

Although obesity has become a world epidemic, our understanding of this condition in childhood is limited by a lack of representative data from different countries for their comparison, as well as by the different criteria used to define it.

The IOTF has developed charts for an international growth standard that allows the comparison of prevalences across the world. There is evidence that the IOTF classification has a high specificity but a low sensitivity, although many countries continue using their own national charts, including Spain and the United States, where the standards in use were developed from data acquired in nationwide surveys.

At present we do not have a general consensus standard to classify overweight and obesity in children and adolescents. The use of universal criteria for classifying obesity could help make international comparisons.

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R. Llada Suárez<sup>a,\*</sup>, L. del Fresno Marqués<sup>b</sup>, J.J. Díaz Martín<sup>c</sup>, S. Málaga Guerrero<sup>d</sup>, C. Rey Galán<sup>e</sup>

<sup>a</sup> *Facultad de Medicina, Universidad de Oviedo, Oviedo, Principado de Asturias, Spain*

<sup>b</sup> *Atención Primaria, Servicio de Salud del Principado de Asturias (SESPA), Oviedo, Principado de Asturias, Spain*

<sup>c</sup> *Sección de Gastroenterología y Nutrición, Hospital Universitario Central de Asturias (HUCA), Oviedo, Principado de Asturias, Spain*

<sup>d</sup> *Sección de Nefrología Pediátrica, Hospital Universitario Central de Asturias (HUCA), Oviedo, Principado de Asturias, Spain*

<sup>e</sup> *Sección de Cuidados Intensivos Pediátricos, Hospital Universitario Central de Asturias (HUCA), Oviedo, Principado de Asturias, Spain*

\*Corresponding author.

E-mail address: [lladarubn@gmail.com](mailto:lladarubn@gmail.com) (R. Llada Suárez).

## Congenital lactase deficiency: Identification of a new mutation<sup>☆</sup>



## Déficit congénito de lactasa: identificación de una nueva mutación

Dear Editor,

Congenital lactase deficiency (CLD, OMIM 223000) is a rare genetic disorder that belongs to the subgroup of enteropathies caused by carbohydrate malabsorption.<sup>1</sup> We present a case recently diagnosed in our paediatrics department.

The patient was a newborn of 20 days of age with a history of 6–8 episodes of diarrhoea a day since birth and with stunted growth despite breastfeeding with formula supplementation. He is the first child born to second-degree consanguineous parents. He presented with a dystrophic appearance and signs of dehydration. Laboratory analyses revealed metabolic acidosis, mild hypernatraemic dehydration, and normal blood chemistry, liver function and urine

tests. The main findings of the stool analysis included stool acidity (pH 6), normal ion levels, a high positive level of reducing bodies and an osmotic gap of 282 mOsm/kg (normal gap < 50 mOsm/kg). Intravenous fluids were initiated with the patient kept on an absolute fast, and the watery stools resolved after 12 h. The working diagnosis was chronic osmotic diarrhoea due to carbohydrate malabsorption. Since CLD was suspected, a diet based on lactose-free hydrolysed formula was initiated. The patient tolerated it well and his weight curve rose. Genetic testing was positive and revealed the presence in homozygosis of a new mutation in the LTC gene, c.2232.2253dup22 (p.L752KfsX18). Genetic testing of both parents was positive in heterozygosis. The patient remained asymptomatic and showed adequate growth in subsequent checkups.

Congenital lactase deficiency was first described in Finland in 1959 with an estimated prevalence of 1 in 60,000 inhabitants. It was included in the group of congenital diarrhoeas, a heterogeneous set of rare diseases associated to specific genetic defects. The onset of symptoms typically occurs in early infancy and the course and prognosis vary depending on the underlying cause.<sup>1</sup>

Congenital lactose deficiency is caused by very low levels or the absence of lactase-phlorizin hydrolase (commonly known as lactase) in the gut resulting from a mutation in the LCT gene (MIM 603202), and has an autosomic recessive inheritance pattern.<sup>2</sup> The correct hydrolysis of lactose, the disaccharide found in milk, is essential to adequate nutri-

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tion in the early months of life. Lactase is the rate-limiting enzyme in the hydrolysis of lactose to the monosaccharides that can be absorbed by enterocytes. Its deficiency prevents the hydrolysis of lactose and causes osmotic diarrhoea when the child starts breastfeeding.<sup>2,3</sup> At first it was believed that CLD was a severe form of lactose intolerance with early onset.<sup>4</sup> But while both disorders are due to mutations in the LCT gene, recent studies have shown that their genetic mechanisms differ.<sup>3,5</sup>

The LCT gene is located in chromosome 2q.21 and is composed of 17 exons.<sup>2,3</sup> Eleven mutations have been described to date that cause CLD.<sup>3,6</sup> Genetic testing of the patient revealed the homozygous duplication c.2232\_2253dup22 in exon 7 of the LCT gene, which had not been described before. This is a frameshift mutation that produces a premature stop codon (p.L752KfsX18), resulting in a truncated protein that precludes the correct hydrolysis of lactose.

Congenital lactose deficiency must be suspected in neonates of a few days of age with onset of watery diarrhoea after the start of breastfeeding, usually in the absence of vomiting, with adequate intake and no food refusal. If the diagnosis is delayed, dehydration and metabolic acidosis can become severe and life-threatening. Once the patient is stabilised, more common conditions with compatible symptoms must be ruled out: infection, food allergies and intestinal malformations.<sup>1</sup> If a chronic congenital diarrhoeal disorder is suspected, a basic stool study (pH, ions, reducing substances and osmotic gap) must be performed in a timely manner. First, the mechanism underlying the diarrhoea must be determined (osmotic or secretory) by observing the response of diarrhoea to fasting and the osmotic gap (theoretical gap – measured gap =  $290 - 2 [Na + K]$ ). Osmotic diarrhoea is characterised by a high osmotic gap (>50 mOsm/kg), that reflects the substances that are not absorbed by the bowel and normalises with fasting, contrary to what happens in secretory diarrhoea. The most frequent cause of osmotic diarrhoea is carbohydrate malabsorption, with positive reducing substances and an acidic pH (5–6) in the stool.<sup>1,4</sup> Congenital lactose intolerance is suspected under

these circumstances because lactose is the main carbohydrate in the diet during the neonatal period. A jejunal biopsy will reveal reduced levels or the absence of lactase in the bowel mucosa, with normal levels of the other disaccharidases and a normal jejunal morphology.<sup>4</sup> The diagnosis is confirmed by genetic testing, avoiding invasive tests. Treatment with lactose-free formula improves symptoms and has no impact on growth or psychomotor development.<sup>4</sup>

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J. Sala Coromina\*, A. Vinaixa Vergés, R. Garcia Puig

*Servicio de Pediatría, Hospital Universitario Mútua Terrassa, Terrassa, Barcelona, Spain*

\* Corresponding author.

*E-mail address:* [juliasalac@gmail.com](mailto:juliasalac@gmail.com) (J. Sala Coromina).