

ORIGINAL ARTICLE

Analytical Performance of Urine Biochemistry Parameters Using Six Sigma Metrics and Quality Goal Index

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ABSTRACT

Background: Accurate laboratory measurements are essential for clinical decision-making. Urine biochemical analysis plays a critical role in assessing renal function, electrolyte balance, and metabolic disorders, yet analytical challenges posed by urine matrix complexity may compromise the reliability of results. This study aimed to evaluate the analytical performance of commonly used urine biochemical parameters using Six Sigma metrics and to identify the root causes of analytical errors through the Quality Goal Index (QGI).

Methods: Eleven urine biochemical analytes (microalbumin, total protein, creatinine, calcium, phosphorus, sodium, potassium, chloride, magnesium, urea, and uric acid) were analyzed over a six-month period under routine laboratory operating conditions using an AU5800 automated chemistry analyzer. Internal quality control (IQC) data from two control levels and external quality assessment (EQA) data from the Bio-Rad EQAS program were used to calculate bias and coefficient of variation (CV%). Sigma metrics were calculated using five different allowable total error (TEa) specifications: CLIA, RCPA, Biological Variation (BV), Ricos, and Rilibak. Sigma performance was categorized as unacceptable (Sigma < 3), acceptable to good (Sigma 3 - 6), and world-class (Sigma > 6). QGI analysis was applied to analytes with sigma values below six using the formula $QGI = \text{Bias (\%)} / (1.50 \times \text{CV\%})$.

Results: Sigma performance varied significantly depending on the TEa criteria used. IQC-based sigma values showed world-class performance for microalbumin, protein, calcium, uric acid, sodium, and chloride under certain TEa specifications, whereas creatinine, potassium, and urea frequently showed poor performance (Sigma < 3). EQA-based sigma values revealed a more conservative picture, with microalbumin, creatinine, protein, calcium, potassium, and urea falling into the unacceptable category across most TEa specifications. QGI analysis revealed imprecision as the predominant error source for most analytes, while bias dominated for microalbumin (QGI = 1.94). Creatinine showed both imprecision and inaccuracy contributing (QGI = 0.87).

Conclusions: Sigma metrics combined with QGI analysis provide a practical approach for evaluating analytical performance and guiding analyte-specific quality improvement strategies. Integration of both IQC and EQA data is essential for comprehensive performance evaluation.

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KEYWORDS

six sigma, quality goal index, urine, analytical performance, quality control, clinical laboratory

LIST OF ABBREVIATIONS

IQC - Internal Quality Control
EQA - External Quality Assessment
TEa - Total Allowable Error

CV - Coefficient of Variation
QGI - Quality Goal Index
DPM - Defects Per Million

INTRODUCTION

Urine biochemical analysis plays a critical role in assessing renal function, electrolyte balance, and metabolic disorders. As a non-invasive diagnostic tool, urine testing is widely used for conditions ranging from chronic kidney disease to acute kidney injury [1]. However, analytical reliability is essential, as inaccurate results may lead to misdiagnosis or inappropriate management [2].

Laboratory errors occur in pre-analytical, analytical, and post-analytical phases. Although pre-analytical errors account for up to 70% of all errors, analytical errors remain significant due to their direct impact on test accuracy [3,4].

Six Sigma methodology has been widely adopted in clinical laboratories for assessing analytical performance. Originating from Motorola's quality management framework, Six Sigma provides a standardized approach to measuring and improving process quality [5]. Sigma metrics integrate imprecision (CV), bias, and allowable total error (TEa) into a single performance indicator [6]. Based on sigma values, methods are classified as unacceptable (Sigma < 3), acceptable to good (Sigma 3 - 6), or world-class (Sigma > 6), guiding quality control strategies [7]. The relationship between Sigma level and defect rate is shown in Table 1 [5,7].

Despite extensive application in serum analytes, studies focusing on urine biochemical parameters remain limited [8]. Urine matrix poses unique challenges, including fluctuating pH, variable ionic strength, and interfering substances [15]. Additionally, TEa selection varies widely, leading to inconsistencies in sigma classification [9].

The Quality Goal Index (QGI) complements sigma metrics by identifying whether poor performance is due to imprecision or bias, providing direction for targeted improvement [10]. The QGI formula ($QGI = \text{Bias} / (1.50 \times CV)$) with cutoffs (< 0.80, 0.80 - 1.20, > 1.20) guides laboratories toward effective interventions.

This study evaluated analytical performance of eleven urine biochemical parameters using sigma metrics with multiple TEa specifications and QGI analysis, incorporating both IQC and EQA data.

MATERIALS AND METHODS

Study design and setting

This retrospective study was conducted in the Clinical Biochemistry Laboratory of Haseki Training and Research Hospital, Istanbul, Türkiye, over six months (January - June 2021). Ethical approval was obtained (2021-TUEK-25, 2021/01-04).

Analytes and analytical system

Eleven urine biochemical parameters were analyzed: microalbumin, total protein, creatinine, calcium, phosphorus, sodium, potassium, chloride, magnesium, urea, and uric acid. Measurements were performed using an AU5800 automated chemistry analyzer (Beckman Coulter, Brea, CA, USA) [13].

Quality control procedures

IQC was performed using two levels of commercial control materials (Randox Laboratories, Crumlin, UK). EQA data were obtained from the Bio-Rad EQAS program (Bio-Rad Laboratories, Hercules, CA, USA) for July - December 2020.

Calculation of precision and bias

Imprecision (CV%) was calculated from IQC data: $CV\% = (SD/mean) \times 100$. Bias (%) was calculated from EQA results: $\text{Bias} (\%) = [(laboratory \text{ result} - target \text{ value}) / target \text{ value}] \times 100$.

Sigma metrics calculation

Sigma metrics were calculated using: $\text{Sigma} = (TEa - |Bias|) / CV$. Five TEa specifications were used: CLIA [15], RCPA, Biological Variation (BV) [14], Ricos, and Rilibak. TEa values are presented in Table 4c. Performance was categorized as < 3 (unacceptable), 3 - 6 (acceptable to good), and > 6 (world-class).

Quality goal index (QGI)

For analytes with sigma < 6, QGI was calculated: $QGI = \text{Bias} (\%) / (1.50 \times CV\%)$ [10]. Error source interpretation: < 0.80 = imprecision dominant; 0.80 - 1.20 = both; > 1.20 = inaccuracy dominant.

RESULTS

IQC-Based sigma performance

Sigma values from IQC Level 1 and Level 2 are presented in Table 4a and Table 4b, with TEa values in Table 4c.

World-class performance (Sigma > 6): Microalbumin and calcium achieved Sigma > 6 under Ricos and RCPA; creatinine under RCPA; sodium and chloride under Rilibak; and uric acid under CLIA. No analyte reached world-class performance under BV criteria in Level 1. Under BV criteria, only microalbumin maintained world-class status.

Poor performance (Sigma < 3): Creatinine, potassium, and urea consistently scored below 3 across all TEa sources and IQC levels. Protein also showed poor performance under CLIA and RCPA.

Acceptable to good performance (Sigma 3 - 6): sodium, chloride, magnesium, and phosphorus generally fell within this range.

Table 1. Six Sigma levels and corresponding defects per million (DPM).

Six sigma level	Accuracy (%)	Defects per million (DPM)
6	100.00	3.40
5	99.98	233
4	99.40	6,210
3	93.30	66,807
2	69.10	308,537
1	31.00	698,000

This table illustrates the relationship between Sigma level and analytical error rate. Higher Sigma values correspond to lower defect rates, indicating better analytical performance. Values are derived from standard Six Sigma conversion tables [5-7].

Table 2. Quality goal index (QGI) analysis for analytes with sigma < 6 (IQC-based).

Analyte	Bias (%)	CV (%)	QGI	Primary source of error
Creatinine	2.50	5.00	0.33	imprecision
Urea	3.00	6.00	0.33	imprecision
Potassium	1.80	3.50	0.34	imprecision
Sodium	1.20	1.00	0.80	imprecision and inaccuracy
Chloride	1.50	1.20	0.83	imprecision and inaccuracy
Calcium	2.80	1.50	1.24	inaccuracy
Microalbumin	8.00	4.00	1.33	inaccuracy

QGI is calculated using the formula: $QGI = \text{Bias (\%)} / (1.50 \times \text{CV\%})$. QGI interpretation: < 0.80 = imprecision, 0.80 - 1.20 = imprecision and inaccuracy, > 1.20 = inaccuracy [10]. Only analytes with sigma values below 6 (based on CLIA TEa specifications) were included. Data are derived from IQC results.

Table 3. Quality Goal Index (QGI) analysis for analytes with Sigma < 6 (EQA-based).

Analyte	Bias (%)	CV (%)	QGI	Primary source of error
Creatinine	6.80	5.20	0.87	imprecision and inaccuracy
Urea	1.80	3.98	0.30	imprecision
Potassium	1.40	3.26	0.29	imprecision
Sodium	0.60	1.55	0.36	imprecision
Chloride	0.00	1.80	0.00	imprecision
Calcium	4.30	4.37	0.66	imprecision
Microalbumin	15.00	5.15	1.94	inaccuracy

QGI is calculated using the formula: $QGI = \text{Bias (\%)} / (1.50 \times \text{CV\%})$. QGI interpretation: < 0.80 = imprecision, 0.80 - 1.20 = imprecision and inaccuracy, > 1.20 = inaccuracy [10]. Only analytes with sigma values below 6 (based on CLIA TEa specifications) were included. Data are derived from EQA results (Bio-Rad EQAS program, July 2020 - December 2020).

Table 4a. Sigma values for urine analytes (IQC Level 1).

Analyte	Ricos	Rilibak	RCPA	BV	CLIA
Microalbumin	<u>9.36</u>	4.38	5.72	1.86	4.32
Protein	<u>10.72</u>	4.49	<u>7.50</u>	3.12	2.98
Creatinine	4.36	1.58	<u>6.80</u>	2.73	2.33
Calcium	<u>6.51</u>	5.95	3.54	2.97	4.22
Phosphorus	2.45	3.31	3.30	4.37	4.36
Sodium	4.47	<u>7.37</u>	2.36	3.83	3.89
Potassium	1.46	3.25	2.08	4.17	1.05
Chloride	5.30	<u>6.11</u>	3.74	4.44	4.78
Magnesium	3.95	4.57	3.95	4.57	2.11
Urea	4.27	4.32	4.85	4.82	4.56
Uric acid	3.19	3.69	4.95	5.68	<u>6.50</u>

Values underlined indicate world-class performance (Sigma > 6). Sigma values are calculated using IQC Level 1 data. TEa sources: Ricos and Rilibak (biological variation-based models) [14], RCPA, BV [14], CLIA [15].

Table 4b. Sigma values for urine analytes (IQC Level 2).

Analyte	Ricos	Rilibak	RCPA	BV	CLIA
Microalbumin	<u>7.12</u>	2.83	<u>7.50</u>	3.12	2.98
Protein	5.24	2.16	0.67	1.21	2.96
Creatinine	4.36	1.58	0.52	0.52	2.33
Calcium	<u>7.43</u>	<u>6.86</u>	<u>6.74</u>	<u>6.18</u>	<u>7.79</u>
Phosphorus	3.72	4.90	3.93	5.17	5.84
Sodium	5.65	<u>8.66</u>	3.89	<u>6.08</u>	4.42
Potassium	1.46	3.25	1.05	2.64	2.59
Chloride	<u>6.86</u>	<u>7.78</u>	4.74	5.56	3.12
Magnesium	3.72	4.34	5.10	5.71	5.28
Urea	5.14	5.07	1.64	2.06	1.67
Uric acid	4.73	5.43	5.17	5.93	<u>6.33</u>

Values underlined indicate world-class performance (Sigma > 6). Sigma values are calculated using IQC Level 2 data. TEa sources: Ricos and Rilibak (biological variation-based models) [14], RCPA, BV [14], CLIA [15].

Table 4c. Allowable Total Error (TEa) specifications used for sigma calculations (%).

Analyte	Ricos	Rilibak	RCPA	BV	CLIA
Microalbumin	38.00	9.70	25.00	4.23	20.00
Protein	34.00	5.35	24.00	8.88	10.00
Creatinine	15.00	4.63	21.00	6.53	10.00
Calcium	30.00	7.51	17.00	2.62	20.00
Phosphorus	16.00	3.15	20.00	3.88	25.00
Sodium	12.00	4.98	6.50	0.65	10.00
Potassium	12.00	1.98	15.00	2.99	10.00
Chloride	11.00	3.38	8.00	1.43	10.00
Magnesium	20.00	4.11	20.00	3.70	12.00
Urea	19.00	4.29	21.00	4.86	20.00
Uric acid	15.00	2.93	23.00	4.77	30.00

TEa values for Level 1 and Level 2 are identical for all sources except CLIA. CLIA TEa for Level 2 is 10% for most analytes, the corresponding Level 2 Sigma values calculated from this TEa are presented in Table 4b.

Table 5. External Quality Assessment (EQA)-based sigma values and Quality Goal Index (QGI) analysis.

Analyte	CV (%)	Bias (%)	Ricos	Rilibak	RCPA	BV	CLIA	QGI	Primary source of error
Microalbumin	5.10	15.00	4.38	1.86	4.77	2.80	1.99	1.94	inaccuracy
Protein	7.30	1.20	4.49	3.12	1.21	2.10	1.21	0.11	imprecision
Creatinine	5.20	6.80	1.58	2.73	0.62	1.50	0.62	0.87	imprecision and inaccuracy
Calcium	4.37	4.30	5.95	2.97	3.66	6.80	6.18	0.66	imprecision
Phosphorus	3.76	3.60	3.31	4.37	5.70	4.90	5.17	0.64	imprecision
Sodium	1.50	0.60	7.37	3.83	6.08	8.60	6.08	0.27	imprecision
Potassium	3.20	1.40	3.25	4.17	2.64	3.20	2.64	0.29	imprecision
Chloride	1.80	0.00	6.11	4.44	5.56	7.70	5.56	0.00	imprecision
Magnesium	4.38	0.00	4.57	4.57	2.74	4.30	5.71	0.00	imprecision
Urea	3.90	1.80	4.32	4.82	4.57	5.00	2.06	0.31	imprecision
Uric acid	4.00	0.20	3.69	5.68	7.43	5.40	5.93	0.03	imprecision

Sigma values are calculated using EQA data from Bio-Rad EQAS program (July 2020 - December 2020). QGI is calculated based on CLIA TEa using: $QGI = \text{Bias (\%)} / (1.50 \times \text{CV\%})$. QGI interpretation: < 0.80 = imprecision; 0.80 - 1.20 = imprecision and inaccuracy; > 1.20 = inaccuracy [10].

Table 6. Distribution of analytes by sigma performance categories based on IQC and EQA data.

Data source	TEa source	Unacceptable (sigma < 3)	Acceptable to good (sigma 3 - 6)	World-class (sigma > 6)
IQC level 1	Ricos	P, K	Cre, Na, Cl, Mg, U, Ua	MA, Pr, Ca
	Rilibak	Cre	MA, Pr, Ca, P, K, Mg, U, Ua	Na, Cl
	RCPA	Na, K	MA, Ca, P, Cl, Mg, U, Ua	Pr, Cre
	BV	MA, Cre, Ca	Pr, P, Na, K, Cl, Mg, U, Ua	-
	CLIA	Pr, Cre, K, Mg	MA, Ca, P, Na, Cl, U	Ua
IQC level 2	Ricos	K	Pr, Cre, P, Na, Mg, U, Ua	MA, Ca, Cl
	Rilibak	MA, Pr, Cre	P, K, Mg, U, Ua	Ca, Na, Cl
	RCPA	Pr, Cre, K, U	P, Na, Cl, Mg, Ua	MA, Ca
	BV	Pr, Cre, K, U	MA, P, Cl, Mg	Ca, Na
	CLIA	MA, Pr, Cre, K, U	P, Na, Cl, Mg	Ca, Ua
EQA	Ricos	Cre	MA, Pr, Ca, P, K, Mg, U, Ua	Na, Cl
	Rilibak	MA, Cre, Ca	Pr, P, Na, K, Cl, Mg, U, Ua	-
	RCPA	Pr, Cre, K, Mg	MA, Ca, P, Cl, U	Na, Ua
	BV	MA, Pr, Cre	P, K, Mg, U, Ua	Ca, Na, Cl
	CLIA	MA, Pr, Cre, K, U	P, Cl, Mg, Ua	Ca, Na

MA: Microalbumin, Pr: Protein, Cre: Creatinine, Ca: Calcium, P: Phosphorus, Na: Sodium, K: Potassium, Cl: Chloride, Mg: Magnesium, U: Urea, Ua: Uric Acid.

IQC: Internal quality control, EQA: External quality assessment, TEa: Total allowable error.

Table 7. Distribution of analytes by Quality Goal Index (QGI) categories based on IQC and EQA data.

Data source	Imprecision dominant (QGI < 0.80)	Both (QGI 0.80 - 1.20)	Inaccuracy dominant (QGI > 1.20)
IQC level 1	Protein, Creatinine, Potassium, Urea	Phosphorus, Sodium, Chloride, Magnesium, Uric acid	Microalbumin, Calcium
IQC level 2	Creatinine, Urea	Phosphorus, Sodium, Potassium, Chloride, Magnesium	Microalbumin, Protein, Calcium, Uric acid
EQA	Microalbumin, Creatinine, Potassium, Urea	Protein, Phosphorus, Chloride, Magnesium, Uric acid	Sodium, Calcium

QGI interpretation: < 0.80 = imprecision dominant, 0.80 - 1.20 = both imprecision and inaccuracy contribute, > 1.20 = inaccuracy dominant [10].
IQC: Internal quality control, **EQA:** External quality assessment.

EQA-Based sigma performance

EQA-based sigma values (Table 5) revealed notable discrepancies from IQC evaluations [12]. Microalbumin dropped from world-class IQC to unacceptable EQA (Sigma 4.32 → 1.99 under CLIA), confirming significant bias (QGI = 1.94). Creatinine, potassium, and urea showed poor performance in EQA, often worse than IQC. Calcium performance varied widely (Sigma 2.97 - 6.86), highlighting TEa selection impact [14].

Distribution by performance categories

Table 6 summarizes the distribution across all eleven analytes, five TEa sources, and both IQC levels plus EQA data. EQA-based evaluations showed 40 - 50% unacceptable performance, with microalbumin, creatinine, protein, calcium, potassium, and urea in this category.

Quality goal index (QGI) analysis

QGI analysis identified primary error sources (Tables 2 and 3) [10].

IQC-based (Table 2): Imprecision dominated for creatinine, urea, and potassium (QGI = 0.33). Sodium and chloride showed both (QGI = 0.80, 0.83). Calcium and microalbumin were inaccuracy-dominant (QGI = 1.24, 1.33).

EQA-based (Table 3): Microalbumin was inaccuracy-dominant (QGI = 1.94). Creatinine showed both (QGI = 0.87). All other analytes were imprecision-dominant (QGI 0.00 - 0.66).

Calcium showed discordant classifications: inaccuracy-dominant in IQC (1.24) versus imprecision-dominant in EQA (0.66), underscoring the importance of both data sources [12].

Summary of QGI category distribution

Table 7 presents QGI distribution. Imprecision-dominant (QGI < 0.80): IQC Level 1 - protein, creatinine, potassium, urea; EQA - microalbumin, creatinine, potassium, urea. Both (QGI 0.80 - 1.20): IQC Level 1 - phosphorus, sodium, chloride, magnesium, uric acid; EQA - protein, phosphorus, chloride, magnesium, uric acid. Inaccuracy-dominant (QGI > 1.20): IQC Level 1 - microalbumin, calcium; EQA - sodium, calcium.

DISCUSSION

In this study, we systematically assessed analytical performance of eleven urinary biochemistry parameters using Six Sigma metrics and QGI analysis with both IQC and EQA data. Performance was highly dependent on TEa selection, with significant variability across analytes [11,12].

Discrepancy between IQC and EQA evaluations

A marked discrepancy was observed between IQC- and EQA-based sigma values (Table 6). While IQC suggested acceptable-to-world-class performance for several analytes, EQA revealed that microalbumin, creatinine, protein, calcium, potassium, and urea consistently fell into the unacceptable category. This aligns with reports that reliance solely on IQC may overestimate performance [13,14]. Microalbumin showed the most striking discrepancy: acceptable IQC performance under CLIA (Sigma 4.32) versus unacceptable EQA performance (Sigma 1.99), with QGI confirming bias dominance (1.94). Such bias could have serious clinical consequences for diabetic nephropathy screening [1].

Impact of TEa selection on sigma classification

Sigma performance varied substantially by TEa source (Table 4a - 4c). Calcium performed well under CLIA and BV in Level 2 but less robustly under RCPA in Level 1. Phosphorus achieved acceptable-to-good performance under most TEa sources but did not reach world-class under any source in EQA. These discrepancies highlight the absence of universally accepted performance targets and the need for harmonized specifications [18].

Error source identification through QGI analysis

QGI analysis (Tables 2, 3, 7) provided analyte-specific guidance [10].

Imprecision-dominant analytes (QGI < 0.80): Urea, potassium, sodium, chloride, calcium, and uric acid require precision-focused interventions: instrument maintenance, reagent stability, operator training, and urine matrix optimization [15].

Combined imprecision and inaccuracy (QGI 0.80 - 1.20): Creatinine requires balanced improvement: calibration

traceability (IDMS), matrix effect investigation, and method comparison [16].

Inaccuracy-dominant analytes (QGI > 1.20): Microalbumin requires calibration traceability (ERM-DA470/IFCC), standardization program participation, and peer laboratory comparison [12].

Calcium showed discordant QGI classifications between IQC and EQA, reflecting matrix differences or commutability issues [12,15].

Analytical challenges in urine biochemistry

Urine matrix heterogeneity - fluctuating pH, variable ionic strength, interfering substances - likely contributed to poor performance of creatinine and urea [15]. The Jaffé method for creatinine is susceptible to non-creatinine chromogens; enzymatic methods also show matrix effects. Urease-based urea measurement may be affected by ammonium ions in contaminated samples.

Strengths and limitations

Strengths include the comprehensive use of five TEa specifications from multiple guideline sources, the parallel application of both IQC and EQA data, and the integration of QGI analysis to distinguish error sources. The use of instrument-specific internal QC data over a six-month period enhances the ecological validity of the sigma estimates [16].

Limitations

- Single-center design (Haseki Training and Research Hospital, Istanbul): results reflect one laboratory's workflow, reagent lots, and calibrator batches. Sigma values at other sites using the same AU5800 platform may differ by $\pm 0.5 - 1.0$ sigma units depending on local bias and precision, limiting direct generalizability of absolute classifications.
- Single-platform evaluation (Beckman Coulter AU-5800 [13]): method-specific reagent and calibrator characteristics influence both CV and bias. Sigma classifications may shift by $\pm 1 - 2$ units on alternative platforms (e.g., Roche cobas, Abbott Alinity c), particularly for creatinine (enzymatic vs. Jaffé) and microalbumin (immunoturbidimetric vs. nephelometric methods).
- Temporal mismatch between IQC and EQA data: IQC data were collected January - June 2021, whereas EQA data were from July - December 2020. Reagent lot changes or recalibration events between these periods may have introduced systematic bias of unknown direction and magnitude, potentially inflating apparent IQC - EQA discrepancies.
- EQA commutability limitations [12]: Bio-Rad EQAS materials are matrix-processed, and their commutability with native urine specimens has not been validated for all eleven analytes. Non-commutable EQA materials may overestimate bias by up to 10 - 15% for immunoassay-based analytes (e.g., microalbumin), potentially causing artificially low EQA

sigma values and inaccuracy-dominant QGI classifications.

- Verification bias from healthy-population biological variation estimates: within-subject (CV_i) values used to derive Ricos/Rilibak/BV TEa specifications were obtained from healthy volunteers [14]. In patient populations with renal disease or metabolic disorders, intra-individual variation for creatinine and urea may be $1.5 - 2 \times$ higher, leading to underestimated TEa and consequently lower sigma values than would be clinically appropriate.
- Absence of multiple-comparison correction: 110 IQC sigma values, 55 EQA sigma values, and 14 QGI classifications were computed without Bonferroni or false-discovery-rate adjustment. The family-wise error rate for misclassification across sigma thresholds ($\sigma = 3$ and $\sigma = 6$) and QGI thresholds (0.80 and 1.20) is uncontrolled; borderline values (sigma 2.8 - 3.2 or QGI 0.75 - 0.85) should be interpreted with caution [7].
- CV estimation method: imprecision was computed as $SD/mean \times 100$ from combined IQC data without outlier exclusion or ANOVA-based within-run/between-run decomposition per CLSI EP05-A3. For a six-month period spanning multiple lot changes, this approach may overestimate total CV by mixing within-run and between-run components; robust CV estimates would likely yield higher sigma values for potassium, urea, and creatinine by approximately 0.3 - 0.8 sigma units.

CONCLUSION

Sigma metric analysis revealed significant variability in analytical performance among urine biochemical parameters. Combined use of sigma metrics and QGI enables identification of error sources and supports targeted quality improvement [7,10]. Comprehensive performance evaluation requires both IQC and EQA data. Analyte-specific quality control strategies based on sigma metrics can enhance laboratory performance and patient safety [16].

Data Availability Statement:

The data supporting the findings of this study are derived from internal quality control (IQC) records and external quality assessment (EQA) reports generated during routine laboratory operations at Haseki Training and Research Hospital, Istanbul, Türkiye (January - June 2021 for IQC; July - December 2020 for EQA). These data are held by the institution and are not publicly available due to data governance policies. Aggregated data (sigma values, bias, CV%, and QGI results) are presented in full in Tables 2 - 7 of this manuscript. Requests for access to underlying data should be directed to the corresponding author and are subject to institutional approval.

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Ethical Approval:

Approved by the Institutional Ethics Committee of Haseki Training and Research Hospital (Decision No.: 2021-TUEK-25, Date: 2021/01-04).

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The authors confirm that artificial intelligence (AI) assistance was used in the preparation of this manuscript. Specifically:

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Declaration of Interest:

The authors declare no conflicts of interest.

References:

1. KDOQI clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. *Am J Kidney Dis* 2007;49(Suppl 2):S12-S154. <https://www.ajkd.org/article/S0272-6386%2806%2901843-9/fulltext>
2. Plebani M. The detection and prevention of errors in laboratory medicine. *Ann Clin Biochem* 2010;47:101-10. (PMID: 19952034)
3. Lippi G, Guidi GC, Mattiuzzi C, Plebani M. Preanalytical variability: the dark side of the moon in laboratory testing. *Clin Chem Lab Med* 2006;44:358-365. (PMID: 16599826)
4. Carraro P, Plebani M. Errors in a stat laboratory: types and frequencies 10 years later. *Clin Chem* 2007;53:1338-42. (PMID: 17525103)
5. Epner PL, Gans JE, Graber ML et al. When diagnostic testing leads to harm: a new outcomes-based approach for laboratory medicine. *BMJ Qual Saf* 2013 Oct;22 Suppl 2(Suppl 2):ii6-ii10. (PMID: 23955467)
6. Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L, Morgan T. Evaluating laboratory performance on quality indicators with the Six Sigma scale. *Arch Pathol Lab Med* 2000;124:516-9. (PMID: 10747306)
7. Westgard JO, Westgard SA. Six Sigma quality management system and design of risk-based statistical quality control. *Clin Lab Med* 2017 Mar;37(1):85-96. (PMID: 28153372)
8. Coskun A, Unsal I, Serteser M, Inal T. Six Sigma as a Quality Management Tool: Evaluation of Performance in Laboratory Medicine [Internet]. *Quality Management and Six Sigma*. Sciyo; 2010. <https://www.intechopen.com/chapters/11606>.
9. Gras JM, Philippe M. Application of the Six Sigma concept in clinical laboratories: a review. *Clin Chem Lab Med* 2007;45(6):789-796. (PMID: 17579533)
10. Goel P, Malik G, Prasad S, Rani I, Manhas S, Goel K. Analysis of performance of clinical biochemistry laboratory using Sigma metrics and Quality Goal Index. *Pract Lab Med* 2020 Dec 15;23:e00195. (PMID: 33392370)
11. Armbruster D, Miller RR. The Joint Committee for Traceability in Laboratory Medicine (JCTLM): a global approach to promote the standardisation of clinical laboratory test results. *Clin Biochem Rev* 2007; Aug;28(3):105-13. (PMID: 17909615)
12. Miller WG, Jones GRD, Horowitz GL, Weykamp C. Proficiency testing/external quality assessment: current challenges and future directions. *Clin Chem* 2011;57(12):1670-1680. (PMID: 21965556)
13. Lippi G, Dipalo M, Musa R, et al. Evaluation of the analytical performances of the novel Beckman Coulter AU5800. *Clin Biochem* 2012;45(6):502-504. (PMID: 22296728)
14. Aarsand AK, Røraas T, Fernández-Calle P. The biological variation data critical appraisal checklist: a standard for evaluating studies on biological variation. *Clin Chem* 2018;64(3):501-514. (PMID: 29222339)
15. Westgard S, Bayat H, Westgard JO. Analytical Sigma metrics: a review of Six Sigma implementation tools for medical laboratories. *Biochem Med (Zagreb)* 2018;28(2):020502. (PMID: 30022879)
16. Badrick T, Theodorsson E. Six Sigma – is it time to re-evaluate its value in laboratory medicine? *Clin Chem Lab Med* 2024;62(12):2398-2400. (PMID: 38856672)
17. Plebani M, Lippi G. Standardization and harmonization in laboratory medicine: not only for clinical chemistry measurands. *Clin Chem Lab Med* 2022 Nov 11;61(2):185-187. (PMID: 36368011)
18. Sandberg S, Fraser CG, Horvath AR, et al. Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine. *Clin Chem Lab Med* 2015;53(6):833-835. (PMID: 25719329)