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Article *in* Clinical Laboratory · July 2019

DOI: 10.7754/Clin.Lab.2019.190108

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Clin. Lab. 2019;65:1309-1312

ORIGINAL ARTICLE

Determination of Six Sigma Metric in Control of Enzymes Determination in Human Serum

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SUMMARY

Background: **Clinical Chemistry is the backbone of medical treatment, diagnostics, and prevention. The laboratories are trying to improve the quality and to reduce diagnostic errors and processing time and safeguard traceability of all laboratory procedures to ensure patient safety. Six sigma belongs to statistical quality control and provides a new methodology for measuring and improving process performance in laboratory.**
Methods: **Activities of AST, ALT, CK, LDH, Amy, and γ-GT were determined by standard kinetic methods on a Vitros 5600 biochemistry analyzer. Two daily quality controls (Verifier I and Verifier II) were run over 60 days. Total percent CV was calculated from routine daily QC. Between-instrument bias was also calculated from daily QC.**
Results: **The calculated sigma metrics for AST were 6.9 and 3.8; for ALT 9.3 and 5.6; for CK 6.6 and 5.3; LDH 5.2 and 5.2; for γ-GT 4.9 and 2.7; and for amylase 8.7 and 7.1. Analytical performance for AST, ALT, CK, LDH, and Amylase is world class. On the other hand, γ-GT analytical performance is poor.**
Conclusions: **Six Sigma benefits from earlier quality management approaches that creates new challenges for medical laboratories.**
(Clin. Lab. 2019;65:1309-1312. DOI: 10.7754/Clin.Lab.2019.190108)

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Manuscript accepted January 24, 2019

KEY WORDS

enzymes, six sigma, method evaluation

INTRODUCTION

Clinical laboratories produce analytical results that are used in the diagnosis, prognostic evaluation, follow-up, treatment monitoring, and the prevention of diseases. The overall goal of clinical laboratories is to ensure patient safety through trueness and stability in laboratory analyses. Analytical quality procedures are necessary to improve patient health [1]. Precise results are crucial for physicians and their patients. Laboratories need to produce precise test results before any other dimension of quality becomes important. Since the mid of 1980s Six Sigma methodology represents an evolution in quality assessment and management that has been applied

widely in business and industry [8]. Motorola developed the Six Sigma methodology to decrease the cost of production, reduce defects, and decrease inconsistency in processing. The main goal was to decrease variations in manufacturing and 3.4 defects per million opportunities (DPMO). Healthcare and laboratories have recently started to implement Six Sigma as a statistical quality control method. The Six-sigma method has already been shown to be effective for applications in healthcare. The goal of every operation or production system is to generate a useful product [2]. Laboratories must reduce finances, increasing volumes and personnel shortages. The clinical laboratories are progressively moving to automation to minimize defects [3]. Six sigma activities give the possibility to enhance the process time and save resources [4]. The Six Sigma method characterizes all performed processes on a Sigma scale that ranges from 2 to 6, values less than three are considered unreliable and these results are not used in routine laboratory practice. Based on the data from the real-world health laboratories, it is an obvious statement that current instrumentation performs well [5]. The aim of this study was to measure the levels of enzymes so we could determine the six sigma metrics on a Vitros 5600 System.

MATERIALS AND METHODS

Study setting

The study was performed at the University Clinical Center of Sarajevo, Department of Clinical Chemistry and Biochemistry. The measuring of enzyme levels was performed in the period of March to April 2018, and they were assessed for sigma metrics.

Instruments and reagents

Six enzyme levels were measured: alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine phosphatase (CK), gamma GT (γ-GT), amylase (Amy), and lactate dehydrogenase (LDH). Activities of AST, ALT, CK, LDH, Amy, and γ-GT were determined by standard kinetic methods according to IFCC (International Federation of Clinical Chemistry) on a Vitros 5600 biochemistry analyzer. All measurements were performed with single lot cassettes. Reagents and controls were prepared according Roche diagnostics recommendation.

Determination of the enzyme activity

The catalytic activity of an enzyme is measured by determination of the conversion rate of catalyzed chemical reaction using a specific measurement procedure. It is expressed as the amount of substance converted per unit time, in international units (IU). The catalytic concentration is the catalytic activity contained in a volume of sample and is expressed in U/L. Control samples were tested according CLSI/NCLLS protocol EP15-A2. Bias was calculated using a comparison method. Total percent CV was calculated from routine daily quality controls. Two daily quality controls (Verifier I and Verifier II) were run over 60 days for each parameter tested.

Sigma level calculation

The Sigma-metric is calculated from the quality required for the test (% TE) and the precision (% CV) and trueness (% Bias) observed for the methods, as follows: Sigma-metric = (% TEa - % Bias)/% CV.
The Sigma-metric QC Selection Tool provides an easy way of selecting the right QC procedure. The calculations are simple. The power curves are relatively easy to understand.

Statistical calculations

Data analyses were performed using the statistical software package IBM SPSS Statistics for Windows v 20.0 for Windows (IBM Corp., Armonk, NY, USA).

RESULTS

Two daily quality controls (Verifier I and Verifier II) were run over 60 days. Total percent CV was calculated from routine daily QC. Between-instrument bias was also calculated from daily QC. Monthly Sigma metrics are given in the Table 1 and Figure 1.

DISCUSSION

Clinical laboratories have a critical role in the diagnosis of many diseases. From this point of view, accurate test results are crucial for physicians, and the assessment of laboratory performance is important to maintain precise laboratory results [9]. Laboratory testing process is divided into three phases: pre-analytical, analytical, and post-analytical phases [10]. Errors that occur in each phase may have a negative effect on clinical decision. In this context, the total occurrence of errors in all phases should be calculated. Laboratory professionals for this purpose can use modern quality-management tools such as Six Sigma [11]. The sigma value defines how frequently defects are likely to occur, the higher the sigma value is, the less likely the defects or false test results are. A laboratory method with low sigma levels means cost of laboratory time, effort, and money in order to maintain quality results. Usually, manufacturers or suppliers assert that their tests have excellent quality, but the clear criteria that prove this information are not defined. Laboratory professionals can use sigma metrics that involves simple and minimal calculations. All that is necessary for quality assessment of the analytical phase is to calculate the methods imprecision and bias levels. All of these data are available in method validation studies. Tests with low quality (low sigma value) can lead to the wrong diagnosis and therapy along with expensive follow-up testing. On the other hand, tests with high quality (high sigma value) might turn out to be cost-saving, if it decreases delay of therapy and fu-

Table 1. Sigma levels for the measurement procedures in two months.

Assay	Conc. mean U/L		Total % CV (30 days)		Observed % Bias		Tea target %	Sigma Metric	
	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2		Level 1	Level 2
AST	51	140	2.7	5.5	4.3	2.1	23	6.9	3.8
ALT	44	108	2.1	3.6	3.3	2.6	23	9.3	5.6
CK	17	302	2.6	3.3	2.7	2.4	20	6.6	5.3
LDH	206	312	2.6	2.9	4.3	2.8	18	5.2	5.2
γ-GT	52	227	3.9	6.9	2.7	3.1	22	4.9	2.7
Amylase	88	188	1.4	1.5	2.4	3.9	14.6	8.7	7.1

Level 1- Precinorma U. Level 2 - Precipeth U.
Calculated sigma metrics for AST levels were 6.9 and 3.8; for ALT 9.3 and 5.6; for CK 6.6 and 5.3; LDH 5.2 and 5.2; for γ-GT 4.9 and 2.7; and for amylase 8.7 and 7.1. Analytical performance for AST, ALT, CK, LDH, and Amy is world class.

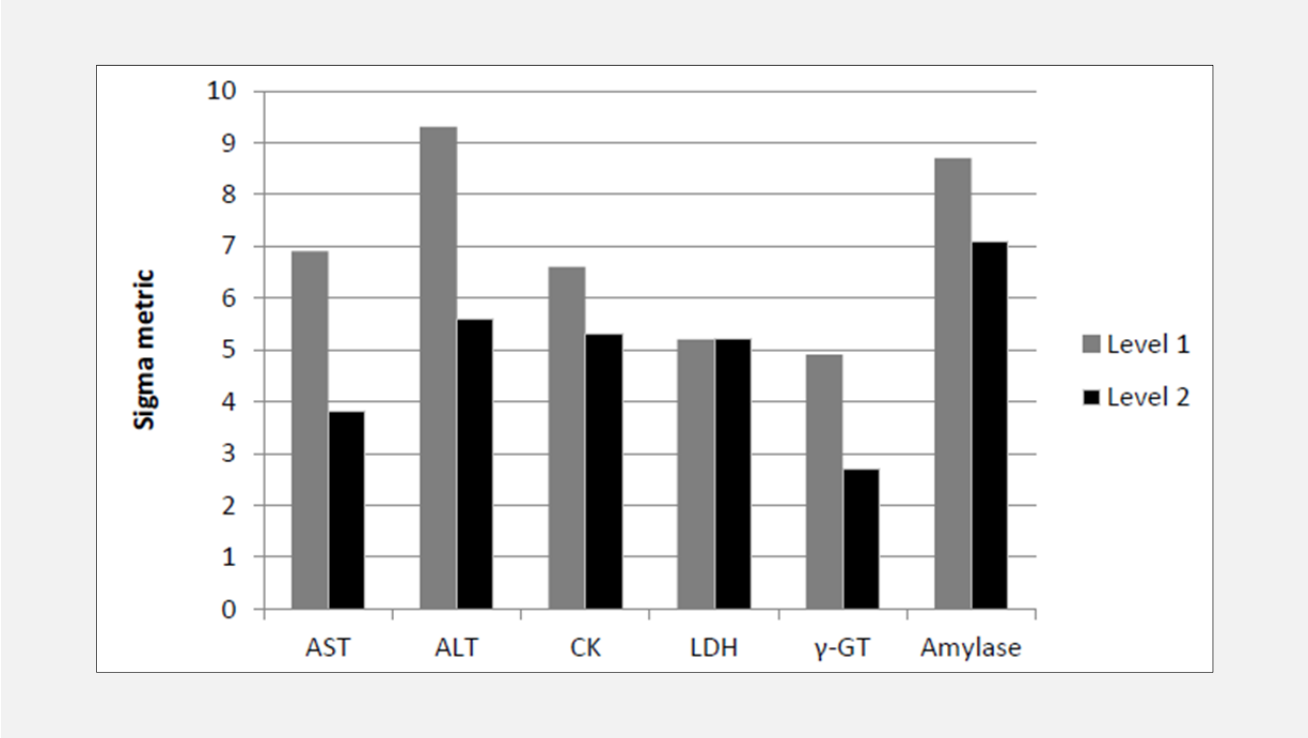

Figure 1. Six sigma levels.

ture costly diagnostic procedures [12]. If the method has a sigma value ≤ 3, the quality of the test result cannot be assured even after multiple QC repetition. We have analyzed six enzyme levels over a period of two months (March - April 2018) and calculated the Six sigma values. Variations in sigma values between our study and other studies performed are due to different instrument use and quality control of used material. We have calculated mean, standard deviation (SD), coefficient of variation (CV), and bias. Analytical performance for AST, ALT, CK, LDH, and Amy is world class. On the other hand, γ-GT analytical performance is poor. Our results, in comparison with other results of the same and different types of instruments, are in full concordance except GGT. Our study shows that the Vitros 5600 analyzer provides stable results for tested analyses.

CONCLUSION

The Six Sigma metrics seem to be the most comprehensive measurements which provide the information on defects or variations that may cause harm to the patients and also create poor quality cost. It is a set of tools and techniques for process improvement to identify and remove the causes of defects and minimize the variability in process and provide cost savings [6,7,13].

Acknowledgment:
Thanks to Prof. Dr. Jozo Ćorić for data collection and paper expertise.

Declaration of Interest:
None.

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