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Original Research Article

Evaluation of analytical performance & quality specification of urine biochemical analytes

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ABSTRACT

Background: Urinary biochemical analytes are very important tools for clinical decision making. Total allowable error (TEa) by integrating internal (IQC) and external (EQC) quality control performances are used to evaluate the performance of urinary biochemical analytes along with quality specifications strategy.
Materials and Methods: Alternate 6 months Coefficient of Variation (CV%) and External Quality Assurance Scheme (EQAS) bias% data for urinary biochemistry analytes were collected for the year 2022. TEa calculated for each analyte was calculated based on average CV% and bias%. Total TEa calculated values are compared with optimal, minimal and desirable TEa of each analyte.
Result: TEa values of urinary biochemistry analytes were performing good and fulfilled minimal, desirable and optimal quality requirements except urine creatinine which did not fulfill the minimal standards.
Conclusion: TEa is an excellent quality management tool and quantitatively evaluates analytical performance. The accurate results generated are useful for clinicians for decision-making.

1. Introduction

The clinical applications of urinary quantitative biochemical analytes such as potassium (K), sodium (Na), calcium (Ca), phosphorus (P) creatinine (Crea), total protein (TP), and microalbumin (mAlb), are becoming increasingly widespread.[1–4] The levels of K, Na, Ca, and P reflect the excretion and reabsorption functions of the kidneys.[5,6] The levels of Crea, TP, and mALB mainly reflect the degree of kidney damage caused by various diseases.[7–9] The biochemical analysis of these urinary analytes can have an important adjuvant role in the diagnosis and evaluation of a number of clinical problems. It may, however, be confounded in ICU settings and ideally should be integrated into the broader clinical context to inform about optimal management.[10] With the widespread application of urinary biochemical analytes in clinics, the testing capabilities of laboratories are increasingly becoming a challenge. Thus, there is an increasing need for, laboratories to urgently design a quality evaluation strategy to evaluate the analytical performance of urinary biochemical analytes. The performances of an analyte are expressed in statistical terms such as CV and Bias. The CV of an analyte can be obtained from IQC while bias can be obtained from EQC data such as EQA. Total allowable error for an analyte is obtained from published literature.

2. Materials and Methods

This study was done in a clinical laboratory setting and the urinary biochemical analytes involved in this study were microalbumin, protein, creatinine, calcium, phosphorous, sodium and potassium. All the analytes were processed in the Roche Cobas 6000 analyzer and with its dedicated reagents. Bio-Rad Laboratories (Bio-Rad Inc., California, USA), including the following two levels: the normal

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level (level 1, lot no:63471) and high level (level 2, lot no: 88192) were used as internal quality control (IQC) materials. Alternate month Bio- Rad EQAS Urine chemistry program cycle 14, lot no:251300 was selected. The methods for detecting urinary biochemical analyte levels are briefly described as follows: K, Na levels were detected using the indirect ion selective electrode method. mAlb levels were detected by using immunoturbidimetric method; TP levels detected using the benzethonium chloride, Crea levels were detected using the alkaline picrate method, Ca levels were detected by using BAPTA method; P levels were detected using phosphomolybdate method.

2.1. Calculation of TEa

Referring to formula: TEa = 2*CV%+Bias %. TEa was calculated for each analyte.

The CV data represent the imprecision of each analyte and were derived from six alternative months of IQC (two levels) analysis from January to December 2022. Two levels of IQC were run at peak time in the morning and one level at every 8 hourly daily protocols was used. Mean and Standard deviation (SD) were calculated. Monthly CV % was calculated by the formula: CV% = SD / Mean * 100. The highest CV% out of two levels was selected for each month and finally the average CV% was calculated.

Bias represents the trueness of each analyte, and it was determined based on EQA samples of urinary biochemical analytes in 2022. Bio- Rad EQAS report was used for the average absolute value of the above single percentage difference was defined as the bias of that analyte and used for the calculation of its TEa.

Bias % = Value(measured) – Value(target) / Value(target) × 100%.

Average Bias % was calculated for each urine biochemical analytes. TEa % calculated for each analytes using the above said formula.

In 1974, the concept of total error was first introduced by Westgard based on analytical imprecision (reproducibility of the result) and bias (systematic error).[11] It must be noted that there are three possible TEa targets for analytes: desirable, minimum, and optimal.[12] (Table 1)

Table 1: Quality specification of TEa

Quality Specifications	TEa
Optimal	TEa = <1.65 * (0.25 CV_I) + 0.125 $\sqrt{(CV_I^2 + CV_G^2)}$
Desirable	TEa = <1.65 * (0.50 CV_I) + 0.250 $\sqrt{(CV_I^2 + CV_G^2)}$
Minimum	TEa = <1.65 * (0.75 CV_I) + 0.375 $\sqrt{(CV_I^2 + CV_G^2)}$

CV_I = CV of within-subject (intra-individual) BV and CV_G = CV of between-subject (inter-individual) BV.

3. Results and Discussion

Coefficient of variation (CV%), obtained from IQC data for each analyte describes the variation of the test & signifies the degree of imprecision in general. Lower CV signifies a better performance method whereas higher CV implies poorer performance.[13] From Tables 2 and 3, in our study, analytical CV% of all analytes was within acceptable limits of minimum, desirable & optimum quality specifications. This suggested good precision & minimum variability of urine chemistry parameters in our laboratory.

Biological variation and CLIA guidelines are the most commonly used sources. In our study, from Tables 2 and 3, it is evident that urine chemistry parameters were within all the three quality specifications except for urine creatinine wherein the bias% was not within acceptable performances as per minimum quality specifications. It is ideal to calculate the bias by using reference method value as "true value".[14]

Table 4 shows comparison of TEa from Ricos and Our lab TEa. All the urine parameters showed lower TEa compared to the Ricos et al. TEa values.[12] There are multiple sources for TEa targets derived from medically important measures or clinical decision thresholds. A laboratory should decide which TEa target is best suited for clinical decision. In our study, from Tables 2 and 3, it is also evident that the Total analytical error adopted as bias (%) + 2CV(%) which is consistent with CLIA recommendations, are within acceptable limits for all the urine parameters except for Urine Crea did not fulfil the minimum quality specification. TEa biological variability values are very stringentand perhaps too challenging for analyzing the analytical performance.[15] The applications of TEa are to evaluate the performance qualification of the instrument, to guide comparison of test results across laboratories and clinics using the same or different analytical methods & to help interpret results from external QA (proficiency testing) programs or inter-laboratory comparison as a part of proficiency testing activity.[16]

Thus, evaluation of the performance of Urinary biochemical analytes helps to minimize the errors and improve process quality. A better analytical quality of these urinary biochemical tests can be fulfilled by setting and implementing evidence-based analytical quality specifications, improving metrological traceability and correcting biases and systematic errors.

4. Conclusion

Quality assurance strategies for urinary biochemical analytes should be incorporated during the analytical phase in laboratory diagnosis to avoid errors & generate accurate reports thereby facilitating proper diagnosis and enabling better patient care and management.

Table 2: Urine biochemical analytes CV% and bias % data for the year 2022

S.No.	Urine Parameters	Jan 2022	March 2022	May 2022	July 2022	Sep 2022	Nov 2022	Average
1	**U. Albumin**							
	CV%	6.68	9.11	3.28	6.1	3.2	7.8	6.02
	EQAS (bias %)	1.22	6.25	7.67	4.42	4.97	2.28	4.46
2.	**U. Calcium**							
	CV%	3.15	4.17	3.42	2.11	1.96	3.25	3.01
	EQAS (bias %)	0.42	0.02	5.45	3.87	2.31	0.27	2.05
3	**U. Creatinine**							
	CV%	1.54	2.89	3.15	2.02	1.96	2.75	2.38
	EQAS (bias %)	6.16	5.17	3.66	1.35	6.42	3.61	4.39
4	**U. Phosphorous**							
	CV%	1.9	2.73	0.71	1.95	2.07	3.15	2.08
	EQAS (bias %)	4.69	4.64	0.93	5.44	4.06	2.29	3.67
5	**U. Potassium**							
	CV%	1.84	3.25	4.23	2.13	1.99	3.03	2.74
	EQAS (bias %)	0.77	5.55	4.04	4.59	4.84	4.42	4.03
6	**U. Protein**							
	CV%	3.45	3.99	2.59	5	6.65	3.29	4.16
	EQAS (bias %)	5.27	0.28	4.21	7.25	2.57	3.72	3.87
7	**U. Sodium**							
	CV%	3.98	4.2	7.72	3.96	3.13	3.36	4.39
	EQAS (bias %)	6.2	1.38	6.88	2.82	2.57	0.93	3.46

Table 3: Total analytical error calculation

	Minimum			Desirable			Optimum			Study result		
Analyte (Matrix: Urine)	**Imp (%)**	**Bias (%)**	**TEa (%) p<0.05**	**Imp (%)**	**Bias (%)**	**TEa (%) p<0.05**	**Imp (%)**	**Bias (%)**	**TEa (%) p<0.05**	**% CVA**	**Analytical BIAS%**	**Total Analytical Error**
Albumin	8.8	6.2	**20.6**	17.5	12.4	**41.2**	26.3	18.6	**61.9**	6.02	4.46	**16.5**
Calcium	6.6	4.7	**15.5**	13.1	9.4	**31.0**	19.7	14.1	**46.5**	3.01	1.57	**7.59**
Creatinine	2.8	3.2	**7.7**	5.5	6.4	**15.4**	8.3	9.6	**23.2**	2.38	4.39	**9.15**
Phosphate	4.5	3.6	**11.0**	9.0	7.2	**22.1**	13.5	10.8	**33.1**	2.08	3.67	**7.83**
Potassium	6.1	4.1	**14.2**	12.2	8.2	**28.4**	18.3	12.4	**42.6**	2.74	4.03	**9.51**
Protein	8.9	5.3	**20.0**	17.8	10.7	**40.0**	26.6	16.0	**59.9**	4.16	3.87	**12.19**
Sodium	7.2	4.2	**16.0**	14.4	8.3	**32.0**	21.5	12.5	**48.0**	4.39	3.46	**12.24**

Table 4: Comparison of TV from BV and our lab study

Urine Parameters	TEa from Ricos	Our Lab TEa
Albumin	40.6	16.5
Calcium	34.1	7.59
Creatinine	42.1	9.15
Phosphate	22.1	7.83
Potassium	28.4	9.51
Protein	40.0	12.19
Sodium	32.0	12.24

5. Source of Funding

None.

6. Conflict of Interest

None.

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