

# Transference of CALIPER total alkaline phosphatase reference interval to a Brazilian pediatric population

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The reference intervals (RI) represent a set of values used to interpret the results of quantitative laboratory tests and are powerful tools that assist health professionals in making decisions during patient care<sup>(1)</sup>. The determination of their own RI gives diagnostic power, but it is one of the most arduous and costly tasks in the Clinical Pathology<sup>(2,3)</sup>. When it comes to defining RI in the pediatric population, the situation is further complicated, since defining a healthy pediatric population involves, among other procedures, obtaining the anthropometric measurements and collecting blood samples. The concern about not plundering the child and the emotional pressure involved in collecting samples in pediatric patients are care for which we must be aware.

For this reason, the Clinical and Laboratory Standard Institute (CLSI)<sup>(4)</sup> defined that one of the simplest and least expensive ways to determine RI could be the transference, which is the way by which a previously defined RI is adapted to a new analytical method or to another laboratory. This technique was proposed by the Nordic Reference Interval Children Project (NORICHILD), and later used by the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER). The latter is a Canadian project, multicenter, aimed at developing a comprehensive database of reference values in the healthy children population.

Considering the transference, a successful validation occurs when a number greater than or equal to 90% of the sample values are within the RI that serve as a comparison and this method must be performed in at least 20 samples.

Alkaline phosphatase (ALP) is a group of enzymes found in several tissues, with emphasis on the liver, epithelium of the bile ducts, bone, placenta and intestinal mucosa. The study of ALP isoenzymes allows us to identify the fraction involved in eventual elevation of total ALP. In physiological conditions, the hepatic fraction contributes with 50% of the total serum level of ALP, the bone fraction with 40%, and the intestinal fraction with 10%. Pregnant women produce the placental isoenzyme.

For many decades, medical concern has always been centered on the elevated levels of this enzyme, which, classically, is a marker of osteoblast activity and hepatic injury, particularly in cholestatic conditions.

In the recent years, however, with the description of hypophosphatasia, attention has been focused on the low activity of this enzyme, characterized by decreased serum levels.

Hypophosphatasia is a rare, potentially fatal inherited metabolic disease caused by a mutation in the gene that encodes the tissue-nonspecific alkaline phosphatase (TNSALP), causing the accumulation of various substances [inorganic pyrophosphate (PPi) in urine, pyridoxal 5'-phosphate (PLP), phosphoethanolamine (PEA)]<sup>(5,6)</sup>. This disease can affect individuals in any age group, with clinical manifestations from the intrauterine period, which are the most severe cases, to adulthood.

The description of cases of disorganized bone mineralization, leading to clinical manifestations of rickets, osteomalacia, fractures, craniosynostosis, skeletal deformities, as well as systemic complications such as convulsions responsive to pyridoxine, respiratory compromise, dental anomalies, nephrocalcinosis, hypercalciuria, hypotonia, weakness, non-progressive proximal muscle weakness, hypercalcemia and muscle and chronic joint pain were related to hypophosphatasia.

The diagnosis is difficult and, most of the time, is mistaken with other orthopedic conditions, but the reduced ALP serum levels are fundamental for its diagnosis.

The major advantage of using the transference to determine the RI is the exemption from collecting and testing samples of reference individuals in each partition (gender and age), which makes the procedure of establishing the RI more feasible.

In this issue of the *Jornal Brasileiro de Patologia e Medicina Laboratorial* (JBPML), there is a study by Fontes *et al.* (2018)<sup>(7)</sup>, which presents the application of the methodology of “Alkaline phosphatase: reference interval transference from CALIPER to a Brazilian pediatric population”. The validation of CALIPER RI for the Brazilian population, will certainly give more power and safety in the diagnostic decision-making in daily practice.

Enjoy reading!

## REFERENCES

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