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Quality of life of caregivers and drug-resistant epilepsy children treated with a ketogenic diet

Qualidade de vida do cuidador e da criança com epilepsia fármaco-resistente em tratamento com dieta cetogênica

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ABSTRACT

Objective

To assess caregivers' burden and quality of life of children and adolescents with drug-resistant epilepsy treated with ketogenic therapy.

Methods

Survey-type study involving caregivers of children and adolescents being monitored at the ketogenic diet clinic of the *Instituto de Medicina Integral Prof. Fernando Figueira*. Socioeconomic data were collected from the patients' medical records. Telephone interviews with the guardians of the child/adolescent were carried out using two instruments: 1) The Quality of Life of Children with Epilepsy, which approaches the physical, psychological, cognitive/educational and socio-familial domains from the parents perspective,; and 2) The Zarit Burden Inventory, which assesses the impact of chronic mental disorders on the physical and emotional well-being, social life and financial aspects of the caregiver.

Results

The sample consisted of 49 children and adolescents of caregivers with a median age of 44 years, 61;2% of whom were male. The results obtained using the Quality of Life of Children with Epilepsy showed that after the cognitive/educational domain, the domain most impaired was the physical domain (median=52.8, Q1=47.2; Q3=61.1) and the most preserved was the psychological domain (median=77.8; Q1=70.8; Q3=83.3). The burden was considered moderate to severe for the majority (55.1%) of caregivers.

Conclusion

A poor quality of life for the child/adolescent and an increase in the caregiver's burden were observed, interfering in the daily life and personal relationships of the guardians. Thus, the multidisciplinary team should also offer support and appropriate technical support to caregivers.

Keywords: Caregiver exhaustion. Epileptic seizures. Ketogenic diet. Palliative care. Refractory epilepsy.

RESUMO

Objetivo

Avaliar a sobrecarga do cuidador e a qualidade de vida da criança e adolescente com epilepsia fármaco-resistente em tratamento com terapia cetogênica.

Métodos

Estudo tipo survey envolvendo os cuidadores das crianças e adolescentes em acompanhamento no ambulatório de dieta cetogênica do Instituto de Medicina Integral Prof. Fernando Figueira. Foram coletados dados socioeconômicos a partir da análise dos prontuários e realizadas entrevistas telefônicas, onde foi aplicado ao responsável pela criança/adolescente dois formulários: 1) Qualidade de Vida da Criança com Epilepsia, que aborda pela perspectiva dos pais os domínios físico, psicológico, cognitivo/educacional e sociofamiliar; e 2) Inventário de Sobrecarga de Zarit, que avalia a repercussão dos transtornos crônicos mentais sobre o bem-estar físico e emocional, vida social e aspectos financeiros do cuidador.

Resultados

A amostra foi constituída por cuidadores de 49 crianças e adolescentes, com mediana de idade de 4,4 anos, sendo 61,2% do sexo masculino. Os resultados obtidos no Qualidade de Vida da Criança com Epilepsia, evidenciaram que após o domínio cognitivo/educacional, o mais prejudicado foi o físico (mediana=52,8, Q1=47,2; Q3=61,1) e o mais preservado foi o psicológico (mediana=77,8; Q1=70,8; Q3=83,3). A sobrecarga foi considerada moderada a grave para a maioria (55,1%) dos cuidadores.

Conclusão

Foi evidenciado baixa qualidade de vida da criança/adolescente e aumento da sobrecarga do cuidador, interferindo na vida cotidiana e nas relações pessoais dos responsáveis. Assim, a equipe multidisciplinar deve também oferecer amparo e suporte técnico apropriado aos cuidadores.

Palavras-chave: *Crises epilépticas. Cuidados paliativos. Dieta cetogênica. Epilepsia refratária. Exaustão do cuidador.*

INTRODUCTION

An epileptic seizure is defined as the transient occurrence of signs and/or symptoms resulting from synchronous or excessive neuronal activity in the brain. Such phenomena include change in consciousness, motor, sensitive/sensory, autonomic or involuntary psychic events perceived by the patient or by an observer [1]. Epilepsy is one of the most common neurological diseases; it predominantly onsets in childhood; part of this juvenile population can develop epileptic seizures but without the most severe form, characterized by difficult medication control [1-3].

Despite the availability of new drugs with different mode of action, the control of newly diagnosed epilepsy cases has not improved and has remained at 63.7% over the years. The probability of seizure control decreases substantially with each new additional drug use [4]. A group of approximately 30.0% patients had no seizure control, despite appropriate therapy with Anti-Seizure Drugs (ASD). Such patients can evolve with delayed neuropsychomotor development and even regression of cognitive functions [4,5].

Care of people with epilepsy has expanded over the years incorporating now the concept of quality of life for patients and their families as a crucial point in health care. The impact of organic-functional impairments caused by epilepsy also involves prejudices that cause patients to suffer a serious stigmatization and restriction process that can lead them to social isolation [6,7].

This group of patients with drug-resistant seizures can benefit from non-pharmacological interventions such as Ketogenic Therapy (KT), which can be effective in controlling epileptic seizures with a possible reduction in ASD, providing better quality of life for the patients and less burden on their families' members [8].

The main objectives of the KT are: to improve the clinical pattern of crises; to reduce the use of anti-seizure medications and, consequently, their adverse effects; and to improve the patient's quality of life (with improved cognition, alertness and behavior) [9].

In an observational study evaluating 32 children with difficult-to-control epilepsy undergoing treatment with ketogenic therapy, it was demonstrated that 35.5% of them had a reduction greater than 50.0% in the frequency of seizures and 19.4% were seizure-free, hence proving the therapy effectiveness [10]. Traditionally, the reduction of the number of seizures has been the only objective of the treatment; however, over time it was found that the impact of epilepsy also involves prejudices that expose patients and families to a serious process of stigmatization and restrictions that can lead them to social isolation and can cause a burden to the caregiver [6].

There is a diversity of feelings experienced by caregivers, especially mothers of epileptic children, such as fear, anxiety, anger, hurt and guilt [3]. A child's illness brings profound and, almost always, unexpected changes in the lives of the caregiver and the family, especially in terms of overload, which occurs due to the intense care routine, restrictions on the activities of the entire family and the lack of social support that the caregiver has to face [11].

To adapt to the new situation of caring for a child with drug-resistant epilepsy, caregivers often need to make a trade-off, such as stop working, building a support network by changing their place of residence to be closer to family members and learning to face the daily care routine [11].

Thus, the concept of quality of life in epileptic syndrome goes beyond the clinical aspects (such as type, frequency, severity and etiology of seizures); behavioral, psychological, cultural, social and emotional aspects should also be considered [12]. Our study aimed to evaluate, from the perspective of caregivers, caregiver burden and the quality of life of children and adolescents with drug-resistant epilepsy undergoing treatment with ketogenic therapy.

METHODS

An observational, survey-type study with an analytical component was carried out. The sample was made up of caregivers of children and adolescents under 18 years of age, diagnosed with drug-resistant epilepsy; they were followed up for a minimum period of 6 months from December 2015 to December 2021, at the Ketogenic Diets Outpatient Clinic of the Institute of Integral Medicine Prof. Fernando Figueira (IMIP).

The IMIP is a philanthropic, non-profit institution serving patients mainly from Recife and the metropolitan region who are users of the government *Sistema Único de Saúde* (SUS, Unified Health System) which provides comprehensive health care for children, women and adults located in Recife/Pernambuco. The Ketogenic Diets for Drug-Resistant Epilepsy outpatient clinic was established in December 2015, being the first in the North/Northeast; it is staffed by trained professionals in Child Neurology and Nutrition who have treated around 200 children since the beginning of their activities, attending a monthly average of 30 visits.

In order to identify the caregivers, the medical records of children and adolescents with at least six months of KT follow-up were evaluated. When applying the questionnaires, patients who were undergoing treatment or who had discontinued the diet either due to discharge or for other reasons were considered. Patients who started ketogenic therapy in other services and those with incomplete data in their clinical records were excluded. They were considered losses when there was no availability of telephone contact with caregivers.

To characterize the patients being monitored, some socioeconomic data were collected from the medical records, such as age, gender, origin, education, categorization of the main caregiver and family income.

Telephone interviews lasting approximately 15 minutes were carried out, where two instruments were applied to the child/adolescent: The Quality of Life in Childhood Epilepsy (QOLCE-50) and the Zarit Burden Inventory (ZBI), both translated into the Portuguese language and validated in Brazil [13, 14]. Each participant interviewed was assigned a number (to maintain anonymity); the responses were transcribed and recorded in a spreadsheet, along with the date and time of the interview.

The QOLCE-50 is a tool that aims to assess the quality of life of children and adolescents with epilepsy from the perspective of their parents/guardians. It contains 50 questions, which assess the physical (9 questions), psychological (18), socio-family (7) and cognitive/educational (16) dimensions. For each question there is a score from 1 to 4 and for each domain the score varies from 25 to 100 [13]; the higher the score, the better the quality of life. At the end of the QOLCE-50 there is a visual analogue scale with a score from 0 to 10 to determine global quality of life; this scale was not used in this study as the interviews were over the telephone and there was no eye contact.

The ZBI is one of the most used instruments to assess burden in caregivers of patients with chronic mental or physical disorders. It consists of 22 questions with a score from 1 to 4, divided into five domains that involve: health, personal and social life, financial situation, emotional well-being and interpersonal relationships. By adding together all the items, we can assess the following results: little or no overload (0-20 points), mild to moderate (21-40 points), moderate to severe (41-60 points) and severe overload (61-88 points) [14].

Descriptive statistical analysis was performed using Stata® software, version 13.0. Relative frequencies were determined for the categorical variables and measures of central tendency and dispersion for continuous variables. The Student's t test was performed to compare the averages of global quality of life according to the burden reported by caregivers.

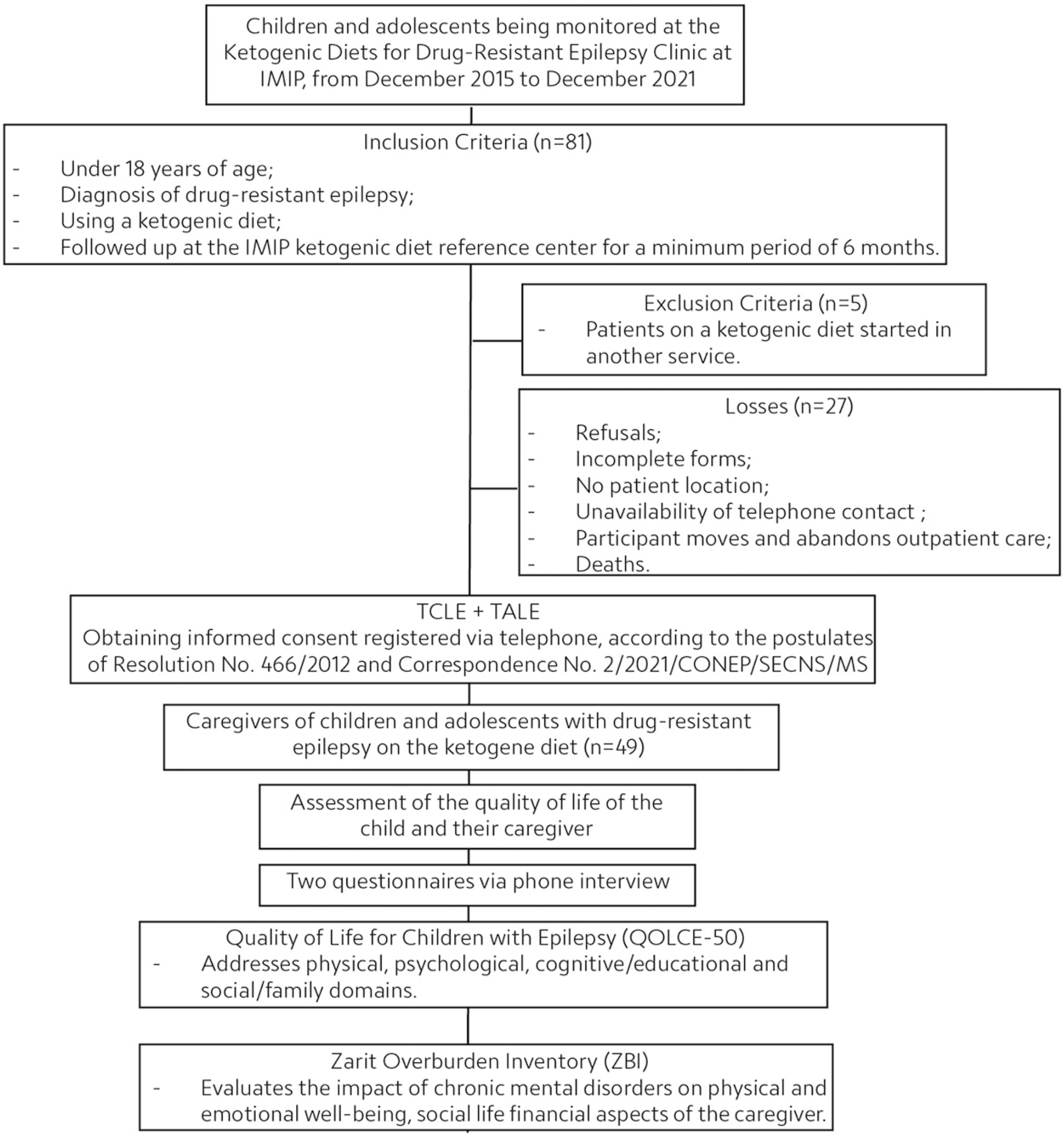
The work was approved by the IMIP Research Ethics Committee (CAAE: 50599821.0.0000.5201) and followed the recommendations of Correspondence nº 2/2021/CONEP/SECNS/MS (Brazil), which addresses research in digital media. The participants gave their consent in advance.

RESULTS

The sample consisted of caregivers of 49 children and adolescents' monitored at the ketogenic diet clinic. The capture and monitoring flowchart is described below (Figure 1).

The main caregiver was the mother (89.8%), 6.1% was the father and only 4.1% were other relatives, such as grandparents or uncles. Regarding the education of these caregivers, almost half of the sample (44.9%) had 12 years or more education.

Table 1 shows the main characteristics of the children and adolescents cared for. Approximately 2/3 (61.2%) were male, with extreme range ages of 5 months and 17 years, median of 4.4 years. The rate of frequency distribution was similar in the four age groups used (<2 years, from 2 to 4, from 5 to 10 and from 11 to under 18 years). The majority came from Recife and the metropolitan region (51.0%).



Children and adolescents being monitored at the Ketogenic Diets for Drug-Resistant Epilepsy Clinic at IMIP, from December 2015 to December 2021

Inclusion Criteria (n=81)

- Under 18 years of age;
- Diagnosis of drug-resistant epilepsy;
- Using a ketogenic diet;
- Followed up at the IMIP ketogenic diet reference center for a minimum period of 6 months.

Exclusion Criteria (n=5)

- Patients on a ketogenic diet started in another service.

Losses (n=27)

- Refusals;
- Incomplete forms;
- No patient location;
- Unavailability of telephone contact ;
- Participant moves and abandons outpatient care;
- Deaths.

TCLE + TALE

Obtaining informed consent registered via telephone, according to the postulates of Resolution No. 466/2012 and Correspondence No. 2/2021/CONEP/SECNS/MS

Caregivers of children and adolescents with drug-resistant epilepsy on the ketogene diet (n=49)

Assessment of the quality of life of the child and their caregiver

Two questionnaires via phone interview

Quality of Life for Children with Epilepsy (QOLCE-50)

- Addresses physical, psychological, cognitive/educational and social/family domains.

Zarit Overburden Inventory (ZBI)

- Evaluates the impact of chronic mental disorders on physical and emotional well-being, social life financial aspects of the caregiver.

Figure 1 – Flowchart of participants' capture and monitoring.

It was also observed that 83.7% of families had a per capita income of less than 1 Minimum Wage (MW), considering that the year 2022 minimum wage in Brazil was R$ 1.212,00 (one thousand, two hundred and twelve *reais*). The years of schooling were not considered for the 24 (49.0%) children under five years of age; ten were over five years old, but did not know how to read, write and interpret; ten had up to four years of study and five between five and eight years schooling (Table 1).

The results obtained in the QOLCE-50 are presented in Table 2 in the form of minimum and maximum values, median and interquartile range in the different domains according to the parents' perspective regarding their children's quality of life. Minimum scores in the cognitive/educational domain were observed, since approximately half of our sample was made up of children under 5 years of age who did not know how to read, write and interpret. Next, the most damaged domain was the physical (median=52.8, Q1=47.2; Q3=61.1) and the most preserved was the psychological (median=77.8; Q1=70.8; Q3 =83.3).

Table 1 – Sociodemographic characterization of caregivers and 49 children and adolescents with drug-resistant epilepsy undergoing ketogenic therapy at *Instituto de Medicina Integral Prof Fernando Figueira* in the period 2015-2021, Recife (PE), Brazil.

Variables	n	%
Gender		
Male	30	61.2
Female	19	38.8
Age of initiation of the ketogenic diet (years)		
<2	13	26.5
2–4	13	26.5
5–10	11	22.5
11–17.9	12	24.5
Origin		
Recife and metropolitan region	25	51.0
Interior of Pernambuco	19	38.8
Other States	5	10.2
Per capita family income in minimum wage (MW)		
<1 MW	41	83.7
1–2 MW	3	6.1
>2 MW	5	10.2
Primary Caregiver		
Father	3	6.1
Mother	44	89.8
Others	2	4.1
Education (years completed)		
Of child		
Not applicable*	24	49.0
Illiterate**	10	20.4
≤4	10	20.4
5 to 8	5	10.2
Of caregiver		
Illiterate	1	2.0
≤4 years	2	4.1
5 to 8	3	6.1
9 to 11	21	42.9
≥12	22	44.9

Note: *Children ≤5 years of age; **Children >5 years old, who cannot read, write and interpret.

Table 2 – Scores referring to the Quality of Life of Children with Epilepsy domains, according to the perspective of caregivers of 49 children and adolescents with drug-resistant epilepsy undergoing ketogenic therapy at *Instituto de Medicina Integral Prof Fernando Figueira* in the period 2015-2021, Recife (PE), Brazil.

Quality of Life in Childhood Epilepsy	Median	Q1; Q3	Min–Max
Physical Domain	52.8	47.2; 61.1	30.6–80.6
Psychological Domain	77.8	70.8; 83.3	62.5–17.5
Sociofamily Domain	67.9	53.6; 75.0	39.3–100
Cognitive/educational domain	37.50	34.4; 60.9	32.8–89.1

Regarding quality of life and caregiver burden, more than half of the sample (55.1%) was considered to have moderate to severe burden, followed by 36.7% as mild to moderate burden (Table 3).

Table 3 – Classification of the Zarit Overload Inventory scale, referring to the caregiver burden of children and adolescents with drug-resistant epilepsy undergoing ketogenic therapy at *Instituto de Medicina Integral Prof Fernando Figueira* in the period 2015-2021, Recife (PE), Brazil.

Zarit Overload Inventory	n	%
Little or no overload (0 to 20 points	2	4.1
Mild to moderate (21 to 40 points	18	36.7
Moderate to severe (41 to 60 points	27	55.1
Severe overload (61 to 88 points	2	4.1

A comparison was made between the average global quality of life according to the burden reported as being mild to moderate by caregivers (average global quality of life=125.6±3.7) with moderate to severe burden (average=117.3±2.65) with p=0.063.

DISCUSSION

Children/adolescents' poor quality of life and increased caregiver burden were evident, interfering with the daily life and personal relationships of the guardians. Instruments for measuring quality of life must evaluate both subjective and objective aspects, both influenced by the patient's degree of cognition which, in the case of refractory epilepsy, is commonly hampered. Therefore, caregivers' reports become extremely important [15]. In our study, patients presented with refractory epilepsy and had significant cognitive deficits; therefore, the instruments applied to the caregivers, such as the QOLCE-50 and ZBI, are the main source of information available about the child's quality of life and the burden on caregivers.

Regarding the characteristics of the 49 children and adolescents with drug-resistant epilepsy whose caregivers, mostly males, participated in this study, are in line with the literature that indicates a slight predominance of this gender in relation to females, in the cases of epileptic juvenile patients [16,17].

As for family income, the *Instituto Brasileiro de Geografia e Estatística* (Brazilian Institute of Geography and Statistics) [18], in its Continuous National Household Sample Survey, estimated the average monthly income for the Brazilian population at R$ 2,265.00 (two thousand, two hundred and sixty-five reais) in 2021. Although the study population earning was below-average, these data correspond to the profile of the population served at the IMIP Ketogenic Diet Outpatient Clinic, which is composed of patients using the Unified Health System (Government Health Service). Furthermore, the below-average income may also be the consequence of one of the parents giving up their job to take comprehensive care of their child affected with severe epilepsy.

It is noteworthy that a large part of these families are supported by the Government disability allowance or the *Benefício de Prestação Continuada* (Continuous Payment Benefit), provided for in the *Lei Orgânica da Assistência Social* (Organic Social Assistance Law) and some people report having those benefits as their only source of income. This factor can impact the social, psychological, educational and physical aspects of the individual, and may even be the cause of the relatively poor quality of life of these patients, even when considering other variables assessed, as we shall discuss hereafter.

Around one third of the patients live in the interior of the State of Pernambuco and claim that they do not always receive social support to be able to have access to health care. These data coincide with data found in the literature, indicating that 60.0% of parents do not receive any help from the government and endure financial hardships due to the costs of medicines and trips they have to make from the place where they live to the city where the quaternary hospital where children are cared for is located [19].

Only approximately one third of the patients cared for had some level of education, which reflects the social contrast existing in the country and the lack of institutions prepared to teach children diagnosed with a chronic illness [20]. The inclusion of children with epilepsy must go far beyond their presence in the classroom; it must aim, above all, at learning and developing skills and potential for their psychomotor development. This low level of education tends to disqualify those patients and make it even more difficult for patients with severe epilepsy to enter the labor market in the future [20].

It was not possible to assess the quality of life of IMIP children and adolescents before the start of KT. However, there are some studies that provide comparative data on quality of life before and after therapy, indicating a significant improvement in quality of life in children undergoing KT treatment [21,22]. In the literature, the clinical efficiency of ketogenic therapy appears relevant, and the reduction in epileptic seizures is estimated to be greater than 50.0%. However, there are cases of patients who are less responsive to KT, and despite there being no reduction in the number of seizures, there is a clear improvement in their intensity, with significant advances in cognitive and neuropsychomotor development, behavior and quality of life of the patient and family, justifying the maintenance of the treatment [23].

The QOLCE-50 and ZBI questionnaires were applied to the main caregivers, most of whom were mothers, which is in accordance with the Brazilian tradition of the mother being the person prominently in charge of taking care of children and adolescents with chronic illnesses [24]. In our society, the issue of the female figure assuming, differently from men, separate roles in her daily life or being culturally induced to reconcile work activities, inside and outside the home, is indeed well-grounded [25,26].

According to the findings in the literature, the results obtained through the application of the QOLCE-50 showed that one of the domains considered to be most affected was the physical domain. This dimension evaluates the essential elements for a child's good physical health, vitality and energy for physical activities, quality of rest and sleep and opportunities for leisure and sport; which are possibly jeopardized due to the severity of the clinical condition [13].

A survey carried out with parents on the quality of life of uncontrolled epileptic seizures children showed that the damage to the child's quality of life was significantly greater in the physical domain, when compared to the responses of parents with children with controlled seizures. The fact that children present daily crises in an age range of important acquisitions in neuropsychomotor development may be signaling a greater physical impairment for those children [27].

There is a shortage of Brazilian research on caregivers, as the patient is always given priority. Caring for someone with a chronic illness is a somewhat complex activity, which often causes overload for the caregiver, even more so if this caring relationship is between mother and child [28]. In a literature review, it was demonstrated that questionnaires answered by closer people (such as parents or family members) of chronic diseases patients, were generally similar, but the quality of life is underestimated when compared with the answers provided by the patients themselves [29]. In the case of children who are not able to provide information about their quality of life due to age, health status or functional capacity, the only way to obtain the assessment is through complementary sources, such as that of caregivers [15].

In our study, most caregivers responding to the questionnaire, justified that the burden of care was generally associated with the child's developmental delay and multiple impairments: cognitive, motor, pulmonary, gastrointestinal, orthopedic as well as sleep disorders and often with mobility restrictions demanding the use of a wheelchair. Concordant data in the literature report that the fact that children are totally dependent creates a greater burden on the physical well-being of caregivers, as they have an exhausting routine and spend heavy physical efforts daily [30].

Some authors enhance that caregiver's physical and/or psychological symptoms directly interfere with their ability to deal with stressful situations, causing a greater feeling of overload. Furthermore, the most jeopardized aspects in the care process were the development of stress, depression, anxiety and the worsening of quality of life [31,32].

The presence of a social support network can help family members to overcome adversities. In line with our study, some authors state that when interviewing caregivers, different responses regarding the burden may be given, and this fact can be influenced by the social and emotional support network that caregivers have available [33,34].

A difference was observed when comparing the average global quality of life between caregivers who reported mild to moderate burden and those who reported moderate to severe burden; however such difference was not statistically significant, probably due to the small sample size.

This study has as a limitation: the small size sample, which forestalled a multivariate analysis of subgroups, as there was a significant number of losses due to lack of information in the clinical records or the unavailability of a contact telephone number. Furthermore, another important limitation was that data collection took place during the COVID-19 pandemic period, an important milestone that may have generated impacts on quality of life beyond those that would perhaps be expected solely from dietary treatment or the disease itself.

One of the strengths of our study is the analysis of the quality of life of patients on ketogenic therapy and the comparison with the burden reported by caregivers. Comparisons of quality of life before and after ketogenic therapy could add information, but such comparison was not performed in the present study as the application of the quality of life questionnaire is not part of the current outpatient care protocol.

Therefore, for future investigations, it is highly advisable to conduct a multicenter study. This approach would not only allow for a more comprehensive analysis, but would also facilitate data comparison within a larger and diverse sample of this specific population, which would yield results with greater statistical significance.

CONCLUSION

Juvenile drug-resistant epilepsy implies in a negative impact on the caregiver's quality of life, since children are seriously impaired and dependent, demanding exclusive attention thus causing physical and emotional overload. Our results show that it is up to professionals in the multidisciplinary health team, who work with the child as well as with family members and caregivers, to identify situations in which caregivers need to be advised and guided, offering informative and technical support and exchanging experience and appropriate support for care.

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