Analytical evaluation of Sysmex Clinical Chemistry analyzer JCA-BM6010/C

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The study objective was to perform the analytical evaluation of the clinical chemistry analyzer JCA-BM6010/C (BM6010/C; Sysmex Corporation, Kobe, Japan). The JCA-BM6010/C is a new high throughput compact and efficient analyzer from Sysmex Corporation. Results were obtained for within-run and between-day imprecision, interference, linearity and comparison with cobas c501 [cobas c501; Roche Diagnostics (Schweiz) AG, Switzerland]. Altogether 12 analytes including glucose, creatinine, uric acid, total bilirubin, total cholesterol, triglycerides, aspartate aminotransferase (AST), alanine aminotransferase (ALT), HDL-C, urea, total protein and albumin were tested. Satisfactory precision results were obtained, with most assays demonstrating within-run coefficients of variation of less than 3.3% and between-day coefficients of variation less than 3.7%. The linearity for all assays was acceptable over the range tested. Correlation results were adequate. We conclude that the BM6010/C demonstrates good performance capabilities, making this instrument suitable for a medium - to high - volume laboratory.

Key Words BM6010/C, Analytical Evaluation, Imprecision, Correlation, Chemistry Analyzer

INTRODUCTION

Sysmex JCA-BM6010/C (BM6010/C; Sysmex Corporation, Kobe, Japan) is the fully automated clinical chemistry analyzer designed for clinical chemistry laboratories with medium to large number of samples. Analytical evaluation of BM6010/C analyzer was conducted at Clinical Chemistry Department, St. Carolus Salemba Hospital, Jakarta, Indonesia.

According to international guidelines, analytical evaluation of the analyzer and methods should be done before the introduction of the new analyzer into the routine use in order to confirm declared specifications of the analytical methods.

Sysmex BM6010/C is a compact and efficient automated analyzer where the measurements are carried out using the spectrophotometry, turbidimetry and indirect potentiometry (using ion-selective electrode - ISE unit) in serum, urine, cerebrospinal fluid, and other types of body fluids. The analyzer can process maximum up to 1200 tests per hour, including 600 ISE unit tests. It has capacity to program maximum of 99 different test parameters and can process 50 assays simultaneously (53 assays with ISE unit).

The analyzer uses inert oil as reaction bath oil which provides stabilized optical path and ensures homogenous incubation temperature within the reaction carousel. In addition, the inert oil prevents stains and odors; therefore no maintenance is required for the reaction bath.

It also has the ability of continuous control monitoring, and statistical data processing obtained during operation (daily control and day-to-day control).

In this study we aimed to assess the analytical performance of 12 analytes determined on BM6010/C analyzer. For these analytes, a comparison with the cobas c501 analyzer [Roche Diagnostics (Schweiz) AG, Switzerland] was also performed.

MATERIAL AND METHOD

The chemistry analytes evaluated were chosen based on the different spectrophotometric measurement wavelengths used by BM6010/C analyzer and were as follows:

Glucose (Glu), Creatinine (Cre), Uric acid (UA), Total Bilirubin (T-Bil), Total Cholesterol (T-Chol), Triglycerides (TG), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Serum urea (Urea), High density lipoprotein-Cholesterol (HDL-C), Total protein (TP), and Albumin (ALB).

Testing was conducted at the Clinical Chemistry Department, RS. St. Carolus Salemba Hospital, Jakarta, Indonesia. The evaluation study was approved by the Hospital Board of Directors and patient samples were included after receiving their informed consent. Sysmex reagents (SYSMEX WUXI CO., LTD., China) were used in the study. Methods and reagents used for this validation are presented in ***Table 1***.

Sysmex lyophilized control samples of human origin (Control Serum Level 1, M-Trol 1, lot M-120 & Control Serum Level 2, M-Trol 2, lot M-217) were used for evaluation. Calibrations for the tested analytes were performed using the recommended procedures for the evaluated analyser and the assigned calibrators (SYS-Multicalib1, lot R-1001, SYS-Multicalib 2, lot R-1001 and Lipid Calibrator lot S1001).

We evaluated the basic performance of BM6010/C by performing within-run and between-day imprecision, linearity and interference studies. BM6010/C was also compared for speed of sample processing in comparison to cobas c501. Correlation comparison was also performed using patient samples with consent.

Within-run imprecision was determined in duplicate on 20 consecutive measurements of different analyte concentrations in control sera (M-Trol 1, M-Trol 2) and pooled serum. Imprecision was expressed as the coefficient of variation (CV %).

Table 1 *Method and reagents used in the evaluation of BM6010/C along with manufacturer's linearity claim*

Analyte	Unit	Method	Linearity
AST	U/L	UV Method, IFCC	0 - 1,500
ALT	U/L	UV Method, IFCC	0 - 1,400
T-BIL	mg/dL	Stabilized diazo	0 - 30
UREA	mg/dL	Urease-GLDH UV – NH3	0 - 300
CRE	mg/dL	Enzymatic	0 - 80
UA	mg/dL	Uricase-EHSPT	0 - 100
TG	mg/dL	GK-GPO, Free Glycerol Elimination	0 - 1,800
T-CHOL	mg/dL	COD-POD	0 - 750
HDL-C	mg/dL	UV Method, reaction inhibiting method	0 - 100
GLU	mg/dL	Hexokinase	0 - 900
ALB	g/dL	BCG	0 - 7
TP	g/dL	Biuret	0 - 10

Table 2 *Imprecision and Recovery Study*

Analyte	Within run CV%			Between day CV%			Recovery%	
	M-Trol 1	M-Trol 2	Pooled serum	M-Trol 1	M-Trol 2	Pooled serum	M-Trol 1	M-Trol 2
AST	1.21	0.69	1.57	1.04	0.75	1.99	105	102
ALT	3.18	1.20	3.34	3.06	1.12	3.23	109	102
T-BIL	1.04	0.70	1.25	0.76	0.82	1.75	107	107
UREA	1.49	1.23	1.17	1.39	0.72	1.47	101	101
CRE	0.88	0.56	0.68	0.68	0.67	1.35	100	99
UA	1.05	0.82	0.00	1.21	0.85	1.45	98	99
TG	1.08	0.56	0.64	1.16	0.78	1.84	108	104
T-CHOL	0.66	0.95	0.71	0.64	0.76	1.52	99	99
HDL-C	0.93	1.65	0.65	0.77	2.11	1.70	102	95
GLU	1.07	0.71	0.98	0.66	0.91	1.35	99	100
ALB	1.06	0.71	0.89	0.66	0.67	1.51	97	96
TP	2.01	1.52	1.57	3.74	1.51	2.14	99	94

Between-day imprecision was determined measuring the concentration of analytes in the control sera of different concentration ranges (M-Trol 1, M-Trol 2) and pooled serum in duplicate over the period of 5 days and also expressed as a coefficient of variation (CV%). The mean value of replicates and percentage of deviation from target value was calculated and was presented as a percentage recovery.

Linearity studies were performed using a high level check E, S plus, bilirubin, TG and lipid linearity kit (SIRC, Japan) with ten serial dilutions for each analyte, covering the ranges listed in ***Table 3***. HDL-C Control High (Thermo Scientific, U.S.A) was used for HDL-C linearity studies.

Interference studies were performed using 4 different serum pools spiked with increasing amounts of 4 different interference material; free and conjugated bilirubin, hemoglobin and chyle which is expressed as Formazin Turbidity Unit (FTU). These spiked serum pools were further serially diluted to obtain ten different concentration levels for each interfering substance. The concentration levels tested for each substance ranged from 0.0 to 197.0 mg/dL for bilirubin F; 0.0 to 210.0 mg/dL for bilirubin C; 0.0 to 4,880 mg/dL for hemoglobin and 0.0 to 15,500 FTU for chyle. A substance was considered to show interference at that particular concentration level when +/- 10% limits of the measured value without interfering substance were exceeded.

Table 3 *Linearity study*

Analyte	Unit	Expected	Obtained
AST	U/L	0 - 1,250	0 - 1,344
ALT	U/L	0 - 1,250	0 - 1,381
T-BIL	mg/dL	0 - 45	0 - 45.17
UREA	mg/dL	0 - 250	0 - 285.7
CRE	mg/dL	0 - 22	0 - 23.57
UA	mg/dL	0 - 55	0 - 58.5
TG	mg/dL	0 - 1,400	0 - 1,545
T-CHOL	mg/dL	0 - 700	0 - 742
HDL-C	mg/dL	0 - 80	0 - 84.8
GLU	mg/dL	0 - 600	0 - 661
ALB	g/dL	0 - 5.0	0 - 5.0
TP	g/dL	0 - 13	0 - 13.06

Table 4 *Results of the interference study*

Analyte	Interference substance			
	Bil-c	Bil-f	Chyle	Hemoglobin
AST	-	-	-	↑
ALT	-	-	-	-
T-BIL			-	↓
UREA	-	-	-	-
CRE	-	-	-	-
UA	-	-	-	-
TG	-	-		-
T-CHOL	-	-	-	-
HDL-C	-	-		-
GLU	-	-	-	-
ALB	-	-	-	-
TP	-	-	-	↑

↑ / ↓ Positive/negative influence > 10%

\- no influence

Comparison of results obtained on BM6010/C and cobas c501 analyzers was conducted on approximately 160 serum samples with a wide range of values. The sera used for the comparison were collected at different hospital departments of St. Carolus Hospital mainly from patients coming for the routine health check-up. The samples were randomly selected for the comparison study and were centrifuged immediately upon arrival in the laboratory. All the samples were collected in plain tubes. The serum obtained was aliquotted and stored at -20°C until the analysis.

Statistical analysis
Statistical methods included the calculation of mean, standard deviation and coefficient of variation (CV%). Pearson correlation coefficient and linear regression were calculated for the method comparison. The level of significance was set at $P < 0.01$.
Statistical analysis, including descriptive statistics, was performed using SPSS software version16.

RESULTS

Results of between-day imprecision are shown in ***Table 2***. Coefficients of variation for between-day imprecision ranged as follows: in M-Trol 1 from 0.66 % to 3.74%; in M-Trol 2 from 0.67 to 2.11%; and in pooled serum from 1.35% to 3.23%. Percentage recovery was calculated and was found to be 100% for most of the assays; however, they ranged from 94% to 109%.

Table 5 *Throughput comparison*

Criteria		BM6010/C	cobas c501
Number of	Samples	84	84
	Parameter (each sample)	12	12
	Test	1008	1008
Time needed (minutes)	Warming up	30	30
	Order Entry	15	15
	Analysis time	90	120

Table 6 *Method Comparison*

Parameter	Correlation Between BM6010/C & cobas c501		
	R^2	R	Equation
AST	0.9939	0.9969	y = 1.0203x + 0.0606
ALT	0.9986	0.9993	y = 0.9666x + 1.6416
T-BIL	0.9978	0.9988	y = 0.7247x + 0.1006
Urea	0.9979	0.9989	y = 1.0591x + 0.8953
CRE	0.9981	0.9990	y = 1.0106x + 0.1082
UA	0.9734	0.9866	y = 1.0076x + 0.0173
TG	0.9897	0.9948	y = 1.0505x + 3.3760
T-CHOL	0.9846	0.9922	y = 0.9669x + 5.5297
HDL-C	0.9127	0.9553	y = 1.0048x + 0.8090
GLU	0.9862	0.9930	y = 1.0032x + 0.4429
ALB	0.9608	0.9802	y = 1.0092x + 0.2271
TP	0.8305	0.9113	y = 1.1431x + 0.0795

The results of within-run imprecision are also shown in ***Table 2***. Coefficients of variation for within-run imprecision ranged as follows: in M-Trol 1 from 0.66% to 3.18%; in M-Trol 2 from 0.56% to 1.65%; and for pool serum from 0.00% to 3.34%.
Table 3 shows the linearity range obtained for different assays. All the assays showed good linearity in the tested range (data not shown).

1. Interference Studies
Table 4 shows the results of interference study. Hemolysis is supposed to falsely elevate AST results, as the enzyme is contained in the erythrocytes. Similar, results were found in our study also. Hemoglobin also showed a slight influence on the T-Bil and TP at higher concentration levels. The other tested interfering substances did not show any interference at the tested concentrations on all the other tested analytes.

2. Speed Comparison
The throughput of BM6010/C was compared with cobas c501 under similar conditions (number of tests, number of parameters, warming up time, order entry and analysis process). ***Table 5*** shows that BM6010/C speed was found to be comparable to cobas c501.

3. Method Comparison
The statistical parameters for the correlation between BM6010/C and cobas c501 for the analysis of the routine chemistry parameters are reported in ***Table 6***. All R values obtained were between 0.91 and 0.99.

DISCUSSION

The results of this analytical validation showed acceptable coefficients of variation for between-day imprecision, within-run imprecision, as well as a satisfactory degree of recovery. In setting the criteria for acceptable imprecision, we considered the manufacturer's recommendation. Depending on the measurement procedure, measuring instruments and compliance with a reference or definitive method, we can assess whether the new method or analyzer is suitable for routine use, and whether they are of acceptable accuracy. For most analytes tested in this study, the results of imprecision were in the range of desirable specifications for imprecision, derived from CLIA guidelines [1].
Correlation analysis yielded high correlation coefficients proving high correlation for all the tested parameters.
Linear regression analysis showed that most of the analytes did not differ by a constant amount (95% CI of intercept includes 0), and also there were no proportional differences between methods (95% CI of slope includes 1) except for T-CHOL and TG which could be attributed to the difference between the methods used on the two analysers [2].

In conclusion, Sysmex BM6010/C analyzer showed acceptable performance for the majority of evaluated analytes. It is fully comparable with cobas c501 analytical analyzer for all the evaluated analytes and have been implemented in our laboratory.

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