Communication

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High prevalence of congenital generalized lipodystrophy in Piura, Peru

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SUMMARY Congenital generalized lipodystrophy (CGL) is an autosomal recessive rare disease, with a worldwide prevalence of around 1 in every 12 million people. There are several case reports of patients with CGL in Piura, a region in northern Peru; however its regional prevalence is unknown. The objective was to determine the prevalence of CGL in the region of Piura, Peru during the years 2000-2017. A descriptive, observational study was carried out. A search of clinical histories of patients with the diagnosis of CGL attended between 2000 and 2017 in the pediatric and endocrinology services of the reference hospitals of the department of Piura and in the genetic and endocrinology services of the "Instituto Nacional de Salud del Niño". A patient was considered to have CGL if they met the clinical criteria and or if they had a molecular diagnosis, in addition to patients with CGL from the department of Piura reported in previous publications. A total of 23 cases of CGL were found in Piura, the highest prevalence was in 2014 with 1.2 per 100,000 people, and by 2017 the prevalence was 0.86 per 100,000 people. In conclusion, the department of Piura has a high prevalence of CGL.

Keywords congenital generalized lipodystrophy, rare diseases, Peru (Mesh Terms)

1. Introduction

Congenital generalized lipodystrophy (CGL) is an autosomal recessive disease characterized by an almost total absence of adipose tissue from birth, muscular prominence and low levels of leptin. There are 4 molecular subtypes of CGL, based on the genes involved: CGL 1, related to the *AGPAT2* gene, CGL 2 with the *BSCL2* gene, CGL 3 with the *CAV1* gene and CGL 4 with variants in the polymerase I and *PTRF* gene (*1*). Patients with CGL may develop multiple complications, such as insulin resistance that may progress to diabetes mellitus, hepatic steatosis and severe hypertriglyceridemia leading in some cases to cirrhosis and end-stage chronic kidney disease (*2*).

Globally the prevalence of CGL is estimated at 1 in 12 million people (*3*), however, the prevalence varies according to the region under study, for example in Rio Grande Do Norte (RN), Brazil, the prevalence of CGL is 3.23 per 100,000 people (*4*).

In Peru, the first 5 cases of patients with CGL from Piura, a region in northern Peru, were reported in 1999 (*5*). In 2017, a series of 5 cases as well as one other were reported, all from Piura (*6,7*). Although there are multiple reports of CGL from the department of Piura, their prevalence has not been determined. The objective of the study was to estimate the prevalence of CGL and its distribution in the region of Piura, Peru during the years 2000-2017.

2. Methodology

A historical record of patients with a diagnosis of

CGL from the department of Piura was made between the years 2000-2017. A search was made for patients with the diagnosis of CGL between the years 2000-2017 in the services of pediatrics, endocrinology of the reference hospitals of the department of Piura: Hospital III José Cayetano Heredia, Hospital Jorge Reátegui Delgado, Hospital Santa Rosa, Hospital de Apoyo Sullana and also in the services of genetics and pediatric endocrinology of the National Institute of Child Health in Lima, the latter one is considered to be the pediatric reference site in Peru. In addition, patients with CGL from the department of Piura reported in previous publications were included. Patients with CGL were considered if they met the clinical criteria (*8*) and/or if they had molecular diagnosis.

The patients' place of birth, age, sex and current status were recorded and a database was created in *Microsoft Excel* 2017. The annual prevalence was calculated at the departmental and provincial levels, using the annual population reported by the National Institute of Statistics and Information. The study was approved by the Ethics Committee of the National Institute of Child Health, Lima, Peru.

3. Cases of congenital generalized lipodystrophy in Piura

In the initial review, we found a total of 22 patients with a probable diagnosis of CGL and 3 publications with a total of 11 CGL patients (*5-7*). A publication that included 5 patients was excluded because it did not correspond to the study period. Of the 6 patients reported in the other two publications, 3 were not found recorded in clinical histories.

A total of 23 cases of CGL were found, all from the department of Piura, the majority were from the province of Piura (73.9%), they are living (73.9%) and only 34.8% had genetic confirmation (Table 1). All patients had the pathogenic variant homozygote c.213-1336_c.294+1921delinsCA in the *BSCL2* gene.

The highest prevalence of CGL in the department of Piura was in 2014 with 1.2 per 100,000 people, and by 2017 the prevalence was 0.86 per 100,000 people (Table 2). Patients were found in only 3 provinces of the department of Piura: Morropón, Sullana and Piura (Figure 1), and their prevalence by 2017 was 0.6, 1.23 and 1.33 per 100,000 people respectively.

Our study found a high prevalence of CGL (0.86 in 100,000 habitants) in the department of Piura during the year 2017. This prevalence is higher than that reported worldwide, USA, Norway, Lebanon, Portugal (*3,9*), however it is lower than that reported in other regions such as Rio Grande do Norte and Oman, which can reach 3.23 in 100,000 habitants (*4,10*).

The reason for the high prevalence is the founder effect proposed by Purizaca *et al*. (*7*), which described a genetic variant in the *BSCL2* gene associated with type 2 CGL which, to the authors' knowledge, has not been reported in patients outside Piura (*11*). The same pathogenic variant was detected in all the patients in our study who underwent the genetic test; likewise, in patients without genetic confirmation it is assumed that they may have type 2 CGL due to the fact that they share the same clinical and geographic origin.

The department of Piura is divided into 8 provinces and only 3 of them have presented patients with CGL, coming from small agricultural areas that are difficult to access. The authors propose that migration between different agricultural villages in the department of Piura for work, and sometimes precipitated by natural events such as the El Niño phenomenon (*12,13*), may have caused patients carrying the same genetic variant to be found in different provinces due to the movement of groups to areas with better living conditions. The latest verbal reports of patients with and without genetic confirmation from other provinces where no cases had

Table 1. General characteristics of patients with CGL between 2000-2017, Piura, Peru

Variable	*n*	%
Age (median)		6
Age at death (median)		8
Gender		
Male	12	52.2
Female	11	47.8
Province of origin		
Sullana	5	21.7
Morropon	1	4.3
Piura	17	73.9
Current status		
Living	17	73.9
Deceased	6	26.1
Genetic Confirmation		
Yes	8	34.8
No	15	65.2

Table 2. Prevalence of CGL in the department of Piura, 2000-2017

Year	Cases	Prevalence (/100,000)
2000	2	0.12
2001	2	0.12
2002	2	0.12
2003	3	0.18
2004	3	0.18
2005	4	0.24
2006	4	0.23
2007	6	0.35
2008	7	0.40
2009	12	0.68
2010	13	0.73
2011	15	0.84
2012	17	0.94
2013	19	1.05
2014	22	1.20
2015	21	1.14
2016	19	1.03
2017	16	0.86

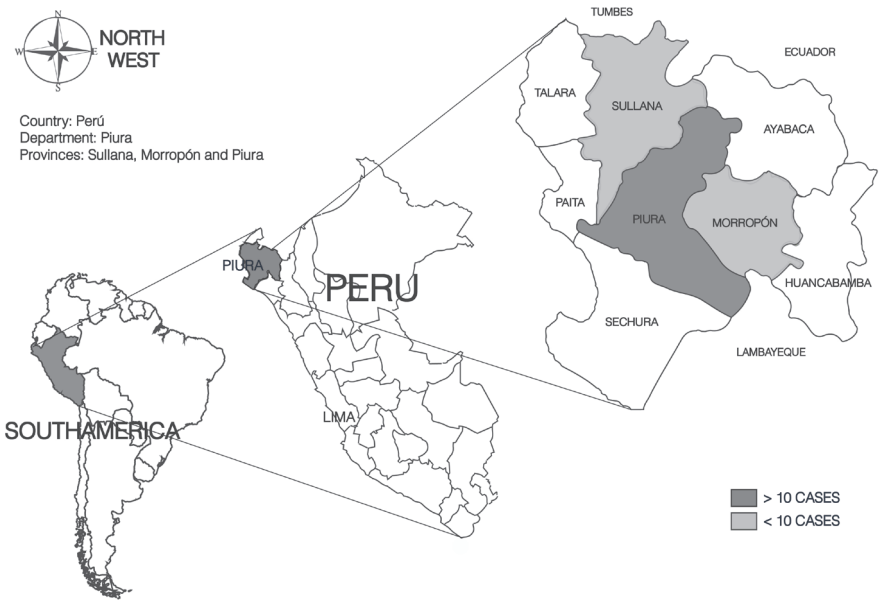

Figure 1. Geographic location of patients with CGL in Piura, Peru.

been registered to reinforce our assumption and oblige us to optimize the active search for them at the regional level. Due to the fact that the first cases were reported in the province of Piura and that this is the one that registers the greatest number of patients, it is assumed that it is where the type 2 CGL index case was presented.

Within the limitations it is necessary to highlight that the prevalence is based on a hospital registry, however, to the knowledge of the authors there are patients with a probable diagnosis of CGL who have not gone to a health center for different reasons such as cultural, economic and geographic, so the actual prevalence could be higher than reported in this study. In conclusion, the department of Piura has a high prevalence of CGL.

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