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Brief Report

Parents' Perspectives of Children with PKU: Assessing Parental Stress and Psychological Adjustment

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Abstract: Phenylketonuria (PKU) is an inborn error of metabolism resulting from a deficiency of phenylalanine hydroxylase enzyme activity. Diagnosis in the first days of life allows early initiation of dietary therapy. The maintenance of this treatment raises demanding management issues in everyday life, often resulting in a psychological burden for patients and families. In this brief report, we aimed to investigate parenting stress and parents' perceptions of their child's adjustment, focusing on correlations between the perspectives of mothers and fathers. We conducted an observational study, enrolling parents of pediatric patients (aged 2–18) diagnosed with PKU and treated from birth. A total of 20 parenting couples of 20 PKU-affected children were included. The mean Phe level was 301.60 µmol/L (SD = 128.39). Most PSI-SF and SDQ-P scores were below the clinically relevant threshold. Significant correlations emerged between paternal parenting stress and the child's Phe level and, additionally, between mothers' and fathers' scores. Parents of PKU-affected children reported acceptable levels of parenting stress and their children's psychological adjustment. However, fathers perceived greater stress in maintaining adequate Phe levels for their children. Our results suggest a similar perspective of both parents in relation to their child's psychological adjustment. Therefore, the psychological well-being of PKU patients and their parents must be monitored to provide family-centered care and psychological support in the process of accepting a rare disease.

Keywords: phenylketonuria; PKU; parents; parenting stress; psychological adjustment

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1. Background

Phenylketonuria (PKU) is a rare autosomal recessive metabolic disorder that affects about one in every 10,000 births in Europe [1]. PKU is determined by a deficiency in the activity of the enzyme phenylalanine hydroxylase (PAH), which converts phenylalanine (Phe) into tyrosine (Tyr). A deficiency in the activity of this enzyme results in increased levels of phenylalanine and reduced levels of tyrosine. Early diagnosis through neonatal screening and prompt initiation of therapy prevents the development of severe neurological damage such as intellectual disability, motor disturbances, psychiatric symptoms, aberrant behavior, and epilepsy [2]. The three known disease subtypes range in severity from hyperphenylalaninemia (HPA) (blood Phe at birth: 120–600 µmol/L) to mild PKU (blood

Phe at birth: 600—1200 µmol/L) and classic PKU (blood Phe at birth: 1200 µmol/L) [3]. A low-Phe diet based on restriction of natural protein, integration of Phe-free protein substitutes, and frequent Phe monitoring are the mainstays of treatment of mild and classic PKU, with the aim being to promote normal brain development and cognitive function [3]. Adherence to the diet requires a significant amount of time and additional resources from families [4,5]. Other subtypes of PKU also imply a psychological burden: indeed, a study by Becsei and colleagues showed that people with mild PKU had higher anxiety prior blood tests, which may be due to their more limited engagement in disease management [6]. Therefore, PKU can impact the psychological well-being of people with PKU and their families.

Moreover, patients with PKU often exhibit emotional problems, low self-esteem, low achievement motivation, decreased autonomy, and reduced social competence. Indeed, adult and adolescent patients may present mood and anxiety disorders and social withdrawal [7,8].

This study investigated parental stress and perceived problems in children's psychological adjustment among the parents of children with PKU diagnosed through newborn screening (NBS) and receiving treatment. The main objectives were to explore possible correlations between parents' psychological well-being and Phe levels and to explore parental differences in their subjective perception of stress associated with disease management and of their child psychological adjustment.

2. Materials and Methods

2.1. Patients

Forty parents of twenty pediatric patients (age 2–18 years) with classic phenylketonuria (Phe level > 360 µmol/L at neonatal screening) were enrolled between June 2022 and March 2023 at the Inherited Metabolic Diseases Department of the University Hospital of Padua. All of these PKU patients had commenced dietary therapy in the first days of life, avoiding several neurological issues.

We did not consider parents with communication difficulties related to language of origin. Parents' sociodemographic data and biochemical data were collected, including plasma Phe and Tyr levels at outpatient visits and Phe and Tyr values measured in dried blood spots collected and sent from home (Table 1).

Table 1. Sociodemographic data for the study sample.

	Fathers	**Mothers**
Ethnicity		
Western European	19	17
African	1	1
Asian	0	1
Latin-American	0	1
Occupation		
Employed	19	15
Homemaker	1	4
Unemployed	0	1
Scholastic level		
Lower secondary school level	3	3
Upper secondary school level	9	10
Bachelor's degree or higher	8	7

Table 1. *Cont.*

	Fathers	Mothers
Marital status		
Married	15	15
Cohabiting	1	1
Divorced	3	3
Unmarried	1	1

The 20 patients included 19 Western European infants and 1 Asian infant, of which 10 were firstborns; 1 child had a sibling with PKU. The patients had a mean (± SD) Phe level of 302 (±128) µmol/L based on a mean (±SD) of 25 (±16) dried blood spots tested.

The research survey and questionnaires were administered during routine care and required approximately 20 min to complete.

The principles of good clinical practice (GCP) were adhered to throughout the study, in accordance with the Declaration of Helsinki (as amended) and the International Conference on Harmonization (ICH)/GCP guidelines. The study was performed in compliance with local regulatory requirements (Ethics Committee Approval No. 5637/AO/23, University Hospital of Padua).

2.2. Materials

2.2.1. Strengths and Difficulties Questionnaire-Parent Report (SDQ-P)

The Strengths and Difficulties Questionnaire-Parent Version (SDQ-P) [9,10] consists of 25 items with which parents assess their child's level of psychological adjustment, made up of four subscales that assess perceived difficulties (Emotional Symptoms, Conduct Problems, Hyperactivity–Inattention, and Peer Relationship Problems). A Total Difficulties Score (TDS) is calculated by summing the scores for these four subscales, where higher scores indicate more perceived problems in the child's psychological adjustment. An additional subscale assesses the perceived level of positive social behavior (Prosocial Behaviors), where higher scores indicate the perception of greater positive social behavior.

2.2.2. Parenting Stress Index-Short Form (PSI-SF)

The Parenting Stress Index-Short Form (PSI-SF) [11,12] is a 36-item self-report assessing parenting stress made up of three subscales (Parental Distress, Parent–Child Dysfunctional Interaction and Difficult Child), which are summed to provide a total score. Higher scores indicate higher levels of parental stress.

2.3. Statistics

Statistical analyses were performed using JASP software (version 0.17.1) [13] with a significance threshold set at $p < 0.05$. The cut-off scores for the SDQ-P and PSI-SF were calculated. Three scoring ranges were identified for the SDQ-P (normal, borderline, and abnormal) [10] and two for the PSI-SF (normal and abnormal) [14]. Controlling for the children's ages, Spearman's rho was then used to assess correlations between the variables: mean Phe levels, SDQ-P, and PSI-SF.

3. Results

A total of 20 parents provided responses to the research survey and questionnaires during routine care at the Inherited Metabolic Diseases Department of the University Hospital of Padua. All the parents interviewed participated actively and with interest in this research.

Correlations were explored between the child's metabolic control (Phe levels) and parental outcomes on the SDQ-P and PSI-SF subscales. Additional analyses investigated correlations between the SDQ-P and PSI-SF scores and between results for mothers and fathers.

3.1. Parenting Stress and Perception of the Child's Psychological Adjustment

3.1.1. Mothers

Most of the mothers had SDQ-P total scores below the clinically significant threshold when evaluating their child's psychological well-being (84.21%). A similar pattern was observed with the SDQ-P subscales, for which more than 85% had values in the normal range. All mothers had non-clinical levels of parenting stress, as reflected by their total scores and scores on each subscale.

3.1.2. Fathers

Similar results were obtained with fathers. Most reported that their children exhibited adequate psychological adjustment (88.24%). The same pattern was observed on the SDQ-P subscales, with more than 70% scoring in the normal range. With regard to parenting stress among fathers, all the participants reported non-clinical values on the total score and on each subscale.

3.2. Phe Values, Parenting Stress, and Parental Perception of the Child's Psychological Adjustment

3.2.1. Mothers

No significant correlations emerged between a child's blood Phe levels and the mother's perception of the child's psychological adjustment or her reported parenting stress (both $p > 0.05$).

3.2.2. Fathers

There was no correlation between a child's blood Phe levels and that child's psychological adjustment as reported by the father ($p > 0.05$). However, the "Total PSI-SF Score" among fathers was significantly and negatively associated with mean Phe values ($r = -0.532$; $p = 0.034$). Moreover, a significant negative association emerged between the PSI-SF subscale "Difficult Child" and mean Phe levels ($r = -0.641$; $p = 0.007$).

3.3. Parenting Stress and Perception of the Child's Psychological Adjustment: Comparing Mothers and Fathers

Significant correlations were found between six scores for the mothers' and fathers' psychological parameters (Table 2), with the strongest correlation being for the PSI-SF "Parent–Child Dysfunctional Interaction" subscale ($r = 0.778$; $p < 0.001$).

Table 2. Correlations between SDQ-P or PSI-SF scores for fathers and mothers.

Father	Mother	Correlation
SDQ-P "Peer Problems"	SDQ-P "Total Difficulties"	($r = 0.485$; $p = 0.049$)
PSI-SF "Total Score"	PSI-SF "Parent–Child Dysfunctional Interaction"	($r = 0.527$; $p = 0.036$)

4. Discussion

An inherited metabolic disease can be a significant burden for patients and their families. The complexity of PKU dietary therapy and the need for frequent biochemical testing increase the difficulties associated with daily management of the disease. This can result in anxiety and fear of not being able to control the course of the disease in an optimal manner [15]. Our results show that the stress experienced by parents and the perception of their child's psychological adjustment were in the normal range for mothers and fathers in our cohort. In accordance with Shaji et al. [16] and Thiele et al. [17], these positive results could be the consequence of the medical and psychological support provided by the multi-professional team that assists caregivers in managing their children's PKU and offers the possibility of recognizing and processing emotions and experiences. Physicians, dieticians, and psychologists work together, establishing shared communication to alleviate parental stress, which starts at diagnosis and lasts throughout the patient's life.

Borghi and colleagues [18] highlighted associations between better mental health among parents and better adherence to diet and biochemical control in their children. Moreover, they investigated psychological differences between mothers and fathers of children with PKU, but no relationship between the mothers' and fathers' perceptions and experiences with the disease emerged.

We evaluated the correlation between the level of parenting stress among mothers and fathers as well as their perceptions of their children's psychological functioning. The results suggest that they perceive similar difficulties in their children's daily management, especially regarding a somewhat dysfunctional interaction with their children. Indeed, various correlations between mothers' and fathers' perspectives on the psychological adjustment of their children suggest that they have a similar point of view on their children, and this suggests that parents agree on the general psychological well-being of their children.

In our study, in contrast to a previous work [18], higher parental stress in fathers was correlated with lower Phe levels in children. Fathers seemed to perceive greater fatigue in the process of maintaining adequate Phe levels in their children. Specifically, the correlation with the scale "Difficult Child" on the PSI highlighted the fact that fathers reported higher stress in the management of behavioral difficulties in their children, frequently linked with more issues in the practical care of children's problems. This aspect could be related to the more limited engagement of the fathers in daily disease management, compared to mothers. This result is in line with the findings of a qualitative study related to psychosocial outcomes of parents of children with renal transplants [19]. The authors highlight the fact that fathers sometimes take less responsibility than mothers for mobilizing family-coping resources and are less involved in healthcare communication. Moreover, in a quantitative study by Weiner and colleagues (2001) [20], the authors underline the finding that the fathers experienced significantly elevated stress levels and distress compared to standardized norms. An extensive narrative review from 2012 [21] analyzing the contribution of fathers in the management of children with chronic conditions demonstrates that stresses associated with diagnosis and treatment were compounded by their expectation that they themselves should be "strong and silent". This approach is correlated with the tendency of fathers to express fewer feelings of sadness or vulnerability and consequently a failure to provide them with the support they need.

Furthermore, this review highlights how promoting the involvement of fathers was not previously viewed as a priority in workplace, healthcare, or child-care legislation or provision. Strategies for supporting the role of fathers are needed, such as health professionals being available to meet with fathers during evening or weekend hours or using the internet for information sharing. Based on these results, we underline the importance of evaluating the role of fathers and mothers separately in children with PKU.

5. Conclusions

The strict requirement for adherence to dietary therapy in PKU underscores the need to establish patient- and family-centered care at diagnosis, with regular follow-up visits by the metabolic team. This approach can support parents in the process of accepting a rare disease and help to sustain them through a lifelong treatment process.

There is a need for future studies to better understand the correlation between parenting styles and aspects of chronic disease management of children with phenylketonuria, specifically focusing on the engagement of fathers in the management of their children's PKU.

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