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ORIGINAL ARTICLE – OPEN ACCESS

Factors Affecting Lipid Profile in Pediatric Palliative Care

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ABSTRACT

Objective: Hyperlipidemia can develop as a consequence of a sedentary life or becoming bedridden, malnutrition, and the use of drugs such as carbamazepine, and is associated with a greater risk of morbidity and mortality. The most common diagnoses in pediatric palliative care (PPC) patients are neurological diseases, metabolic diseases, and genetic and congenital conditions. This is the first study to collect and analyze data of the lipid levels of children receiving palliative care support in Türkiye.

Materials and Methods: Hospital records of PPC patients were used to gather the data used in this retrospective study. Hyperlipidemia was defined by a triglyceride (TG) value of >75 mg/dL for patients aged 0–9 years and >90 mg/dL for those aged 10–19 years of age, along with a total cholesterol (TC) level of >170 mg/dL, a low-density lipoprotein (LDL) level of >110 mg/dL, and a high-density lipoprotein (HDL) level of ≤45 mg/dL.

Results: A total of 89 cases were included. The mean age of the participants was 6.2±4.8 years (range: 0.1–17 years), and 53.9% (n=48) were female. Lipid level examination revealed a mean TC level of 147.65±38.22 mg/dL, TG level of 141.76±111.61 mg/dL, HDL level of 38.98±11.43 mg/dL, and LDL level of 85.29±47.14 mg/dL. A correlation was found between the alkaline phosphatase, phosphorus, vitamin B12, hemoglobin, mean corpuscular volume, albumin, and lipid levels.

Conclusion: PPC patients may have particularly high TG levels and low HDL levels. It is important to meet the nutritional needs of those in PPC, to keep the albumin, hemoglobin, and phosphorus levels high, and to monitor vitamin B12 and mean corpuscular volume. Larger and multicentered studies are needed to more fully identify and address PPC needs.

Keywords: Lipid level, palliative care, pediatrics

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INTRODUCTION

Epidemiological, clinical, and experimental studies have revealed that serum lipids and lipoproteins are associated with atherogenesis (1). Both case-control and prospective observational studies have definitively demonstrated a relationship between an elevation in serum total cholesterol (TC) and low-density lipoprotein (LDL) levels with coronary artery disease (1, 2). Two studies conducted in the USA reported high cholesterol levels in the pediatric age group at a rate of 19% and 36.5% (3, 4). Several epidemiological studies have concluded that mortality due to heart disease associated with atherosclerosis is higher in patients receiving antiepileptic therapy than in the general population (5, 6).

Pediatric palliative care (PPC) is a high-level care system designed to increase the quality of life of children with life-threatening/life-limiting diseases and that of their families. The concept gained prominence with oncology patients, and with developments in medicine and technology, it has since been incorporated for children with neurological, metabolic, genetic, and other congenital disorders (7). Hypertension and epilepsy are common in this challenging and vulnerable population with complex problems that may require the use of multiple drugs. Hyperlipidemia can be a consequence of a sedentary life or becoming bedridden, malnutrition, and the use of drugs such as carbamazepine, and is associated with a greater risk of morbidity and mortality. PPC is a new field in Türkiye and, to our knowledge, there are no published data of the lipid levels of these children. The objective of this study was to review the lipid profile of children admitted to PPC and examine influential factors.

MATERIALS and METHODS

Ethics Considerations

Ethics approval for this retrospective, cross-sectional study was obtained from the Noninterventional Clinical Research Ethics Committee of HSUT İzmir Dr. Behçet Uz Children's Hospital on December 9, 2021 (no: 09/12/2021-365). All of the patients or their guardians provided consent for inclusion in the study.

Pediatric Palliative Care Unit

HSUT Dr Behçet Uz Children's Hospital is a tertiary care hospital that includes a PPC center established in November 2018. It was the first PPC center in the country, created based on the examples in Europe and the USA. The care center has 12 beds and is staffed by a multidisciplinary team of 2 doctors, 8 nurses, 4 support staff, a psychologist, a dietitian, a social worker, a physiotherapist, a moral support specialist, and a secretary. The unit accepts children whose illness provides hope for treatment but it has thus far been unsuccessful, those with progressive conditions, those without therapeutic options, and children with non-progressive but irreversible disease. The center works in cooperation with the emergency service, pediatric intensive care, and home health units in an interdisciplinary effort to provide comprehensive care.

Study Design

The study was designed as a cross-sectional, retrospective study of the records of PPC patients hospitalized between December 2, 2018 and December 1, 2019. These data were the first annual data of the clinic. A case report form consisting of 8 sections and 25 questions was used to record the data. The child's gender, age, primary diagnosis (neurological, metabolic, genetic, other), disease duration, level of care (light, medium, intense), number of drugs used, and the lipid profile as well as other laboratory findings were noted.

Children hospitalized in the unit who were between the ages of 1 month and 18 years and had lipid level findings were included in the study and factors that may have had an effect on the lipid profile were examined. Children who were not PPC patients and cases without sufficient lipid level data were excluded. Since it was a retrospective and cross-sectional study, no sample calculation was made.

Laboratory Analysis

The lipid profile was evaluated at least once to determine cardiovascular risks, since almost all of the PPC patients were bedridden with multiple diseases and using multiple drugs. Fasting lipid levels could not be determined in 18 patients (20.2%) as a result of the need for parenteral nutrition due to gastrointestinal symptoms that included respiratory distress and vomiting. Fasting blood sampling was performed at 8:00–10:00 AM in the remaining patients. Measurement of total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and triglycerides (TG) was performed with a Cobas c702 device (Roche Diagnostics, Basel, Switzerland). The low-density lipoprotein (LDL) cholesterol value was calculated by subtracting the HDL result from the TC. Evaluation of lipid level was performed according to age groups: Hyperlipidemia was defined by a TG value of >75 mg/dL for patients aged 0–9 years, and >90 mg/dL for those 10–19 years of age, along with a TC value of >170 mg/dL, an LDL of >110 mg/dL, and an HDL of ≤45 mg/dL (8).

Statistical Analysis

SPSS for Windows, Version 16.0 software (SPSS Inc., Chicago, IL, USA) was used to perform the statistical analysis. Descriptive statistics were presented as the number (%) and the mean and SD values for normally distributed variables, while the median and the minimum and maximum (min–max) values were used for non-normally distributed variables. The Kolmogorov-Smirnov test was used for non-normally distributed variables. An independent sample t-test was employed to compare the mean values between two groups (male vs. female). Pearson's correlation analysis was performed to assess the correlation between lipid levels and other parameters. Correlation coefficients were accepted as very weak at 0.00–0.21, weak at 0.21–0.40, moderate at 0.41–0.60, good at 0.61–0.80, and excellent at ≥0.81. A p value of <0.05 was considered statistically significant.

Table 1. General characteristics of the working group (n=89)

	n	%
Gender		
Male	41	46.1
Female	48	53.9
Primary disease		
Cerebral palsy	36	40.4
Metabolic disease	17	19.1
Muscular dystrophy	12	13.5
Genetic syndrome	7	7.9
Other	17	19.1
Respiratory support		
Normal	57	64.0
Oxygen	14	15.7
CPAP/NIMV	4	4.5
MV	14	15.7
Nutritional support		
Oral	25	28.1
Nasogastric tube	40	44.9
Gastrostomy	24	27.0
Total parenteral nutrition	–	–
Additional diseases		
Tubulopathy	1	1.1
Hydronephrosis	10	11.2
Chronic renal failure	2	2.2
Nephropathy	1	1.1
Epilepsy	65	73.0
Cardiomyopathy	5	5.6
Hypertension	6	6.7
Congenital heart disease	4	4.5

CPAP: Continuous positive airway pressure; MV: Mechanical ventilation; NIMV: Noninvasive mechanical ventilation; SD: Standard deviation

RESULTS

During the study period, 131 patients were hospitalized in the PPC unit. Of these, 89 cases with a lipid level measurement were included in the research. 53.9% (n=48) of the study group were female, and the median age was 5.00 years (IQR=7.5). In the group, 40.4% (n=36) had a diagnosis of cerebral palsy, 19.1% (n=17) had a metabolic disease, 13.5% (n=12) had a muscle disease, 7.9% (n=7) had a genetic disease, and 19.1% (n=17) had other diagno-

Table 2. Lipid and related laboratory parameters of the study group (n=89)

	Mean±SD
Cholesterol	147.65±38.22
Triglyceride¶	141.76±111.61
HDL¶	38.98±11.43
LDL	85.29±47.14
B12¶	852.99±471.53
MCV*	82.73±8.22
Hemoglobin*	11.31±1.88
Albumin*	3.72±0.47

*: Mean laboratory parameters were low for age; ¶: Laboratory parameters were high for age; B12: Vitamin B12; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; MCV: Mean corpuscular volume; SD: Standard deviation

ses. In all, 57 (64%) patients were followed up with normal room air breathing capability, 14 (15.7%) were on oxygen support, and 14 (15.7%) were on home mechanical ventilation (Table 1). Examination of the lipid levels revealed a mean TC level of 147.65±38.22 mg/dL, TG of 141.76±111.61 mg/dL, HDL of 38.98±11.43 mg/dL, and LDL of 85.29±47.14 mg/dL. The average values of laboratory parameters associated with the lipid profile are presented in Table 2. No significant difference was observed in the lipid levels of cerebral palsy patients when compared with other disease groups (p=0.514, p=0.519, p=0.123, p=0.145, respectively). Additionally, the lipid level was not correlated with drugs used, including antiepileptics (p=0.324). A correlation was found between alkaline phosphatase, phosphorus, vitamin B12, hemoglobin, mean corpuscular volume (MCV), albumin, and lipid levels. Laboratory parameters and the relationship between lipid level and disease is summarized in Table 3.

DISCUSSION

The current study is believed to be the first to examine the lipid profiles of patients hospitalized in a PPC unit in Türkiye. The results revealed that the TG and HDL levels were significantly high, and that the TG level was negatively correlated with the phosphorus level and positively correlated with the MCV. Moreover, the HDL level was negatively correlated with B12 and MCV and positively correlated with hemoglobin and albumin values.

Serum lipid levels in PPC patients can be affected by various conditions and become elevated in comparison with normal controls. Especially in children with chronic renal failure, high TC, TG, and LDL levels represent a risk for cardiovascular disease (9). It has been reported that mean LDL levels are higher and HDL levels were lower in children diagnosed with epilepsy who used carbamazepine than in controls (10). The relationship between serum lipid levels, chronic obstructive pulmonary disease, and cardiovascular disease has also been investigated with some interesting findings (11, 12). The TC and LDL values of our patient group were within the normal percentile values, while the TG and HDL levels were high. Kurt et al. (10) reported high HDL and LDL values in their study of epilepsy patients. A very significant relationship between partial oxygen pressure and lipoprotein lipase activity and serum heparin levels has been demonstrated in patients with chronic lung disease. It has been reported that cholesterol levels decrease in a state of hypoxia due to increased lipoprotein lipase activity and heparin levels (11). Similarly, we did not determine high cholesterol levels, which may be associated with the fact that 36% of our patients had respiratory failure.

The relationship between phosphorus level and serum lipid levels has also been investigated recently, and 2 studies have reported that phosphorus intake decreased cholesterol levels and LDL levels (13, 14). Dietary phosphorus has been observed to increase the fecal excretion of cholesterol, thus reducing cholesterol levels (15). In our study, a negative correlation was seen between TG level and phosphorus level, which supports the data in the literature. The TG level in our study showed a positive correlation with the mean erythrocyte volume (MCV). It has been established that the MCV is closely related to endothelial dysfunction and cardiovascular events and is an independent predictor of other factors (16, 17). The mean MCV value of our study group was low, although the B12 level was high. A low MCV was accompanied by low hemoglobin values. Iron deficiency anemia affects the lipid profile. Iron stimulates the activity of lipoprotein lipase, which regulates the blood lipid level (18). Anemia may have been associated with high TG levels in our patient group. The correlation between an increased TG level and elevated MCV may be related to iron deficiency. This parameter bears consideration.

Table 3. Correlations associated with lipid profile (n=89)

	ALP	P	B12	Hb	MCV	Albumin	Heart disease	Kidney disease
Cholesterol coefficient#	0.256	0.079	-0.294	0.132	0.085	0.149	0.222	0.223
p value	0.016*	0.472	0.008*	0.226	0.436	0.169	0.036*	0.035*
Triglyceride coefficient#	0.034	-0.241	0.143	-0.130	0.216	0.023	0.059	0.016
p value	0.752	0.026*	0.203	0.234	0.046*	0.836	0.584	0.884
HDL coefficient#	-0.006	0.154	-0.405	0.220	-0.212	0.264	-0.077	0.025
p value	0.953	0.159	0.000*	0.041*	0.050*	0.014*	0.473	0.814
LDL coefficient#	0.257	-0.090	-0.178	0.101	0.134	0.151	0.128	0.122
p value	0.015*	0.415	0.112	0.353	0.218	0.162	0.231	0.253

#: Pearson correlation coefficient; *: P value≤0.05; ALP: Alkaline phosphatase; B12: Vitamin B12; Hb: Hemoglobin; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; MCV: Mean corpuscular volume; P: Phosphorus

Some studies have reported that HDL levels were high in patients using antiepileptic drugs (19). Furthermore, vitamin B12 deficiency has been associated with dyslipidemia (20, 21). The serum vitamin B12 level was found to be negatively correlated with the TG level and positively correlated with the HDL level in other research (22, 23). In our study, the mean B12 level was high, it was not associated with TG, and there was a negative correlation with HDL. This result may not be surprising in a patient group with severe and complicated diseases and who are often bedridden and taking multiple drugs. It may also be associated with prognosis and mortality; however, we cannot hypothesize about such a relationship since mortality rates were not evaluated in our study. Nonetheless, a high B12 level and a low HDL level may be a valuable and important indication for clinicians.

Individuals with the neurological disease typically have a lower mean serum albumin level and a higher hypoalbuminemia percentage than healthy individuals (24). Eating disorders, swallowing and chewing disorders, and dysphagia are examples of conditions that may lead to insufficient protein intake and hypoalbuminemia. In addition, drugs, especially anticonvulsants, can result in hypoalbuminemia by reducing synthesis in the liver (25). Most of our patient group had a neurological disease and used multiple anticonvulsant drugs. The albumin level was below the lower reference values and positively correlated with HDL. Low serum albumin has been associated with mortality, but mortality rates were not evaluated in this study, and it therefore it cannot be cited as an indicator of prognosis. The correlation between the serum albumin level and HDL was significant and similar to other findings in the literature (26–28). These results may guide future studies in terms of prognosis and mortality.

Study Limitations

The small sample size and the cross-sectional design are the primary limitations of the study. The results cannot be generalized and causality cannot be established.

CONCLUSION

Children followed in PPC may have especially high TG levels and low HDL levels. It is important to monitor and adjust their nutrition, including the levels of albumin, hemoglobin, and phosphorus, as well as vitamin B12 and MCV values. These new data may prove valuable to future research, including examinations of prognosis and mortality. Larger, multicenter studies are needed to fully identify and address the needs of PPC patients.

Ethics Committee Approval: The İzmir Dr. Behçet Uz Children's Hospital Non-Interventional Clinical Research Ethics Committee granted approval for this study (date: 09.12.2021, number: 365).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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