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Analysis of performance and comparison study of two clinical chemistry auto analyzers using six sigma methodology and quality goal index

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Abstract

Background: Accurate and reliable results in clinical laboratories are essential for effective diagnosis and treatment. This necessitates continuous monitoring and improvement of pre-analytical, analytical, and post-analytical processes. The Six Sigma methodology, which evaluates total testing error, is a statistical tool for assessing laboratory performance, with sigma values above 6 indicating world-class performance. Additionally, the Quality Goal Index (QGI) helps identify whether performance issues stem from imprecision, inaccuracy, or both. Comparison of methods using regression and Bland-Altman analysis helps ensure consistency between instruments.

Aim: To evaluate the performance of routine biochemical tests on two clinical chemistry auto analyzers using Six Sigma metrics and QGI, and to compare results using patient samples.

Subjects and Methods: This six-month study (May-November 2024) was conducted at the Biochemistry Department of the National Center of Teaching Laboratories and Baghdad Teaching Hospital. Eight analytes (glucose, uric acid, creatinine, urea, cholesterol, triglycerides, ALT, AST) were tested using Abbott Architect c4000 and Beckman Coulter AU480. Sigma metrics and QGI were calculated using internal and external quality control data. A comparison study was conducted per CLSI EP15 guidelines using 20 patient samples.

Results: Triglycerides achieved $\sigma > 6$ on both analyzers. Uric acid (Abbott) and cholesterol ($\sigma \approx 6$) showed strong performance. Urea showed acceptable performance ($\sigma > 3$), while glucose, creatinine, ALT, and AST had $\sigma < 3$. QGI analysis revealed imprecision and/or inaccuracy issues with specific parameters. Regression and Bland-Altman plots confirmed strong agreement and no significant difference in results between analyzers.

Conclusion: Both analyzers demonstrated acceptable performance for several analytes, with comparable results across platforms. However, improvements are required for parameters with lower sigma values.

Keywords: Performance, comparison, clinical chemistry, auto analyzers, six, sigma, methodology, quality, goal index.

Introduction

In modern clinical laboratories, quality is no longer a matter of post-production inspection but a continuous, proactive process integrated into every phase of testing. The origins of Quality Management (QM) can be traced back to the 1930s, when Walter Shewhart shifted the paradigm from detecting errors after they occurred to preventing them by controlling process variability [1]. Today, QM has evolved into a comprehensive set of principles that guide organizations in consistently meeting customer expectations through structured management and improvement practices [2]. Central to these principles is the implementation of a Quality Management System (QMS) a formal framework that organizes the structure, responsibilities, and processes needed to ensure high standards of patient care and laboratory results [3]. QMS is deeply rooted in the technical disciplines of internal quality control (IQC) and external quality assessment (EQA), both of which continue to underpin laboratory quality operations. The International Organization for Standardization (ISO), particularly ISO 15189, provides a widely recognized model for laboratory accreditation. This standard links quality practices to competence in executing all procedures across the total testing process [4].

It is closely aligned with the Clinical and Laboratory Standards Institute (CLSI), which outlines 12 Quality System Essentials (QSEs) essential for a comprehensive QMS [5]. Quality assurance (QA) is a component of QM that focuses on ensuring all laboratory operations from sample handling to result reporting adhere to defined quality standards. QA addresses the infrastructure required for accurate testing, including staff competency, equipment maintenance, and procedural integrity. Importantly, it also encompasses the total testing process: pre-analytical, analytical, and post-analytical phases. Notably, most laboratory errors (46-68%) occur in the pre-analytical phase, while 18-47% occur post-analytically, and only 7-13% arise during actual analysis [6]. At the heart of performance evaluation are analytical performance characteristics such as trueness, precision, and accuracy. These concepts are rigorously defined in metrological standards such as VIM3 and the newer VIM4, ensuring universal understanding and application [7]. Bias reflects systematic error and is often linked to calibration issues, while precision denotes random error and is measured through repeatability, intermediate precision, or reproducibility studies [8]. Accuracy is the combination of both trueness and precision and is crucial for clinical decision-making [9]. Another critical component is measurement uncertainty (MU), which quantifies the doubt around a test result and influences medical decisions near clinical thresholds. According to ISO15189:2012, MU should be assessed under intermediate precision conditions to reflect real-world variability [10]. Errors in measurements random or systematic can significantly impact clinical outcomes. Random errors introduce variability, while systematic errors cause consistent biases, both of which must be minimized through calibration, method adjustments, and quality controls [11]. To ensure clinical usefulness, the concept of Total Allowable Error (TEa) was introduced. TEa sets the acceptable limits of error in terms of both bias and imprecision, and forms the basis of Sigma metrics, a performance evaluation method that assesses process quality on a six-level scale, from unacceptable ($\sigma<2$) to world-class ($\sigma\geq6$) (21-24,41). Quality Goal Index (QGI) further helps identify whether performance shortcomings are due to imprecision, inaccuracy, or both, thereby guiding targeted quality improvements [12]. To evaluate the equivalence of results from different analytical systems, method comparison studies are conducted. Guidelines such as CLSI EP09-A3 and EP15 provide structured approaches to assess agreement and identify systematic or random differences. Analytical techniques like regression analysis and Bland-Altman plots are employed to determine correlation and detect biases across the full measurement range [13].

Aim

To evaluate the performance of routine biochemical tests on two clinical chemistry auto analyzers using Six Sigma metrics and QGI, and to compare results using patient samples.

Methods

This study was conducted over six months, from May to November 2024, at two government laboratories in Medical City, Baghdad, Iraq: the National Center of Teaching Laboratories and the Baghdad Teaching Hospital. The study was divided into two main parts. The first part involved calculating Sigma metrics and Quality Goal Index (QGI) values for eight routine biochemical analytes glucose, uric acid, creatinine, urea, cholesterol, triglyceride, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) using internal and external quality control (QC) data from two automated chemistry analyzers: Abbott Architect c4000 and Beckman Coulter AU480. Sigma metric was calculated using the formula: σ = (Tea-Bias%)/CV%, where TEa% values were obtained from EFLM (Sigma1), BCQ-2024 (Sigma2), and RIQAS TDPA (σA1/σB1). The coefficient of variation (CV%) was computed as (SD/Mean) × 100 using internal QC data at two control levels (L2 and L3), and the average CV% was derived as [(CV1 + CV2)/2]. Bias% was derived from EQAS reports provided by Bio-rad (May-August) and RIQAS (September-November). QGI was calculated using the formula: Bias/(1.5 × CV). The second part of the study involved a method comparison using 20 serum samples collected from outpatients, selected to represent both normal and abnormal values across the analytical measurement range. Samples were first analyzed on the Abbott Architect c4000 and then transferred in a cooled box to the Beckman Coulter AU480 for re-testing. Comparison was conducted using linear regression analysis via Microsoft Excel 2010 and Bland-Altman plots generated using DATA Tab (Online Statistics Calculator 2024). All procedures were conducted with ethical approvals from the Iraqi Board for Medical Specializations and both participating institutions.

Results

In the first three months of the study (from May to August), the sigma metric was calculated by using the TEa that was obtained from Bio-rad EQAS data as biological variation data (desirable BV% data) updated by EFLM and referred to as (Sigma 1, σ1), then, it was calculated by using BCQ-2024 values and referred to as (Sigma2, σ2). The quality goal index (QGI) ratio was calculated for low sigma (< 3), as shown in tables (3-1) & (3-2).

Table (1): The values of sigma metric (σ 1) & (σ 2), mean CV%, mean bias% & QGI, on Abbott Architect C4000 auto analyzer from (May to August)

Analyte	Mean bias%	CV 1%	CV 2%	Mean CV%	TEA%		Sigma σ1	Sigma σ2	QGI
					Desirable BV% EFLM updated	BCQ 2024%			
Cholesterol	1.9	0.7	0.8	0.75	8.6	10	8.9	10.8	#
Creatinine	1.5	3.8	2.8	3.3	7.3	10.55	1.8	2.8	0.3
Glucose	4.3	1.5	1.1	1.3	6.4	8	1.7	2.9	2.2
Triglyceride	6.2	2.03	1.2	1.6	27.0	15	13	5.5	#
Urea	3.5	7.4	3.8	5.6	17.7	12	2.5	1.5	0.4
Uric acid	0.7	1.4	1.3	1.4	12.7	10	8.6	6.6	#

CV1%-is the mean of CV% of level 2 (L2) from (May to August). CV2%:-Is the mean of CV% of level 3(L3) from (May to August). Mean CV%:= (CV1%+ CV2%)/2. Mean bias% = the mean of three participations in EQAS. #:-QGI wasn't calculated for good sigma metric values.

Results of sigma are in general comparable on the two platforms & are low. Depending on the quality specifications used for TEa% to calculate these sigma values, desirable BV% probably yielded better sigma scales when used in these calculations than what has been seen when BCQ-2024 or TDPA defined acceptable limits are used. As in Table 2.

Table 2: Sigma metric values on Abbott Architect C4000 & Beckman Coulter AU480 using three quality specification for TEa% Desirable BV% EFLM updated (σ1), BCQ 2024% (σ2) & TDPA% (σA1& σB1) over two time durations during the study.

Analyte	Abbott			Beckman		
	May-August		Sep-Nov	May-August		Sep-Nov
	Sigma σ1	Sigma σ2	Sigma A1 σA1	Sigma σ1	Sigma σ2	Sigma B1 σB1
ALT	-	-	0.5	2.8	2.6	1.7
AST	-	-	1.2	0.7	0.9	1.6
Cholesterol	8.9	10.8	1.3	1.2	1.6	2.04
Creatinine	1.8	2.8	1.4	-0.4	0.1	-1.05
Glucose	1.7	2.9	0.6	1.7	2.2	0.1
Triglyceride	13	5.5	0.2	6.8	3.7	0.7
Urea	2.5	1.5	1.2	4.3	2.8	1.2
Uric acid	8.6	6.6	2	3.8	3.9	1.9

The values of σA for (ALT, AST, creatinine & glucose) are low, σ< 2 indicating unacceptable performance. The value of σA for cholesterol is high, (5 ≤ σ <6) indicating excellent performance. The value of σA for urea is 3≤σ<4 indicating marginal performance. The values of σA for (triglyceride& uric acid) are high, ≥ 6 indicating world-class. The values of σB for (AST, creatinine & glucose) are low, σ< 2 indicating unacceptable performance. The values of σB for (AST & cholesterol) are (2 ≤ σ <3) indicating poor performance. The value of σB for uric acid is 3≤σ<4 indicating marginal performance. The value of σB for urea is 4 ≤ σ1 <5 indicating good performance. The value of σB for triglyceride ≥ 6 indicating world-class. The values of QGI A for (creatinine, glucose & urea) are < 0.8 indicating an imprecision problem. The values of QGI A for (ALT & AST) are between (0.8-1.2) indicating a problem in both imprecision & inaccuracy. The values of QGI B for (ALT, cholesterol, glucose & uric acid) are < 0.8 indicating an imprecision problem. The value of QGI B for AST between (0.8-1.2) indicating a problem in both imprecision & inaccuracy. The value of QGI B for creatinine is >1.2 which indicate an inaccuracy problem.

Table 3: Sigma metric values & QGI on Abbott Architect c 4000 referred to as (σ A) & Beckman Coulter AU480 referred to as (σ B) over six months duration (May-November) using EFLM updated desirable BV% quality specifications for TEa%

Analyte	Abbott				Beckman			
	Mean CV%	Mean bias%	Sigma σ A	QGI A	Mean CV%	Mean bias%	Sigma σ B	QGI B
ALT	5.5	-7.2	1.6	0.9	4.6	3.2	2.8	0.5
AST	5.4	-10.1	0.6	1.3	6.1	5.8	1.3	0.9
Cholesterol	1	2.95	5.7	#	2.8	2.9	2.03	0.7
Creatinine	3.6	1.7	1.6	0.3	4.9	9.9	-0.5	1.3
Glucose	3.2	3.15	1	0.7	2.7	2.65	1.4	0.7
Triglyceride	1.8	6.95	11.2	#	3.7	3.4	6.9	#
Urea	4.8	2.95	3.1	0.4	3.3	2.5	4.6	#
Uric acid	1.3	1.6	8.5	#	3.2	1.5	3.5	0.3

#:-QGI wasn't calculated for good sigma metric values.

Uc, is representing an intermediate precision for six months. The resulting measurement uncertainty should be integrated into the data that will provide the correct laboratory response to the clinician's requirements. UcA for ALT is out of (DI) but within the (MI). UcA for AST is out of (DI) but within the (MI). UcB for ALT is within both (DI) & (MI). UcB for AST is out of (DI) but within the (MI). UcA for creatinine is out of the (DI) but within the (MI), but UcB for it out of both the (DI) & (MI). So the lab must look for problem, (as reasonably possible in the standard operation of a measurement procedure e.g. changes of reagent and calibrator batches, different operators, scheduled instrument maintenance). UcA for (urea, uric acid, cholesterol, triglyceride) is within both (DI) & (MI). UcB for (urea, uric acid, triglyceride) is within both (DI) & (MI), but UcB for cholesterol is out of (DI) but within (MI). UcA &UcB for glucose is out of the (DI) but within the (MI) as in Table 4.

Table 4: The values of Uc on both instrument Abbott Architect c 4000 referred to as (UcA) & Beckman Coulter AU 480 referred to as (UcB).

Analyte	UcA on Abbotte	UcB on beckman	Desirable imprecision%(DI)	Minimum Imprecision% (MI)
ALT	5.8	4.6	5.0	13.50
AST	5.4	6.1	4.8	8.93
Cholesterol	1	2.8	2.7	4.05
Creatinine	3.6	4.9	2.2	4.50
Glucose	3.2	2.7	2.5	4.58
Triglyceride	1.8	3.7	10.0	15.68
Urea	4.8	3.3	7.0	9.23
Uric acid	1.3	3.2	4.1	6.75

The calculated t of the eight measurements was smaller than the critical T (2.093) at degree of freedom of (19) & the significance level mentioned above α-value ≤ (0.05), therefore, it was concluded that there was no significant difference between the means of all the parameters measured on Abbott & Beckman auto analyzer. Since p-value > α, the difference between the sample variances of the two groups is not statistically significant. As in table 5 and 6.

Table 5: Comparison of means of the analytes of the (20) patient samples on the (2) platforms using paired t-test with a significant level of α-value ≤ (0.05).

		Abbott			Beckman			Calculated t-test paired
Analyte	Unit	Mean ± SD	Min value	Max value	Mean ± SD	Min value	Max value	
ALT	U/L	42.8±44.355	6.0	176.0	42.6±43.802	6.5	174.7	0.46
AST	U/L	64.9±74.476	14.0	304.0	66.8±79.343	15.5	323.1	0.27
Cholesterol	mg/dL	187.3±66.604	55.0	358.0	193.7±70.785	59.1	375.5	0.02
Creatinine	mg/dL	1.6±1.602	0.3	6.0	1.6±1.434	0.2	5.6	0.5
Glucose	mg/dL	107.6±73.246	46.0	333.0	119.2±78.527	49.7	353.7	0.00
Triglyceride	mg/dL	161.8±132.685	33.0	524.0	198.1±150.244	39.0	618.8	0.00
Urea	mg/dL	48.2±40.731	10.0	164.0	47.3±40.762	9.2	159.8	0.13
Uric acid	mg/dL	5.1±1.602	2.7	7.8	5.5±1.681	3.1	8.2	0.00

SD:-Standard deviation, Min:-Minimum, Max:-Maximum.

Table 6: Comparison of equality of variances of the two sets of data for each analyte on the two platforms using Levenes test with a significance level of α ≤ 0.05.

Analyte	Unit	F-Statistic	P-Value
ALT	U/L	0.0006392	0.98
AST	U/L	0.01723	0.8963
Cholesterol	mg/dL	0.08732	0.7693
Creatinine	mg/dL	0.04826	0.8273
Glucose	mg/dL	0.02492	0.8754
Triglyceride	mg/dL	0.249	0.6207
Urea	mg/dL	0.0001127	0.9916
Uric acid	mg/dL	0.06539	0.7995

Discussion

Sigma metrics offer a quantitative and objective measure of analytical performance, incorporating both precision and accuracy to identify deficiencies in laboratory processes. In this study, sigma values (σA & σB) for ALT, AST, creatinine, and glucose were found to be < 3, reflecting suboptimal performance that does not meet the minimum acceptable sigma threshold of 3. According to Westgard rules (Figure 1), such low sigma levels necessitate stringent quality control (QC) procedures, including the use of multirule systems like 13s/22s/R4s/41s/8x to reduce the risk of reporting erroneous patient results [14, 15].

This study's findings for ALT, AST, and creatinine align with results from Lincy Raj C *et al*. in India using the Erba Mannheim EM200 analyzer, where sigma values for these analytes were also < 3 (40). However, these results contradict studies by Saniye Basak Oktay *et al*. in Turkey (Abbott Architect c16000), where ALT and AST both showed σ >3 [16], and Bushra Mahmood *et al*. in Iraq, where σ for AST was >6 and ALT >3, although creatinine still remained < 3 [17]. Additionally, Çevlik T *et al*. (Beckman AU5800) reported σ >3 for ALT and AST but < 3 for creatinine, consistent with our study's finding for creatinine [18]. For glucose, our study's sigma values (< 3) concur with Çevlik's findings [18] and Monica Verma's report using the Randox Suzuka analyzer [19], but differ from Lincy Raj and Oktay's studies where glucose sigma values were >3 [16, 20]. This discrepancy could be attributed to differences in analyzer models, reagent quality, instrument calibration, and maintenance protocols. Cholesterol displayed σA >3 and σB <3 in our study, indicating better performance on the Abbott analyzer. This agrees with Oktay's findings for Abbott [16] but partially disagrees with Lincy Raj and Çevlik, where σ was consistently < 3 [18, 20]. For triglycerides, both σA and σB were ≥ 6, reflecting world-class performance and aligning with studies by Lincy Raj, Oktay, and Ahmed Naseer Kaftan [16, 20, 21], but contradicting Çevlik's findings of intermediate sigma (3<σ<6) [18]. Urea and uric acid demonstrated acceptable sigma values (>3) in our study, consistent with Oktay [16] and Çevlik [18], but differing from Lincy Raj and Bushra's reports where urea fell below the acceptable threshold [17, 20]. The variation in results among studies may be attributed to differences in instruments, lot variations in QC materials, laboratory protocols, and especially the source of TEa% used in sigma calculation EFLM [22] in the present study versus CLIA [19] or Ricos 2014 [17] in others. These factors significantly influence bias and precision estimations, thereby affecting sigma outputs.

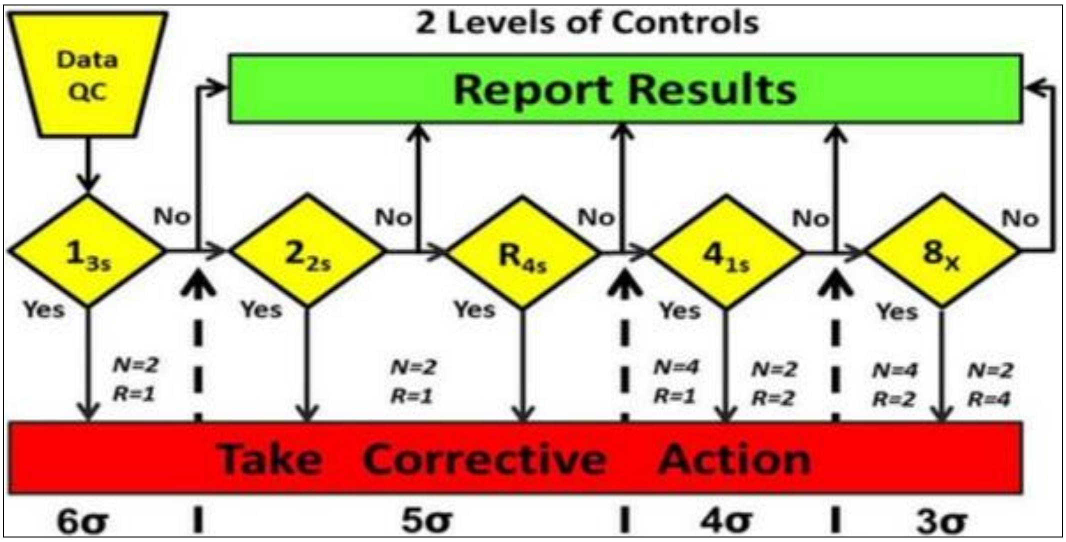

Fig 1: The westgard sigma rules for 2 levels of control materials

Conclusion

The performance of the two auto analyzers (Abbott Architect c 4000 & Beckman Coulter AU 480) was acceptable for some of the studied analytes but needs for improvement for others depending on the results of sigma. Performance was in general comparable for most of the analytes on the two platforms and the correlation between them was good.

Conflict of Interest

Not available

Financial Support

Not available

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