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Abstract

Background: Phenylketonuria (PKU) is one of the most common metabolic disorders. Parents of
children with the disease are at risk of physical problems and mental disorders.

Aims: This study aimed to determine the quality of life of parents of children with PKU in Tehran.

Methods: This study was conducted on 240 parents of children with PKU who were referred to the Children's Medical Center, Mofid Hospital and Ali Asghar Hospital in 2015. Data were collected by World Health Organization Quality of Life Questionnaire. Questionnaires were analyzed by SPSS. 21. ANOVA, t-Test, Pearson’s correlation coefficient and multiple linear regressions at the significant level of 0.05.

Results: The mean age of parents was 36.82 ± 7.8. Of the participants, 55% were mothers and 45% were fathers. Quality of life in parents with psychological, social and environment aspects were lower than average. There was significant relationship between physical dimension and age of disease diagnosis (P = 0.044). There was significant relationship between psychological dimension and parents age (P = 0.019), child age (P = 0.007) and education level of parents (P = 0.033). There also was significant relationship between social dimension and parents age (P = 0.003), marital status (P = 0.025), education level of parents (P = 0.003), parents’ job (P = 0.022), child age (P = 0.007), and age of disease diagnosis (P = 0.026). There was significant relationship between environment dimension and place living (P = 0.034), education level of parents (P = 0.039), and child age (P = 0.049).

Conclusion: Due to low levels of quality of life in studied parents and problems that arise in families of children with PKU, education and more financial support for them are suggested.

Keywords: Quality of life, parents, PKU, Iran

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Introduction

Phenylketonuria (PKU) is an autosomal recessive disorder of amino acid metabolism. The enzyme phenylalanine hydroxylase (PAH) is necessary to metabolize phenylalanine (Phe) to tyrosine in liver. This enzyme is defective in PKU. It leads to Phe increase in the blood and the brain (1). High levels of Phe in the plasma cause mental retardation, seizures, behavioural difficulties, and motor delay and retarded language development. Although children with PKU who are treated early have average intelligence, they differ in cognitive performance when compared to their healthy peers. Academic and cognitive functions of children with PKU are significantly lower than peers in the control group (2). It has also been reported that there are mental afflictions such as low self-esteem, less motivation, loss of independence and reduced social confidence in children. Adolescents and adults may be at risk of depression, anxiety and social isolation (3).

Lifelong dietary treatment is recommended to prevent mental retardation from birth for all patients with PKU. Treatment includes severe restriction of natural protein and supplementation with the Phe-free formula (4). Diet for PKU is considered a heavy burden for patients and health staff, and management of PKU can be time-consuming for both adult patients and caregivers of children. In addition, Phe intake should be monitored carefully by regular blood tests. PKU may impose economic burden to patients and caregivers. These costs include direct costs related to the use of resources in the management of disease such as low-protein foods, supplements, medications, laboratory monitoring, and visits to healthcare services, and also indirect costs of productivity loss (5).

During the last two decades, favourites to assess and improve the quality of life (QoL) of chronic patients have increased significantly (6). Health-related quality of life (HRQoL) can be considered as the impact of disease and treatment on physical, psychological, social and welfare dimensions (7). Health-related QoL can be used in the evaluation of disease outcomes, use of effective interventions and assessment of the effectiveness and benefits of different treatments, healthcare service evaluation, and health policy (8).
With early detection and treatment, PKU is a relatively benign disease, without physical symptoms and with fewer hospitalizations (9). However, to monitor regular blood tests, the need to adapt to a more complex diet, the occurrence of neurological symptoms and stigma associated with diagnosis of a congenital metabolic disorder, are the characteristics that we assume PKU may affect patients’ QoL (10).

Quality of life assessment in these parents can identify those with undiagnosed disorders due to the chronic burden of disease of their children. In addition to the usual stress associated with caring for a newborn baby, parents have to cope with greater demands such as the grief and despair of having a sick child, and learning to manage diet (11). Parents of children with chronic diseases are at risk of disorders and mental problems and have lower health status than parents of healthy children (12).

In this regard, a study carried out on the comparison between the QoL of parents of sick children and parents of normal children showed that more than half of those of children with chronic diseases are at risk of QoL impairment (13). Considering the relatively high incidence of PKU in the Islamic republic of Iran (2) and the lack of studies on the QoL in parents of children with PKU, this study aimed to determine the QoL of parents with children diagnosed with PKU in Tehran Province.

Methods

This cross-sectional study was conducted in three hospitals: Children’s Medical Center, Mofid Hospital and Aliasghar Hospital in 2015. These three government hospitals were the only children's hospitals that provided specialized services to patients with PKU in Tehran Province. Using census sampling, all 240 parents (mother or father) referred to children’s hospitals in Tehran, from March to December 2015, were entered into the study. The inclusion criteria included Iranian nationality, father or mother of patients with PKU, residence in Tehran Province, and ability to write and read. Exclusion criteria were unwillingness to participate in this research and inability to remember the events which occurred in the last 4 weeks.

The World Health Organization Quality of Life- Brief (WHOQOL-BREF) was used as the HRQoL instrument. This 26-item questionnaire included four domains: physical health (7 items), psychological health (6 items), social relationships (3 items) and environment (8 items), and also consisted of two general questions about overall QoL and overall satisfaction of health. Each item was rated on a five-point Likert scale from 1 to 5 and according to the manual, raw scores were converted to transformed scores (14). The mean score of items was used to compute the domain score. A higher score indicated a better QoL. Validity and reliability of the Iranian version of this questionnaire have been proven in the Farsi language (15–17). In this
study, the validity of the instrument was confirmed by expert opinion and its reliability was acceptable with Cronbach’s alpha equal to 0.95.

**Ethical considerations**

The study was approved by the Committee for Ethic in Faculty of Public Health of Shahid Beheshti University of Medical Sciences (Code SBMU.REC.1393.812). The study purpose and procedure was explained to children’ parents and verbal informed consent was obtained. Data were analyzed by IBM SPSS Statistics version 22.0. A significance level was set at $P < 0.05$. Mean and standard deviation (SD) were computed as descriptive statistics for demographic variables. Pearson's correlation coefficient, ANOVA, t-Test and multiple linear regressions using the "enter method" were performed as statistical tests.

**Results**

Of the 240 participants, 55% were mothers and 45% were fathers. The mean ages of parents and their children were 36.82 ± 7.8 and 8.73 ± 8.1 years respectively. 89.6% of parents were married, 49.8% were housewives, 42.5% had high school education, 49.3% earned US$ 295 or less per month, and 51% lived in 22 districts of Tehran city. 55.8% of children were boys and 44.2% were girls. Only 52.8% of patients were diagnosed in a timely fashion. The average age of diagnosis in patients was 14 ± 26 months (1 day–9.8 years). The demographic characteristics of parents and patients with PKU are shown in Table 1.

Most of the participants (43.6%) reported an average level of QoL overall and had little satisfaction with their health status. The mean score for Overall QoL was 2.92 ± 1.1 (1–5), and mean score for satisfaction of health was 2.51 ± 1 (1–5). The mean scores of physical health, psychological health, social relationships and environment levels in parents were 21.23 ± 2.5, 17.53 ± 4.3, 7.96 ± 2.4 and 19.79 ± 2.9 respectively. Highest score was shown for physical health (21.23 ± 2.5) and the lowest mean score was shown for environmental health (19.79 ± 2.9). Quality of life in parents with psychological, social and environment aspects were lower than average. Mean scores of WHOQOL-BREF domains are shown in Table 2.

There was significant relationship between physical dimension and age of disease diagnosis ($P = 0.044, r = -0.133$). There was significant relationship between psychological dimension and parents age ($P = 0.019, r = -0.158$), child age ($P = 0.007, r = -0.183$) and education level of parents ($P = 0.033$).

There was also a significant relationship between social dimension and parents age ($P = 0.003$, ...
r = 0.2), marital status (P = 0.025), education level of parents (P = 0.003), parents’ employment (P = 0.022), child’s age (P = 0.007, r = -0.188), and age at disease diagnosis (P = 0.026, r = -0.146). There was a significant relationship between environment dimension and place of living (P = 0.034), education level of parents (P = 0.039), and child’s age (P = 0.049, r = -0.130). There was no significant relationship between QoL domains and studied hospitals, sex of parents, household income and sex of child. Variables related to QoL domains are shown in Table 3.

The multiple linear regression analysis identified the psychological dimension including marital status of parents and child’s age; in social dimension comprising age of parents, education level of parents, and child’s age; and finally, in environment dimension including education level of parents and place of living as predictive for QoL.

**Discussion**

The purpose of this study was to evaluate the QoL in parents of children with PKU in Tehran Province. The findings of this study showed a low level of QoL in parents of children with PKU.

A study in the Netherlands found low HRQoL in the parents of children with PKU (18). In a survey conducted in the Islamic Republic of Iran, caregivers of patients had a lower QoL level than the general population (19). In contrast to this study, other results were not consistent (7,12). Mentally retarded children in the family, in addition to imposing psychological stress, can causes many physical ailments such as pain and a higher incidence of mental disorders such as depression and anxiety in families, leading to reduced QoL of mothers (20–21). The reasons for differences between this study and others could be due to variations in population, social and cultural conditions of communities, and presence of support organizations.

The findings indicate that parents with older children had lower QoL with regard to psychological health. This was not consistent with results of other studies (7,12). Reasons could be parents not coping with the condition of their children and concern for their future. As children grow older, adherence to treatment becomes difficult, increasingly because meals have to be well planned (22). Non-compliance with diet in low- and middle-income countries is due to the lack of experienced support centres, large families, the neglect of parents, financial constraints, Low perception of risk in parents, and low supply of low-protein products (23). Parents with early diagnosed children had better QoL with regard to physical and psychological health. Patients who are treated early, generally indicate a favourable outcome along with normal development.
IQ in PKU patients treated at an early age is defined within the normal range (24). Therefore, patients with late diagnosis are faced with mental and physical disabilities that impact all family members. The results indicated that older parents had better QoL with regard to the social dimension. It appears that more experience, communication with other parents, and setting up non-governmental organizations by some parents play an important role. Better educated parents had improved QoL with regard to psychological and environment dimensions. A study in the United Kingdom found that there was a positive relationship between higher educated parents and a lower level of blood phenylalanine in children (25). A study in Sweden indicated that education level is significantly associated with blood phenylalanine concentration (26). It appears that better educated parents are more adept at managing anxiety, fear and depression and usually live in a better environment. Parental education with multiple sources of psycho-social support and a positive home environment are likely to be associated with protection against depression (23).

**Limitations**

The limitations of this study were missing data in certain demographic variables such as income and employment, due to unwillingness of participants to share such information. In addition, this cross-sectional study does not measure causality. Other study limitations include patients' absence from the hospital and unwillingness of some parents to complete questionnaires. These problems were largely resolved with repeated follow-up visits that explained objectives of the study to parents and reassured them of confidentiality of information. In the other hand, despite the rareness of the disease, a large number of parents referring to three large children's hospitals can be the strength of the study.

**Conclusions**

There were low QoL levels in parents of children with PKU. The results of this study can be used to design appropriate interventions for parents to cope better with the problem of their diagnosed child and the effects. Family education can increase awareness and improve attitudes by parents. In this regard, the latest information on PKU should be available. Also, more financial support for families, more involvement by support organizations to help fund PKU patients, and acceptance of the medical costs associated with PKU patients by insurance organizations would be beneficial.

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