

Porphyria: analysis of register from Brazilian association of porphyria (ABRAPO)

Abstract

Background: The porphyria is a group of rare metabolic disorders that arise from deficiencies in the heme biosynthetic pathway. The prevalence in Europe is 1-2:100,000 inhabitants. These disorders occur mostly due to mutations in the genes encoding enzymes involved in heme production. They are classified and divided into acute (ALA Dehydratase Deficiency [ALADP], Acute Intermittent Porphyria [AIP], Variegated Porphyria [VP], Hereditary Coproporphyrinuria [HCP]), chronic (Congenital Erythropoietic Porphyria [CEP], Erythropoietic Porphyria [EPP], Porphyria Cutanea Tarda [PCT] and Hepato Erythropoietic Porphyria [HEP]). AIP is the most common form of hepatic porphyria and symptoms often begin after puberty and consist of acute neurovisceral signs, abdominal pain, vomiting, constipation, tachycardia, fever, hypertension and alterations in the central nervous system.

Aim: To study the porphyria frequency in Brazil by Associação Brasileira de Porfiria (ABRAPO- Brazilian Porphyria Association).

Methods: We study the frequency of porphyria in 439 cases of patients with porphyria diagnosis from ABRAPO from 2007 to 2015 and data were analyzed with Microsoft Excel® program.

Results: We analyzed 439 cases consisting of 74.2% female. 59% percent had been diagnosed with AIP, 22% PCT, 4% HCP, 4% EPP, 2.5% VP, 1.1% CEP, 0.9% HEP and 0.4% ALADP.

Conclusion: Our analysis revealed similar epidemiological characteristics as seen in the United States and United Kingdom. In Brazil, porphyria should be studied more carefully to assess, properly diagnosis and treatment.

Keywords: porphyria, acute porphyria, cutaneous porphyria

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Abbreviations: ABRAPO, associação brasileira de porfiria; ALADP, ALA dehydratase deficiency; AIP, acute intermittent porphyria; VP, variegated porphyria; HCP, hereditary coproporphyrinuria; CEP, congenital erythropoietic porphyria; EPP, erythropoietic porphyria; PCT, porphyria cutanea tarda; HEP, hepato erythropoietic porphyria

Introduction

Porphyria is a group of rare metabolic disorders. These disorders result in decreased activity of enzymes involved in the heme biosynthesis pathway, leading to an accumulation of porphyrins and its precursors.^{1,2} The prevalence in Europe is 1-2 cases per 100000 inhabitants (1-2:1000) and about 1:1000 in the northern region of Sweden. According to Bonkovsky HL et al.,³ characteristics of porphyria and its epidemiology is not yet well defined, but is observed to a greater prevalence in psychiatric patients (210:100000).^{4,5} The pathogenesis caused by mutations in genes encoding enzymes involved in heme biosynthesis is classified and divided into acute (ALA Dehydratase Deficiency [ALADP], Acute Intermittent Porphyria [AIP], Variegated Porphyria [VP], Hereditary Coproporphyrinuria [HCP]) and chronic (Congenital Erythropoietic Porphyria [CEP], Erythropoietic Porphyria [EPP], Porphyria Cutanea Tarda [PCT] and Hepato Erythropoietic Porphyria [HEP]).^{1,3,6}

AIP is autosomal dominant and the most common form of hepatic porphyria. The estimated prevalence is approximately

5:100000 in United States (US) and 1:75000 in Europe. Symptoms often begin after puberty and consist of acute neurovisceral signs, abdominal pain, vomiting, constipation, tachycardia, fever, hypertension and alterations in the central nervous system.⁷⁻⁹ HCP is an inherited autosomal dominant and rare recessive disorder type of hepatic porphyria. The prevalence in Denmark is approximately 2:100000.¹⁰ VP is an autosomal dominant genetic disorder with severe neurovisceral symptoms or chronic blistering skin lesions. The estimated prevalence in Finland is 1.3:10000 and in Europe in general is 0.3:100000. ALADP is the rarest type of porphyria and is an autosomal recessive disorder.^{10,11}

PCT is a porphyria that causes chronic blistering skin photo toxicity but has no neurological manifestation and is the most common type or form (estimated incidence of 1:10000 or 2-5:1000000 in the United Kingdom). Affected areas exposed to ultraviolet light result in skin fragility, atrophic scars and milium.^{7,8} CEP is a very rare autosomal recessive disease characterized by blistering cutaneous photosensitivity and is estimated to affect about 3:10000000 of the population in the UK.^{10,12} HEP is a rare form of cutaneous porphyria that occurs in both females and males worldwide. Cutaneous features increase severity leading to disfigurement. EPP is the third most common porphyria (10-20:100000) and the most common in children. It affects both genders but is more common in Orientals than Caucasians.¹⁰ Our objective was describing the epidemiological profile of porphyria from 2007 to 2015 using data from Associação Brasileira de Porfiria (ABRAPO) databases located in Curitiba/Paraná.

Materials and methods

We studied the frequency of porphyria in 439datas of patients with porphyria from 2007 to 2015 as listed in ABRAPO and analysed by Microsoft Excel® program. We evaluated gender, types of porphyria and mean age at diagnosis for each type. We correlated absolute and relative frequencies between males and females, absolute and relative frequencies with each type of porphyria, absolute frequency of each type and mean age at diagnosis in both genders.

Results and discussion

439 patients were analysed in this study 74% (326/439) were female (Figure 1) (Table 1). Results studied by Szlendak et al.⁶ (17/25cases) and Bonkovsky et al.³ (88/108cases) agreed with these findings. The mean age at diagnosis for each type was 40years for AIP, 44 years for PCT, 38years for HCP, 38years for CEP and 39years for VP (Table 2).⁹ Several authors described AIP as the most common porphyria form and was observed in this study at a rate of 59.4% (261/493cases) (Figure 2) (Table 3).^{6,7,10} It is the most frequent acute hepatic porphyria and has a higher incidence in females. Patients present with abdominal pain, vomiting, gastrointestinal disorders, development seizures and psychiatric symptoms.^{7,11}

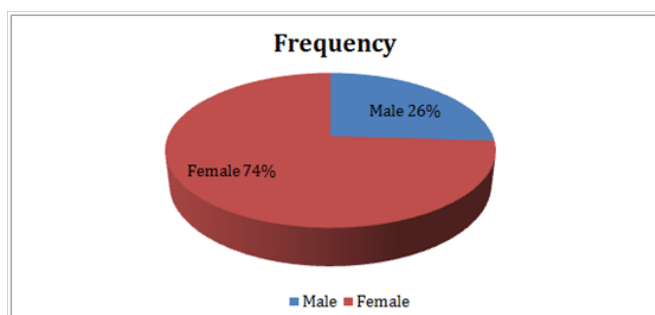


Figure 1 Frequency of porphyria by gender.

Table 1 Cases of porphyria by gender

| Gender | Absolute frequency | Relative frequency (%) |
|--------|--------------------|------------------------|
| Male | 113 | 26 |
| Female | 326 | 74 |

Table 2 Mean age (years) for each porphyria types

| Type | Mean age (years) |
|-------|------------------|
| HCP | 38.56 |
| AIP | 40.34 |
| ALADP | 36 |
| PCT | 44.56 |
| CEP | 38.4 |
| HEP | 53 |
| EPP | 30.24 |
| VP | 39.8 |

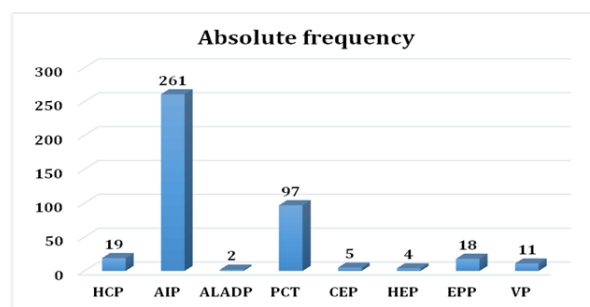


Figure 2 Absolute frequency of porphyria by type.

Table 3 Frequency of porphyria by type

| Type | Absolute frequency | Relative frequency (%) |
|-------|--------------------|------------------------|
| HCP | 19 | 4.3 |
| AIP | 261 | 59.4 |
| ALADP | 2 | 0.4 |
| PCT | 97 | 22.1 |
| CEP | 5 | 1.1 |
| HEP | 4 | 0.9 |
| EPP | 18 | 4.1 |
| VP | 11 | 2.5 |

According to Ramanujam et al.,¹⁰ PCT, AIP and EPP are most common in Europe and AIP is the most frequent acute porphyria. AIP increased in females using contraceptives, hormone replacement therapy and increased alcohol consumption, which can be cause of the increased prevalence in our female population.¹³ However, PHE prevalence was the same in both genders and EPP was the only type that showed higher frequency in males (Table 4). PCT was the second porphyria type with 22.1% (97/493 cases). The mean age at diagnosis was 44years with a higher prevalence in females. Our results differ from other authors that describe PCT as the most common type, but with the same mean age at diagnosis (44years) (Tables 2– 4) (Figure 2).^{3,13} PCT was the third most frequent in Argentina.¹⁴ EPP was the fourth porphyria type and showed a frequency of 4.1% (18cases). Ten cases in men and 8 in women were observed. The mean age at diagnosis was 30years. It was the third most common porphyria (10-20cases per diagnosed individuals) and the most common type in children. Our data and data from other authors showed different outcomes. In contrast to some of these findings, we observed a fourth type of porphyria and incidence around 30 years at diagnosis.^{7,8,13}

Table 4 Cases of porphyria by type and gender

| Type | Females | Males | Total |
|-------|---------|-------|-------|
| HCP | 10 | 9 | 19 |
| AIP | 215 | 46 | 261 |
| ALADP | 2 | 0 | 2 |
| PCT | 66 | 31 | 97 |
| CEP | 3 | 2 | 5 |
| HEP | 2 | 2 | 4 |
| EPP | 8 | 10 | 18 |
| VP | 8 | 3 | 11 |

VP was the fifth porphyria type and showed a frequency of 2.5% (11 cases). Eight cases in women and 3 cases in men were observed. The mean age at diagnosis was 39.8 years. The prevalence of VP has been estimated as 1.3:100000 in Finland and 0.3:100000 in Europe and is particularly prevalent in the white South African population consisting of approximately 3:1000.^{10,11} CEP or Günter disease is the rarest form of porphyria showing severe photosensitivity and scarring and no differences in clinical symptoms between men and women.^{13,15,12} Our results showed a frequency of 1.1% with 3 cases in females and 2 cases in males and the mean age at diagnosis was 38 years. HEP was the seventh porphyria type and showed a frequency of 0.9% (four cases). Two cases in men and 2 in women were observed. The mean age at diagnosis was 53 years. Approximately forty patients were reported up to 2010.¹⁰ ALADP was the last porphyria type with a frequency of 0.4% (two cases). All cases were in females and the mean age at diagnosis was 36 years. According to Ramanujam et al.,¹⁰ it is a rarest type of porphyria with only 6 cases reported world wide. All 6 cases were males. Differences in frequency between genders are unknown.

Conclusion

Patients with Porphyria in Brazil have the same epidemiological characteristic as the US and UK. In Brazil, porphyria should be studied more carefully in order to assess, properly diagnose and treat.

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Conflict of interest

The author declares no conflict of interest.

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