Use of big data for verification of decision levels for biotinidase deficiency and galactosemia

Tijen Tanyalçın[1], Diler Aslan[2]

[1]Tanyalcin Medical Laboratory Selective Screening and Metabolism Unit 1359 sokak No:4/1 Alsancak 35220 Izmir/Turkey

[2]Emeritus Prof. Pamukkale University Medical Faculty Dept. of Biochemistry Address: D-Tek Technology Ltd. Company Pamukkale Technology Development Area D Blok No: 112 Denizli/Turkey

Introduction

To decide for further testing, the percentages of mean/median enzyme activity of individuals, and cutoff are needed for biotinidase (BTD) deficiency and galactosemia (GALT), respectively. Each laboratory that performs screening tests should estimate these decision levels. The mean (263 Enzyme Unit-Eu) and the cut-off (3.5 U/g Hb) were determined for BTD and GALT, respectively. The reference intervals (RIs) are being estimated from big data. Our aim is to assess whether these values determined from small numbers of healthy newborns will be similar with the values estimated by the indirect methods for determination of RIs.

Materials and Methods

The histograms and Q-Q Plots of 33998 BTD, and 23438 GALT screening results generated in Tanyalçın Laboratory from 2004 were evaluated. The RIs were estimated according to the Hoffmann and Bhattacharya Methods. The Microsoft Excel and SPSS Statistical Package were used.

Results

The Q-Q Plots of two analytes are shown in the Figures. The results are listed in the Table.

Normal Q-Q Plot of Biotinidase (Eu)

Normal Q-Q Plot of GALT (U/g Hb)
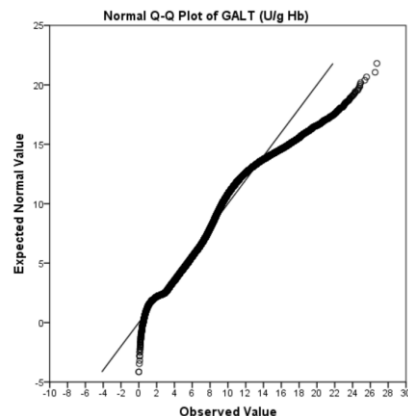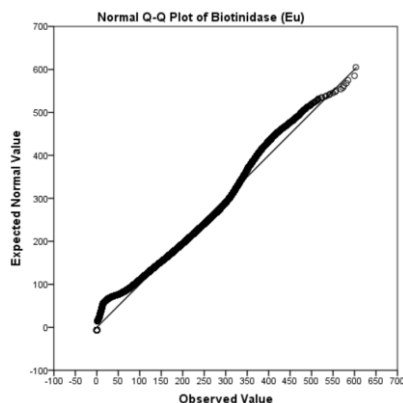
Test:	BTD	GALT
Unit	EU	U/g Hb
Original data		
Group	Neonates	Neonates
n	33 988	23 438
Mean	242	8.6
Median	251	8.4
SD	87.9	3.26
CV	36	38.8
Min	0	0
Max	603	26.73
Bhattacharya		
Bin	30	2
Bhat Cent	270	9.5
Bhat SD	84	3.09
Bhat -2SD	102	3.3
Bhat + 2SD	438	15.69
n	33 364	22 862
Hoffman		
Mean	247	8.29
Median	254	8.36
SD	81	2.21
-2SD	80	3.75
+2SD	384	12.79
n	33 226	21 309

The values determined were compatible with the decision levels estimated before.

Conclusions

The indirect methods for RI determination from big data can be helpful for verification of decision levels for the screening tests.

References

1. Clinical and Laboratory Standards Institute (CLSI). EP28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2010.
2. Clinical and Laboratory Standards Institute (CLSI). NBS03-A Newborn Screening for Preterm, Low Birth Weight, and Sick Newborns; Approved Guideline. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2009.
3. Farrell CJL, Nguyen L. "Indirect Reference Intervals : Harnessing the Power of Stored Laboratory Data." Clin Biochem Rev 2019;40(2): 99–111.
4. Graham RJ et al. "Indirect Methods for Reference Interval Determination – Review and Recommendations." 2019;57(1): 20–29.
5. Ozarda Y. "Reference Intervals: Current Status, Recent Developments and Future Considerations." Biochemia Medica 2016;26(1): 5–16.