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EDITORIAL

The importance of determining reference intervals for Laboratory Medicine

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Exactly 20 years ago, Forsman has shown that at least 70% of clinical decisions made within hospital setting were very dependent on the results of laboratory tests[1]. Nowadays, with the remarkable technological evolution, probably this contributory percentage is even higher.

The performance of a laboratory test may have different purposes such as the diagnosis of a particular disease, monitoring a patient undergoing a therapeutic regimen, the staging of a disease already diagnosed or risk prediction for a particular, among other reasons. With the purpose that the result can be correctly interpreted and, therefore be useful in the medical practice, it needs to fulfill some requirements, such as having been obtained by reliable and robust methodology, have positive and negative predictive values relevant, and high levels of sensitivity and specificity[2, 3]. Additionally, it is essential that their limits of significance and limitations are well known, which means, it is crucial to have their reference intervals well determined[4].

The Word Health Organization (WHO), the International Federation for Clinical Chemistry (IFCC) and the Clinical Laboratory Standard Institute (CLSI) define reference interval as the set of results obtained by observation or quantitative measurement of an analyte in a selected group of individuals, based on well-defined criteria[5].

In the United States of America, since 1988 there are regulatory standards on how clinical laboratories should create and evaluate, periodically, the reference intervals adopted[6]. In Brazil, the legislation (RDC 302) of the Agência Nacional de Vigilância Sanitária (Anvisa)[7] and the Programa de Acreditação de Laboratórios Clínicos (PALC) of the Sociedade Brasileira de Patologia Clínica/Medicina Laboratorial (SBPC/ML) only determine that all clinical laboratory should provide some reference value with the test result. Thus, it is granted to the laboratory to set its own intervals, validate the values provided by the manufacturer of the supplies, or even adopt the values available in the literature. Clearly, determining their own reference intervals, although very desirable, is more laborious and costly than the other options because it entails literature review, selection of reference individuals, application of detailed questionnaires, and analysis of biological variables, such as gender, age and genetic variability, among other tasks. Furthermore, the characteristics of the population in which the reference range was determined and the population to which it is applied must be compatible[8]. For the pediatric population, the difficulties may be even greater, but there is a number of studies on the determination of reference intervals[9-12]; regarding the geriatric population, the data are still scarce or outdated[13, 14]. Data submitted by the College of American Pathologists (CAP) in a interlaboratory study involving 163 clinical laboratories, with special focus on the origin of the reference intervals used, showed that for the adult population approximately 50% of laboratories used their own reference intevals, but when the pediatric population was assessed, this percentage decreased to 25%[15]. Thus, it is with great enthusiasm that we observe some research centers get involved in this subject, as demonstrated in the publication of this issue of the Jornal Brasileiro de Patologia e Medicina Laboratorial (JBPML), in the study of Cruz *et al*. (2016) "Reference intervals of amino acids by high performance liquid chromatography in plasma samples of Brazilian children"[16].

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REFERENCES

1. Forman RW. Why is the laboratory an afterthought for managed care organizations? Clin Chem. 1996; 42(5): 813-6.

2. Dybkaer R, Solberg HE. Approved recommendations (1987) on the theory of reference values. Part 6. Presentation references of observed values related to reference values. J Clin Chem Clin Biochem. 1987; 25: 657-62.

3. Ferreira CES, Andriolo A. Reference ranges in clinical laboratory. J Bras Patol Med Lab [Internet]. 2008; 44(1). Available at: http://dx.doi.org/10.1590/S1676-24442008000100004.

4. Andriolo A, Rocha MH. Características e interpretação dos resultados dos exames laboratoriais. In: Andriolo A, Carraza FR, editors. Diagnóstico laboratorial em pediatria. 2 ed. São Paulo: Sarvier; 2007. Cap. 1; p. 3-13.

5. Clinical and Laboratory Standards Institute. How to define and determine reference intervals in the clinical laboratory. Document C 28-A2; 2000.

6. Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 CFR §493.1253(b) (1) (ii) (2003).

7. Ministério da Saúde. Agência Nacional de Vigilância Sanitária (Anvisa). Dispõe sobre regulamentação técnica para funcionamento de laboratórios clínicos. Resolução da Diretoria Colegiada. RDC nº 302; 2005.

8. Solberg HR. Establishment and use of reference values. In: Burtis CA, Ashwood ER, Bruns DE, editors. Tietz textbook of clinical chemistry and molecular diagnostics. 4 ed. Philadelphia: Elsevier Saunders; 2006. p. 425-48.

9. Meites S. Pediatric clinical chemistry reference (normal) values. 3 ed. Washington, DC: AACC Press; 1989.

10. Soldin SJ, Brugnara C, Wong EC. Pediatric reference ranges. 4 ed. Washington, DC: AACC Press; 2003.

11. Colantonio DA, Kyriakopoulou L, Chan MK, et al. Closing the gaps in pediatric laboratory reference intervals: a CALIPER database of 40 biochemical markers in a healthy and multiethnic population of children. Clin Chem. 2012 May; 58(5): 854-68. doi: 10.1373/clinchem.2011.177741. Epub 2012 Feb 27. PMID: 22371482.

12. Slhessarenko N, Jacob CMA, Azevedo RS, Cor JF, Novak GV, Andriolo A. Serum lipids in Brazilian children and adolescents: determining their reference intervals. BMC Public Health. 2015; 15: 18. doi: 10.1186/s12889-015-1359-4.

13. Faulkner W, Meites S. Geriatric clinical chemistry reference values. Washington, DC: AACC Press; 1994.

14. Figueira JL, Netto MP, Carvalho Filho ET, et al. Perfil lipídico em indivíduos idosos normais. Arq Bras Cardiol. 1987; 48(2): 77-81.

15. Richard C, Friedberg RC, Souers R, Wagar EA, Stankovic AK, Valenstein PN. The origin of reference intervals. A College of American Pathologists Q-Probes study of "normal ranges" used in 163 clinical laboratories. Arch Pathol Lab Med. 2007; 131(3): 348-57.

16. Cruz AF, Barbosa TMCC, Adelino TER, Lima WP, Mendes MO, Valadares ER. Amino acid reference intervals by high performance liquid chromatography in plasma sample of Brazilian children. J Bras Pathol Med Lab. 2016; 52(2): 70-7.