores of symptoms in children are at higher levels, it can be said that children don't follow the diet, but it must be checked the blood Phe concentrations. Continuously high Phe-concentrations lead to impaired executive function [15]. However, even if blood levels of phenylalanine are at normal levels, a patient with PKU can feel less happy, cheerful or believer. The only blood Phe results may not reflect health status of PKU patients. The correlation between level of metabolic control and severity of symptoms suggests a biological basis of psychiatric dysfunction. Additionally, psychosocial factors such as the burden of living with a chronic illness may contribute to psychological and psychiatric outcomes in PKU. The lack of a PKU-specific psychiatric phenotype combined with the observation that not everyone with PKU is affected highlights the complexity of the problem. Referral to a psychologist may be helpful. More research on psychiatric and psychological outcomes in PKU is required [16].

PKU in general module; The emotional effects of PKU affected the group of 9–11 age at most (50,0) and affected the least 18–35 age group (37,5). Previous studies support these results [17–19]. Also, results indicated that PKU patients had quite anxiety about blood Phe levels. It is clear that the most affected group in the PKU in general module is the 9–11 age group. In this case, it can be concluded that young children have problems in acceptance, understanding, comprehension.

Phe-free amino acid supplement administration module; Along with protein-restricted diet, special products to the PKU also constitute a significant part of the treatment of PKU [20]. In our study, there was no significant difference between the groups only in

"taste of PKU supplement" domain. All three groups does not like the taste of supplements, especially children with 75,0. These results are shown in similar studies and was emphasized that studies should be carried out toward to consummability/taste of supplements [21–23].

Dietary protein restriction module; For PKU patients, it is essential to adherence diet for life and it would remain as a major treatment many years [24]. If a person having PKU doesn't follow the diet, it may results a neurocognitive damage in brain [25]. However, one of the most important problems for PKU individuals is adherence to diet. In a study by Finkelson et al. [26], it was found that adherence to protein restricted diet is decreased as age increased, which was observed in our study. It can be result from that children with PKU are faced with significant difficulties when they become adolescent and start to gain independence [27]. There are many studies supporting our results [28–33]. In our study, it was concluded that the foods more attracted the children and they more want the foods that they can not consume. In addition, for children, scores of 'Taste of low-protein food' and 'Food enjoyment', 75.0 and 62.5 respectively, were correlated with adherence to diet. But, considering 'Food temptations' (median = 62.5), childs had liked their diet but desired other foods a lot. Therefore, Glycomacropeptide (GMP) can be useful for PKU patients [34,35]. GMP has a unique amino acid pattern for individuals with PKU in terms of the not contain Phe [36].

In conclusion, PKU have more negative effects on children or younger individuals. Also PKU patients can face various problems in social life due to the diet rules and/or special supplements/formula they consumed. They should evaluated as both biochemically and social life quality. Quality of life for PKU patients is important and there is need to studies towards social life of PKU patients.

Compliance with ethical standards

It was taken an ethics committee approval (report number 2016–004) from ethics committee of Ankara Hematology Oncology Children's Training and Research Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Statement of authorship

General information and introduction section of manuscript were prepared by GÜNDÜZ and KOÇ. ÇAKIROĞLU designed all manuscript. Statistical analyzes were performed by ALPTEKIN. All authors read and approved the final manuscript.

Conflict of interest statement and funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All authors declares that no conflict of interest.

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