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], Variegate Porphyria [VP], Hereditary Coproporphyria [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 are 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: Variegate Porphyria; HCP: Hereditary Coproporphyria; 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], Variegate Porphyria [VP], Hereditary Coproporphyria [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 2:1000000 [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 439 datas 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 U et al. [6] (17/25 cases) and Bonkovsky HL et al. [3] (88/108 cases) agreed with these findings. The mean age at diagnosis for each type was 40 years for AIP, 44 years for PCT, 38 years for HCP, 38 years for CEP and 39 years 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% (261/493 cases) (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].

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

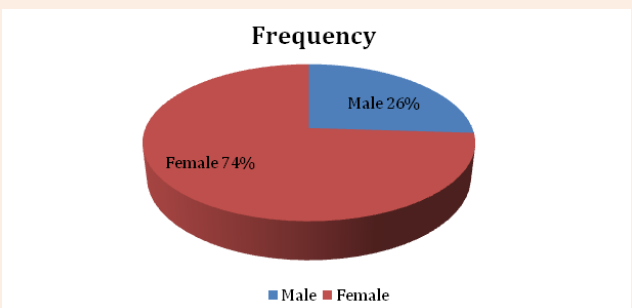

Figure 1: Frequency of porphyria by gender

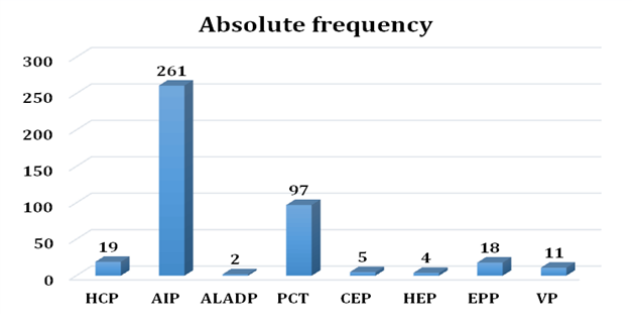

Figure 2: Absolute frequency of porphyria by type

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 VM 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 44 years 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 (44 years) (Tables 2-4) (Figure 2) [13,3]. PCT was the third most frequent in Argentina [14]. EPP was the fourth porphyria type and showed a frequency of 4.1% (18 cases). Ten cases in men and 8 in women were observed. The mean age at diagnosis was 30 years. It was the third most common

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porphyria (10-20 cases 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 VM et al. [10], it is a rarest type of porphyria with only 6 cases reported word 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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