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Implementation of Six Sigma in Glucose POCT Quality Control at Dr. Soetomo General Academic Hospital

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ABSTRACT

Point of Care Testing (POCT) is important for the examination of critically ill patients in the emergency room and intensive care unit. The evaluation of the analytic quality of POCT is needed to ensure the quality of patient care at Dr. Soetomo General Academic Hospital. The purpose of this study is to evaluate the analytical quality of POCT at Dr. Soetomo General Academic Hospital. This was an observational analytical study that was done at Dr. Soetomo General Academic Hospital Surabaya in July 2017. Point of care testing quality analysis was based on 20 within run Internal Quality Control (IQC). Internal quality control data was used to calculate the mean, SD, and CV%. CV% was calculated with the following equation "CV%=(SD × 100)/mean". Bias % = [control mean – control true value]/control true value x 100. The sigma value was obtained from Total Error Allowance (TEa) – Bias/CV. TEa in this study was based on ISO 15197:2003. The results of the glucose examination (58 samples) from Dimension EXL 1, 2, 3 (hexokinase method) compared with 7 glucose POCT (glucose oxidase:i-STAT Nova Biomedical method). The correlation was calculated with Spearman statistical analysis using the SPSS version 23.0. the mean CV of seven POCTs=3.5% (1.7%-5%), mean bias of seven POCT=7.75% (4.8%-12.5%), the mean six sigma of 7 POCT=6.77 (4.0–11.6). The best POCT with a six sigma value of $\geq$ 6 was glucometer K14_2, Palem 1 and GRIU. The glucometer with the lowest six sigma values but still had good quality control were K14_1 and ROI. All glucometers had a good correlation with r value $\geq$ 0.8 (p=0.000). Glucose POCT in Dr. Soetomo General Academic Hospital all had good quality and met world-class standards. Further study using IQC 2 levels is recommended for a better POCT quality evaluation.

Keywords: Glucose, six sigma, POCT, IQC, Dr. Soetomo General Academic Hospital

INTRODUCTION

Laboratory services based on quality services are divided into pre-analytical, analytical, and post-analytical phases. Each of these levels has a chance of a mistake affecting the results of the examination. The pre-analytical phase has the highest chance, but both the other phases must also be taken to light. The analytical phase determines the accuracy of the results of the examination, so an evaluation of the analytical process is needed for a good quality of the examination results.[1]

Point of Care Testing (POCT) is a laboratory service that is executed near the patient and the results can be immediately obtained. Point of care testing is also useful in situations that need a fast Turn Around Time (TAT) and immediate care of disease in the Inpatient Clinic, Outpatient Clinic, emergency room, and intensive care unit. The mostly used POCT at Dr. Soetomo General Academic Hospital is the glucometer. Glucometer results must be accurate to determine the right therapy. A significant variation between glucometer results encouraged the International Standardization Organization (ISO) to make a first edition international standard, ISO 15197:2003, that states that the accuracy of glucose results that is acceptable must be + 20%.[2,3]

This study aims to evaluate the quality of glucometers using the six-sigma system based on International Standards first edition, ISO 15197:2003 on POCT glucometers specifically in Dr. Soetomo General Academic Hospital, Surabaya and generally in Indonesia.

METHODS

This was an observational analytic study with a cross-sectional design that was conducted at Dr. Soetomo General Academic Hospital Surabaya from July–to August 2017. Internal Quality Control (IQC) data from glucose examinations between July and August 2017 were used to calculate the six sigma value. The dimension RXL 3, a biochemical analyzer was used to measure the blood glucose. Internal control was provided by Nova Biomedical UK (Lot no: 0418046303) and was conducted twice a day.

The blood glucose method used was based on the enzymatic method. The enzymatic method used to measure blood glucose in Dr. Soetomo General Academic Hospital Laboratory is hexokinase using Dimension EXL 1, 2, and 3, which is controlled twice every day. Blood glucose measured was from hospitalized patients and outpatients that were examined with Dimension EXL. Sample inclusion criteria were sample volume >2 mL and measurement was done less than one hour since the blood was drawn. The exclusion criteria were a clotted specimen. The remaining blood was reexamined with 7 i-STAT Nova Biomedical glucometers, before running the samples, each glucometer underwent quality control 20 times. All controls and glucose results from each glucometer were documented and analyzed.

Internal quality control data was used to calculate the mean, standard deviation (SD), and CV%. CV% was calculated with the following equation "CV% = (SD x 100)/mean" . Sigma value was obtained by Total Error Allowance (TEa) – Bias/CV. TEa used in this study was obtained from ISO 15197:2003.

The hexokinase method is the gold standard for blood glucose examination. This study compared 7 glucometers (glucose oxidase method) with the gold standard, the hexokinase method (using Dimension RXL) for validation. The study had 58 samples examined with Dimension and all 7 glucometers. Data analysis was done with Windows Excel and SPSS (version 23.0). Data were analyzed using Kolmogorov-Smirnov to test the data distribution, Spearmen correlation was used to evaluate the relationship between the two methods. The concordance of the two methods was analyzed with the Limit of Agreement (LOA) Bland Altman plot. A p-value < 0.05 was deemed significant. This study was approved by the Ethics Committee for Health Studies Dr. Soetomo General Academic Hospital, Surabaya with number 0461/KEPK/VIII/2018.

RESULTS AND DISCUSSIONS

Mean value, SD, CV%, Bias (%), and Sigma value of IQC level 1 with 20 times within run method are shown in Table 1. The test was divided into 4 groups according to their sigma levels. Group 1 tests are tests with a sigma value of 4–4.99, group 2 are tests with a sigma value of 5–5.99 and group 3 with a sigma value over 6 meaning they had a world-class working performance. The analytical performance of tests in group 1 was low, while those in group 3 had world-class analytical performance (Table 2).

This study uses 58 serum samples from both Inpatients and Outpatients at Dr. Soetomo General Academic Hospital. The lowest glucose blood level

Table 1. Standard deviation, mean, CV, bias, and six sigma of 7 glucometers

Parameters	TEa (%)	TV	SD	Mean	CV (%)	Bias (%)	Six Sigma
Level 1							
Glucose (ER)	20.0	61.0	2.2	54.7	4.0	10.3%	4.9
Glucose (K14-1)	20.0	61.0	2.7	53.4	5.0	12.5%	4.0
Level 2							
Glucose (P-1)	20.0	115.0	3.4	107.1	3.2	6.9%	6.2
Glucose (PW)	20.0	115.0	4.4	109.5	4.0	4.8%	5.0
Level 3							
Glucose (K14-2)	20.0	300.0	4.8	279.1	1.7	7.0%	11.6
Glucose (GRIU)	20.0	300.0	4.9	284.4	1.7	5.2%	11.5
Glucose (ROI)	20.0	300.0	13.3	277.1	4.8	7.6%	4.2

Table 2. Test groups according to six sigma

Group	ISO 15197:2003[2]		
	Level 1	**Level 2**	**Level 3**
Group 1 (σ: 4.0-4.99)	ER K-14 (1)		ROI
Group 2 (σ: 5.0–5.99)		Pandan Wangi	
Group 3 (σ: = 6.0)		Palem 1	K14 (2) GRIU

measured was 51 mg/dL using the glucometer in K-14 (1) and the highest was 319 mg/dL measured using Dimension. Mean glucose levels were lowest using K-14 (1), which was 126.4 mg/dL and the highest mean for glucose levels were measured with Dimension at 149.5 mg/dL as seen in Table 3.

Sample distribution was calculated using Kolmogorov–Smirnov test. Data from Dimension and 7 Glucose POCTs were not normally distributed ($p < 0.05$), so the correlation of the data was analyzed using the Spearman correlation test. The results showed that there was a strong correlation between the 8 instruments that were statistically significant ($p < 0.05$) (Table 4).

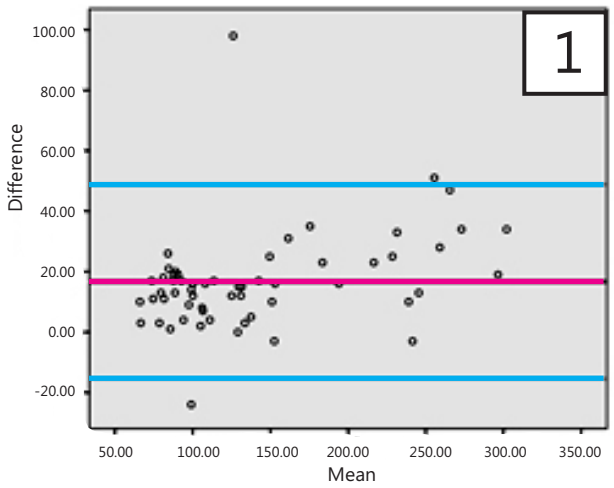
The correlation between the 7 POCTs and Dimension RXL is also shown in the Bland Altman Plot (Fig 1–7). The mean difference in glucose (Dimension-ER) is 16.689 (red line). The LOA limit of 1.96 SD is 15.458 to 48.837 mg/dL, which is shown by the green line (Fig 1). The mean difference in glucose (Dimension–ER) was 16.689 (red line). The LOA limit of 1.96 SD was 15.458 mg/dL up to 48.837 mg/dL,

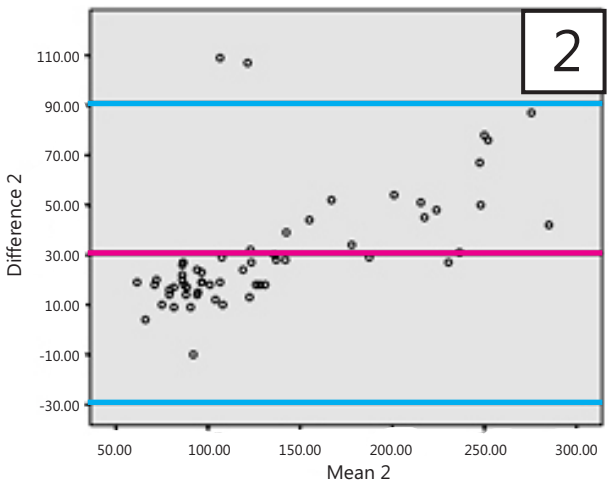
Table 3. Characteristics of 58 patients' serum samples

Instrument	Blood Glucose Levels (mg/dL)		Mean	Standard Deviation
	Minimum	Maximum		
Dimension	71	319	149.5	70.8
K-14 (1)	51	286	126.4	63.2
K-14 (2)	55	263	128.8	63.2
ER	61	287	132.8	64.4
Pandan Wangi	57	275	130.6	62.1
Palem 1	54	263	129.8	61.4
ROI	52	264	118.8	58.6
GRIU	58	264	123.8	56.7

Table 4. Results of the Kolmogorov-Smirnov and Spearman correlation test

Instrument	n	Mean Difference	Standard Deviation	Spearman Correlation (r)	p
Dimension -ER	58	16.68	16.40	0.935	0.000
Dimension -ROI	58	30.65	23.67	0.884	0.000
Dimension -P.Wangi	58	18.94	19.35	0.911	0.000
Dimension -Palem 1	58	19.67	18.34	0.925	0.000
Dimension -K14_2	58	20.72	18.12	0.929	0.000
Dimension -K14_1	58	23.10	19.56	0.911	0.000
Dimension -GRIU	58	25.72	19.89	0.930	0.000





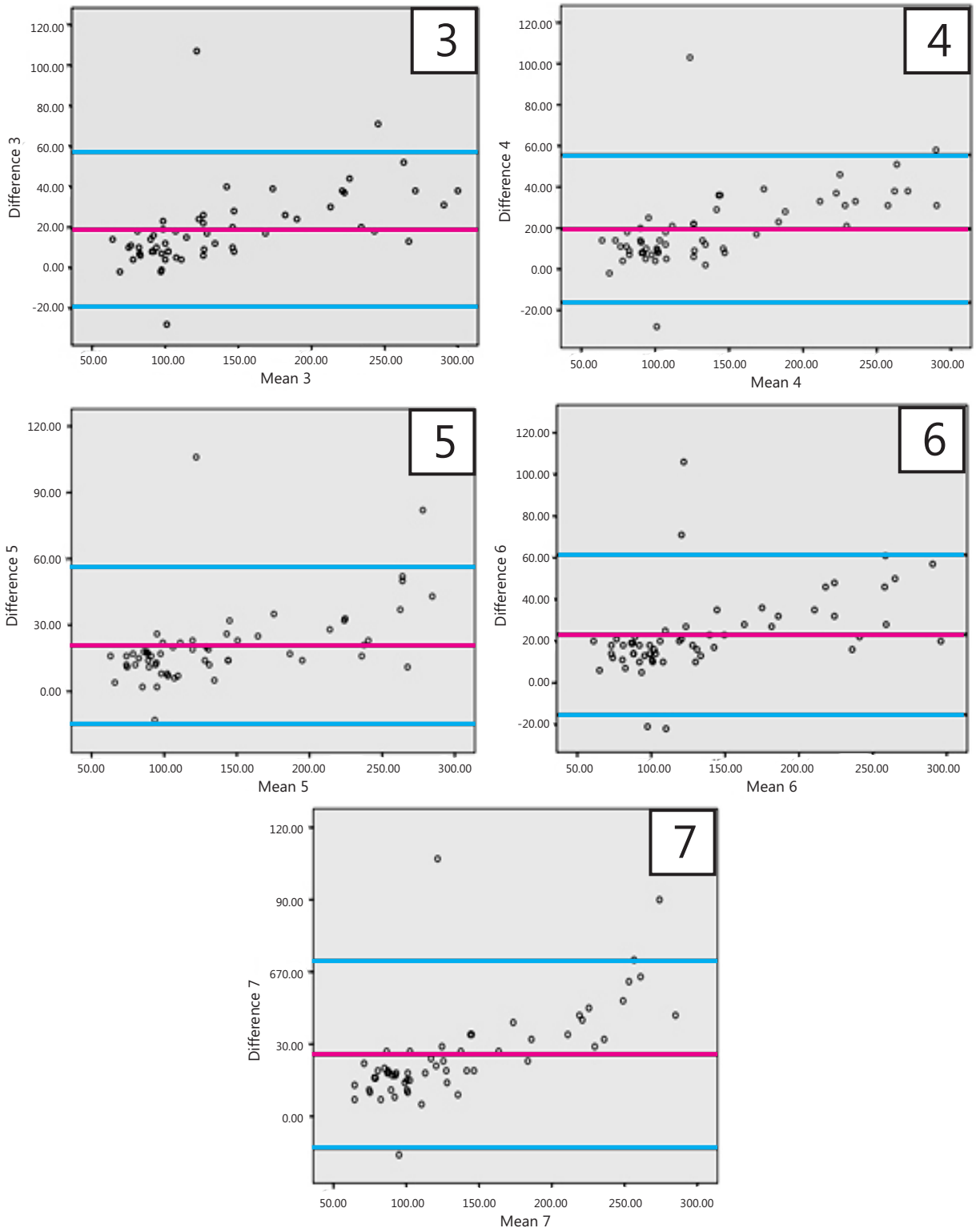


Figure 1-7. Bland Altman Plot for blood glucose using Dimension and glucose POCT in the emergency room, (2) ROI (intensive care unit), (3) Pandan Wangi (Inpatient care), (4) Palem 1 (Inpatient care), (5)K14_2 (Outpatient Clinic), (6) K14_1 (Outpatient Clinic) and (7) GRIU (pavilion)

which is marked by the green line (Figure 1). The mean difference for glucose (Dimension-ROI) was 30.6552 mg/dL with LOA limit between -29.428 mg/dL to 90.739 mg/dL (Figure 2). The mean difference of glucose (Dimension-P. Wangi) was 18.948 mg/dL with an LOA limit between -18.987 to 56.883 mg/dL (Figure 3). The mean difference in glucose (Dimension-Palem 1) was 19.672 (red line).

LOA limit 1.96 SD was –16.291 mg/dL to 55.636 mg/dL marked by the green line (Figure 4). The mean difference of glucose (Dimension-K14_2) was 20.724 mg/dL with LOA limit between -14.808 mg/dL to 56.256 mg/dL (Figure 5). The mean difference of glucose (Dimension- K14_1) was 23.103 mg/dL with LOA limit between -15.240 to 61.447 mg/dL (Figure 6). The mean difference of glucose (Dimension-GRIU) was 25.724 mg/dL with an LOA limit between -13.266 to 64.715 mg/dL (Figure 7).

The clinical laboratory has an important role in diagnosing disease. Turn around time, deemed to be the marker of a laboratory's efficiency, should not be the source of an increase in laboratory error. Laboratory technicians should have enough time to do proper control of analytical performance, so as not to give false results. Glucose, which is the most used laboratory parameter is very important in determining hyperglycemic or hypoglycemic conditions because many diabetic patients are brought to the hospital.[4]

Blood glucose POCT examinations are very useful to help monitor the disease and therapy of patients in hospital settings. The current method used to measure blood glucose is an enzymatic measurement with the hexokinase method as the gold standard.[5-7]

Glucometers at Dr. Soetomo General Academic Hospital are controlled using two levels of control once a week, meaning that the analytic performance of glucose examinations using these 7 glucometers is adequate. Six sigma value was calculated to measure the analytical performance of these glucometers. Sigma matrix are deemed as a modern way to measure quality, that results from the calculation of bias, coefficient of variation, and TEa, as quality parameters of these instruments. Some glucometers at Dr. Soetomo General Academic Hospital had a sigma value > 6 (Table 2) showing world-class quality according to TEa from ISO. Based on these results we can state that these glucometers worked properly to diagnose the disease. There is not yet a standard reference value of six sigma for glucose POCT and usually, the six sigma internal control value is lower than the instrument at the central laboratory as in this study. A six sigma value higher than 5 shows excellent device performance (4 devices), and a six sigma value between 4 and 5 shows optimal device performance (3 devices). Glucose POCTs with a six sigma value between 3 and 4 are usually due to operating errors and not enough competency in measuring blood glucose with POCT as in a study by Vincent *et al*.[8-10]

Prior research, Mariady *et al*. about the comparison of random blood glucose levels using glucometers and spectrophotometers in diabetes mellitus patients in Bandung nirlaba clinic, show results in concurrence with this study. Prior studies obtained mean random blood glucose (263.03 mg/dL) 21.76 mg/dL higher than the mean random blood glucose measured by spectrophotometer (214.27 mg/dL) with $p<0.05$.[10]

The results of this study show a mean CV of the seven POCTs =3.5% (1.7%-5%), mean bias of the seven POCTs=7.75% (4.8% -12.5%), mean six sigma value of the seven POCTs= 6.77 (4.0-11.6). The best POCT with a six sigma value of ≥ 6 were K14_2, Palem 1, and GRIU's glucometer. The lowest six sigma values, but still showed good quality control were K14_1 and ROI's glucometer. Calibration or control of the instrument was accepted if the six sigma value was >4.5, using the classic rule 13s or the six sigma value was ≤ 4.5 using the Westgaard rule. Bland-Altman plot showed a concordance in the 7 glucose POCT with Dimension (confidence interval 95%). All glucometers correlated $r \geq 0.8$ ($p=0.000$). These results validate the use of POCT in the emergency room, intensive care, Outpatient Clinic, Inpatient care, and pavilion in screening hyperglycemic or hypoglycemic conditions that need prompt treatment. This study does not study the effect of glucose POCT on TAT, but there is enough documented data on the role of glucose POCT in decreasing TAT.[11-13]

Further studies with additional data using two control levels are needed to obtain more accurate glucose POCT quality control results.

CONCLUSIONS AND SUGGESTIONS

The use of glucose POCT is feasible in helping emergency cases in inpatients settings, Outpatient Clinics, and intensive and emergency care units. The six sigma results of the 7 glucose POCTs in Dr. Soetomo General Academic Hospital, was a six sigma value of >4 showing good performance. Instruments maintenance and routine control using the 13s classic rule must be done to maintain the performance of the glucose POCTs in Dr. Soetomo General Academic Hospital to obtain accurate results.

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