

## Phenylketonuria at HMIMV Rabat: About 15 Cases

A. Tbatou<sup>1\*</sup>, R. Abilkassem<sup>1</sup>, A. Laaraj<sup>1</sup>, M. Kmari<sup>1</sup>, A. Ourrai<sup>1</sup>, A. Hassani<sup>1</sup>, A. Agadr<sup>1</sup><sup>1</sup>Service de pédiatrie, Hôpital militaire Mohamed V Rabat, MarocDOI: [10.36347/sjmcr.2023.v11i10.041](https://doi.org/10.36347/sjmcr.2023.v11i10.041)

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\*Corresponding author: A. Tbatou

Service de pédiatrie, Hôpital militaire Mohamed V Rabat, Maroc

### Abstract

### Case Report

Phenylketonuria is a disorder of amino acid metabolism causing an intellectually handicapping disease with cognitive and behavioral disorders, caused by elevated serum levels of phenylalanine. The primary cause is phenylalanine hydroxylase deficiency. Diagnosis is based on the detection of elevated phenylalanine and normal or low tyrosine levels. Treatment is lifelong dietary restriction of phenylalanine. The prognosis is excellent under treatment.

**Keywords:** Phenylketonuria, children, aminoacidopathy, phenylalanine, Diagnosis, Treatment, prognosis.

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## INTRODUCTION

Phenylketonuria is an aminoacidopathy resulting from a mutation in the phenylalanine hydroxylase (PAH) gene. Diagnosis is difficult in undetected patients, who may have a highly variable clinical presentation.

## OBJECTIVES

To study the epidemiological profile, clinical, paraclinical and therapeutic features of phenylketonuria in a Moroccan cohort of 15 patients.

## METHODS

Retrospective descriptive study of a cohort of 15 patients with phenylketonuria, managed at the HMIMV pediatric department between January 2006 and September 2019.

## RESULTS

Cohort of 15 patients from 13 families. The percentage of consanguineous marriages was 67% (10/15). The sex ratio was 0.66 (6/9). Patient ages ranged from 2 to 21 years, with a median age of 7.5 years. The median age at diagnosis was 3.5 years, with only one patient screened and treated at 1 month of age. Common symptomatology and examination data at the time of diagnosis were clear complexion in all patients, musty urine odor (13 cases), mental impairment (12 cases) behavioral disorder with agitation and hyperactivity (9 cases), autism spectrum disorder (3 CAS), convulsion (4 cases). Laboratory data showed an increase in phenylalanine in all cases. The electroencephalogram requested in 7 cases was abnormal in 4 cases, with a hypsarrhythmia pattern in 2 cases and generalized epileptic discharges in 2 cases. Treatment was essentially dietary, based on a phenylalanine-controlled diet.

**Table 1: Age at diagnosis and gender**

Age	Masculin	Féminin	Total %
< 12 mois	1	1	2 (13,3)
12-23 mois	1	4	5 (33,3)
2-4 ans	1	0	1 (6,6)
5- 18 ans	3	4	7 (46,66)

**Table 2: Clinical symptoms**

Signe clinique	Nombre de cas
Teint clair des cheveux	13 cas
Odeur de moisi des urines	13 cas
Retard mental	12 cas
Agitation et hyperactivité	9 cas
Convulsion	4 cas
Trouble de spectre autistique	3 cas
Eczéma	1 cas

**Laboratory data:** Increased phenylalanine in all cases.

**Table 3: Electroencephalogram (requested in 7 cases)**

Résultats EEG	Nombre de cas
Normal	3 cas
Pattern hypersarythmie	2 cas
Décharges épileptiques généralisées	2 cas

## DISCUSSION

Phenylketonuria (PKU) is a hereditary disease affecting amino acid (AA) metabolism. In around 98% of cases, it is linked to a deficiency of phenylalanine hydroxylase, the enzyme responsible for converting phenylalanine (PHE) into tyrosine. Blockage of this metabolic pathway leads to PHE accumulation in the blood and brain. This autosomal recessive disease results from mutations in the phenylalanine hydroxylase (PAH) gene, located on chromosome 12, at 12q24.1. Its prevalence varies from 1/4,000 to 1/40,000 in the most affected countries (Ireland and Iceland), and its incidence in France is 1/17,000, with around 50 cases detected every year. In Morocco, national data on the prevalence of PKU are not yet available. The diagnosis of PKU is usually made through systematic neonatal screening, which has been in place in France since 1972. On the other hand, diagnosis remains difficult for patients in countries where screening is not in place, such as Morocco. Clinically, untreated PKU is mainly characterized by severe neurological disorders: mental retardation, behavioral disorders, psychosis, flexion spasms and epilepsy. The electroencephalogram (EEG) is abnormal in 78% to 95% of cases. This neurological symptomatology is associated with dandruff disorders of the overall hypo-pigmentation type, including pale skin, blond hair and blue eyes (eczema is found in 20 to 40% of cases).

Neonatal screening is based on the determination of PHE in whole blood collected on a "Guthrie" card in the first days of life. Biological diagnosis is based on plasma PHE levels (isolated hyperphenylalaninemia). It can be confirmed by molecular study. Urinary bipterins and blood DHPR activity should be routinely measured to detect deficiencies in BH4 metabolism, and liver tests and plasma amino acid chromatography should be performed to rule out other causes of hyperphenylalaninemia. Treatment is essentially dietary. It is based on a low-phenylalanine diet. This diet remains the basis of current treatment, but we are seeing the emergence of therapeutic alternatives, some of which are effective (BH4, neutral amino acids, phenylalanine ammonia lyase (PAL) and, in the future, gene therapy. Treatment is aimed at controlling plasma PHE levels (< 5 mg/100 ml) for at least the first 10 years of life, with gradual relaxation thereafter.

## CONCLUSION

The early diagnosis of phenylketonuria and the good response to phenylalanine-controlled diets prompt us to advocate a national program of neonatal screening for phenylketonuria to prevent mental retardation in our country.

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