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Comparison of Variant Index Score (VIS) of Homemade and Commercial Lyophilized Serum

Ilma Ainun Nisa, Amalia Putri K.A, Anik Handayati, Museyaroh, and Suhariyadi
Medical Laboratory Technology, Health Polytechnic Ministry of Health Surabaya, Indonesia

Corresponding author: Anik Handayati (e-mail: anik_handayati@yahoo.co.id)

ABSTRACT Laboratory quality is related to the analytical test results that are released by the laboratory. Test results that have high quality are expected to have good accuracy and accuracy of results to get laboratory results that can be trusted and lack errors. Quality stabilization is divided into two components, namely Internal Quality Assurance (PMI) and External Quality Assurance (PME). This study aims to provide an overview of alternative control materials to save the high cost of control materials in the implementation of laboratory quality assurance. This research compares the deviation value / Variant Index of commercial control and homemade control materials. The research was conducted at Surabaya health centers, reference laboratories, Ubaya Tecnobiology, and Surabaya Polytechnic Health laboratories from January to May 2023. This type of research is descriptive comparative with sampling using the Purposive Random Sampling method which takes data on the examination of researcher control materials on the parameters of SGOT, SGPT, creatinine, BUN, glucose, uric acid, triglycerides, and cholesterol. The research data obtained were analyzed with T Independent and Mann Withney. The results showed that there was no significant difference with a p-value of $\alpha>0.05$ which means the hypothesis is accepted, indicates that the deviation / VIS value obtained between factory and homemade control materials on the research parameters, both do not have a significant difference in value in terms of deviation of accuracy/inaccuracy so that it indicates that control materials from homemade serum can be used as an option to replace commercial serum.

INDEX TERMS *Quality Control; VIS; PME*

I. INTRODUCTION

Laboratories are expected to be able to release quality examination results, accountable, and lack of errors. Laboratory quality control programs that are carried out regularly and continuously can be an effort to ensure laboratory services [1],[2]. Laboratory quality control is divided into two parts, namely Internal Quality Assurance (PMI) which is carried out by the laboratory independently to see the precision and accuracy of the results, and External Quality Assurance (PME) which is an effort to assess inaccuracy from organizers such as BBLK [3],[4]. In the implementation of quality assurance, control materials are needed for monitoring and supervision of the quality of the results. Currently, laboratories usually use commercial control materials, but the use of commercial control materials is considered very expensive if used regularly. The availability and costs incurred for commercial control materials are a problem for laboratories in developing countries, especially in Indonesia [5]. Some developing countries feel that the amount of money they spend is not always directly proportional to the improvement in the quality of laboratory results [6],[7]. Effective efforts are needed in managing the quality of inspection results, including the selection of the type of control material [8]. The selection of control materials using homemade serum control materials from a collection of remaining daily examination sera (pooled sera) which are categorized as normal / not having high blood chemical levels can be used as an alternative control material for the laboratory quality assurance process [8],[9].

Pooled sera without preservatives can survive at -70°C for 3-4 months [10]. Jamtsho claimed that commercial serum in the form of solid powder/lyophilization can maintain its stability value for up to 2 years at a storage temperature of 2-8°C [11]. The above statement is also supported by Khatri who proved that homemade serum can be used as a substitute for commercial serum quality control because it is easily available and cheap [7]. Previous researchers have conducted research by changing pooled sera from liquid to solid powder/powder which is expected not to change the stability value of serum and can last longer. Cuhadar showed that homemade serum/pooled sera converted into lyophilized form can be stable at -20°C for

up to 4-5 months, even up to ten times the freeze-thaw cycle [12].

Based on this description, the researcher wants to know and evaluate the deviation value of the control material made from the rest of the pooled serum / homemade serum with factory-made control material seen from the results of the examination of the two control materials in 11 health center laboratories to compare the inaccuracy value/variant index score. This research can help laboratory installations and medical workers, especially laboratory technicians, in utilizing the remaining collection of patient serum as an alternative control material used for laboratory quality stabilization.

II. METHOD

The research method used is descriptive comparative with a quantitative approach using homemade lyophilized and commercial control serum test materials. The research population was 11 health center laboratories, which were taken using Purposive Random Sampling techniques with the criteria that health centers use the same examination tools and methods, routinely calibrate laboratory equipment, and routinely carry out internal quality assurance. The research was conducted in January-May 2023 at the Puskesmas, reference laboratory, ubaya technology faculty, and clinical chemistry laboratory of Surabaya Health Polytechnic.

The test material collection method used was blood collection from respondents who were free from HIV, Hepatitis, and Syphilis diseases/history. Blood taken from respondents was first separated into blood and serum. The serum obtained is then checked for blood chemistry levels according to the researcher's parameters, in this examination the respondent is expected to have normal blood chemistry values. The liquid serum obtained is homogenized and converted into powder using a freeze dryer at the Faculty of Technology UBAYA to remove the water content so that it has a longer and more stable shelf life [13].

Serum in solid powder/ lyophilisate form was reconstituted with distilled water 1:1 and then examined at the reference laboratory as true value and tested at 11 health center laboratories using Roche Cobas blood chemistry equipment to determine the variance index value/deviation value.

The results of homemade and commercial serum lyophilization examination were tabulated and the mean/target value was calculated. After calculating the target value, the variance value and variation index score were calculated based on the following calculation formula (FIGURE 1)

$$v = \frac{x - Target\ Value}{Target\ Value}\ x\ 100\frac{\boldsymbol{Value}}{\boldsymbol{CCV}}\ \boldsymbol{x\ 10}$$

FIGURE 1. Variant index deviation value calculation formula

The VIS value is obtained from calculating the variation value divided by the CCV provision as a benchmark in each parameter to determine the results of inspection deviations from the expected results. The obtained variant index value is then grouped into categories according to the quality control book by Siregar in 2018 with details in the following table (TABLE 1)

TABLE 1
Variant Index Score Value

Nilai	Criteria
<100	Good
101 – 200	Simply
201 – 300	Less
>300	Bad

TABLE 2
VIS value of homemade serum based on participant's laboratory target value

No	Public Health Center	Homemade Lyophilized Serum							
		SGOT (U/L)	SGPT (U/L)	Creatinin (mg/dL)	BUN (mg/dL)	Gluc (mg/dL)	UA (mg/dL)	TG (mg/dL)	Choles (mg/dL)
1	A	14	71	108	26	168	118	92	21
2	B	82	53	77	81	46	29	125	2
3	C	55	9	46	5	15	88	24	30
4	D	48	53	92	127	0	59	111	36
5	E	55	40	62	173	61	88	92	45
6	F	55	22	46	224	76	29	30	172
7	G	82	9	46	72	61	88	166	83
8	H	14	40	62	66	76	59	228	83
9	I	48	53	46	173	30	18	24	97
10	J	21	22	62	72	61	88	30	36
11	K	89	40	16	225	76	177	3	36

TABLE 3
VIS value of commercial serum based on participant's laboratory target value

No	Public Health Center	Homemade Lyophilized Serum							
		SGOT (U/L)	SGPT (U/L)	Creatinin (mg/dL)	BUN (mg/dL)	Gluc (mg/dL)	UA (mg/dL)	TG (mg/dL)	Choles (mg/dL)
1	A	97	14	85	240	9	58	31	25
2	B	42	14	97	151	70	29	126	34
3	C	49	55	48	27	40	86	19	140
4	D	79	50	48	151	77	115	5	151
5	E	5	14	85	27	53	29	104	72
6	F	49	41	85	205	4	86	7	107
7	G	13	69	85	116	21	86	19	128
8	H	68	29	60	27	90	115	102	13
9	I	31	55	72	62	70	101	31	60
10	J	49	28	85	205	58	58	90	95
11	K	42	41	60	36	33	29	104	72

TABLE 4
VIS Result of Commercial Lyophilized serum Against True Value

No	Public Health Center	Homemade Lyophilized Serum							
		SGOT (U/L)	SGPT (U/L)	Creatinin (mg/dL)	BUN (mg/dL)	Glu (mg/dL)	UA (mg/dL)	TG (mg/dL)	Choles (mg/dL)
1	A	2	1	125	193	79	37	90	103
2	B	47	1	62	101	13	118	60	168
3	C	129	68	12	83	131	11	79	284
4	D	15	25	87	101	170	198	55	297
5	E	80	28	125	83	144	64	159	51
6	F	129	55	125	266	92	172	67	13
7	G	97	52	125	174	65	172	79	271
8	H	146	42	100	83	184	16	37	116
9	I	113	39	37	9	13	185	90	64
10	J	129	42	50	266	26	37	25	26
11	K	47	55	25	92	52	118	159	51

The grouping of variant index score categories aims to see accuracy deviations. The obtained accuracy deviation can be used as a determinant of laboratory quality, where the smaller the VIS/deviation value, the better the quality stabilization of a laboratory. If the results obtained have a negative sign (-), the value needs to be changed to positive (+) and the VIS value needs to be rounded. The obtained data after further calculations were tested using Independent T-test statistics and Mann Withney to determine whether there was a comparison of deviations between homemade and commercial lyophilized serum on each parameter.

III. RESULT

CALCULATION OF INDEX VARIANCE AND SCORE INDEX VARIANCE CRITERIA

The presented data are homemade serum examination results obtained from a collection of respondents' serum that has tested negative for HIV and HbsAg and commercial serum with Glory Diagnostic level "Contronorm" brand. Homemade and commercial lyophilized control serums were examined on 8 parameters including SGOT, SGPT, Creatinine, BUN, Gluc (Glucose), UA (Uric Acid), TG (Triglyceride), and Choles (Cholesterol). Based on the examination results that have been carried out at the reference laboratory and 11 health center laboratories and have calculated its variant index value, then the VIS value is tabulated to determine the results and categories of homemade and commercial lyophilized serum.

The data of the VIS calculation obtained on the homemade control serum based on the target values of the participant laboratories/ Heath Center laboratories showed that the highest deviation values were in the parameters of BUN and triglycerides (TABLE 2)

The VIS calculation data obtained on the commercial control serum based on the target values of the participating laboratories/public health center laboratories showed that the highest deviation value was in the BUN parameter (TABLE 3). VIS calculation data were also calculated on

TABLE 5
VIS Result of Commercial Lyophilized serum Against True Value

No	Public Health Center	Homemade Lyophilized Serum							
		SGOT (U/L)	SGPT (U/L)	Creatinin (mg/dL)	BUN (mg/dL)	Glu (mg/dL)	UA (mg/dL)	TG (mg/dL)	Choles (mg/dL)
1	A	2	1	125	193	79	37	90	103
2	B	47	1	62	101	13	118	60	168
3	C	129	68	12	83	131	11	79	284
4	D	15	25	87	101	170	198	55	297
5	E	80	28	125	83	144	64	159	51
6	F	129	55	125	266	92	172	67	13
7	G	97	52	125	174	65	172	79	271
8	H	146	42	100	83	184	16	37	116
9	I	113	39	37	9	13	185	90	64
10	J	129	42	50	266	26	37	25	26
11	K	47	55	25	92	52	118	159	51

homemade lyophilized serum based on reference laboratory target values as a reference for true value. The VIS calculation results obtained based on the true value target values showed the highest deviations in SGOT, BUN, glucose, triglycerides, and uric acid (TABLE 4)

VIS calculation data obtained on commercial control serum based on reference laboratory average/true value target values showed that the highest deviation values were in BUN and cholesterol parameters (TABLE 5)

Furthermore, the VIS data are tested for statistical differences using T-Independent or Mann Withney. Below are the results of the comparison test calculation on homemade and commercial lyophilized serum based on the participant's target value and true value (TABLE 6)

TABLE 6
VIS Value Comparison Test Results

Parameter	Parameter	
	VIS Results Against Target peserta	VIS result against True Value
SGOT	0,759	0,070
SGPT	0,983	0,973
Creatinin	0,160	0,224
BUN	0,994	0,616
Glucose	0,413	0,016
Uric Acid	0,797	0,300
Triglyceride	0,318	0,061
Cholesterol	0,262	0,208

The decision-making of the comparison results is seen in the significance value obtained, if the significance value is <0.05 then it is concluded that there is a significant difference between the value of the variant index of homemade and commercial lyophilized serum, otherwise if the significance value is> 0.05 then there is no difference in the VIS value. The significance value obtained in the VIS value based on the target value of participants is greater than 0.05 in 8 parameters. In the VIS value based on the true value target value, there is 1 parameter that has a significance value that is less than 0.05. This can be caused by several factors including limitations in the research due to the presence of enzyme activity in the glucose parameter which easily undergoes the process of glycolysis during sample distribution. This may cause a false high value in one of the samples examined at the reference laboratory. It can also be caused by differences in calibration and quality assurance values between the reference laboratory and the health center laboratory.

IV. DISCUSSION

Jamtsho and Nuchpramol (2012) reported that homemade control serum in solid powder form can survive and be stable at 2-8°C and can be used for EQAS implementation [11]. The application of EQAS can help improve laboratory quality and efficiency [14]. Homemade control serum can be used as a laboratory performance monitoring scheme that can reflect bias (inaccuracy) and precision, improve laboratory quality, and reduce the occurrence of laboratory errors, especially in the parameters of SGOT, SGPT, and Creatinine [15]. Homemade serum can also be used as a laboratory scheme in urea parameters because it can approach the middle of the human physiological range compared to commercial serum [16].

The good and bad results of index variants are caused by factors that affect the quality results of clinical laboratory examinations including pre-analytical, analytical, and post-analytical stages. The pre-analytic stage has the highest error rate of 61% of the total errors, analytic errors of 25%, and errors in the post-analytic stage of 14. % [17]. The pre-analytical stage as a factor affecting quality results consists of patient preparation, collection, shipping, and sample handling. The analytical stage includes the quality of calibration, instrumentation, control materials, reagents, and examination methods, and includes laboratory staff. The inability of laboratory staff to follow procedures and random errors that are not detected in the implementation of quality constraints or misidentification of samples/examination controls can also cause analytical

errors [18]. Other factors that contribute are the lack of periodic quality control/quality assurance implementation, the equipment used, the competence of laboratory assistants, and the method of operation in the examination such as errors in pipetting sample reconstitution or reagents [19].

Commercial serum materials that are different from homemade serum are also a factor in the difference in results, in addition to serum materials in the form of solid powder require proper dilution because error factors can occur during dilution and inaccurate mixing [20]. Improper sample reconstitution can lead to loss of analytes from the serum [21]. Biological variations of the patient do not affect the variation of analyte results because they all come from the same sample [22]. The implementation of quality assurance is very useful to be able to minimize deviations/errors and find out the source of existing deviations. Quality stabilization is carried out to evaluate laboratory results so that the results issued can be precise, thorough, accurate, and reliable [23],[24]. Supported by research by Jamtso (2013), an increase in laboratory performance can increase along with the routine implementation of quality assurance supported by training for laboratory staff to reduce the occurrence of human error and from the routine implementation of quality assurance [25].

The difference in VIS values in this study is supported in Jamtsho's 2010 study, which states that the Mean Variant Index Score (MVIS) value using the GOD / PAP method shows <200, but the semi-automated tool shows MVIS values >200. The VIS values of all laboratories are plotted to assess performance in each month, the results show that performance gradually improves but suddenly decreases in the last round due to reagent drift [16]. In this study, there was a significant difference in the VIS value based on the true value of glucose parameters due to influencing factors, one of which was a decrease in glucose levels due to glycolysis. Glycolysis is the change of glucose into pyruvic acid. Glycolysis can be seen as the first stage of the process of respiration (aerobic) in cells that occur in the cytosol, where glucose is oxidized to pyruvic acid or as a process of energy formation (ATP) in anaerobic conditions [26]. When the blood specimen has not been tested, the process of glycolysis can occur by the cellular components in it and can consume 5% - 7% of the glucose contained in the specimen every hour [27].

The ambient temperature at which blood is stored before separation also affects the rate of glycolysis. At refrigerator temperatures, glucose remains stable for several hours in the blood. At room temperature, it is estimated that there is a decrease of 1 to 2% glucose/hour where it can be seen that the longer the examination is delayed, the lower the glucose level [28]. In addition, some factors affect the decrease in glucose levels, namely degradation by microbial agents because the homemade lyophilized serum used does not use preservatives and stabilizers [28]. Other technical factors can come from the cleanliness of the tools used, improper pipetting, staff skills, air bubbles in the spectrophotometer, imperfect homogeneity, and inappropriate incubation time and temperature [29],[30]. In this study, SGOT and SGPT parameters had varying values, this could be due to the loss of enzyme activity in long storage and interference by LDH on SGPT should also be considered [31],[32]. The BUN parameter had the largest deviation value from both homemade and commercial serum, this could be due to the use of reagents/control materials that are almost at the end of their life span, the brand and storage temperature of the reagents are also factors in the results of the BUN parameter examination [11]. The storage temperature of BUN reagents is 2-8℃. Reagents to be used must also be incubated at room temperature 15-25 ℃ for 30 minutes [33].

This statement is supported by Asih Khoerunnisa's research in 2013, which states that serum urea levels in reagents examined at 2-8 ℃ are lower than in reagents examined at room temperature 15-25 ℃, this is due to enzyme reactions where low temperatures can slow down the rate of reaction between enzymes [34].

The research conducted has limitations including the number of participating laboratories limited to 11 health center laboratories that fulfill the research criteria, researchers also pay less attention to calibration schedules and internal quality stabilization assessments in each laboratory so that there are some high deviation values. Researchers are also not good at distributing samples to maintain the temperature of the control material at 2-8 ℃.

V. CONCLUSION

Based on the results of this study through homemade and commercial lyophilized serum examination tests at reference laboratories and health center laboratories, it can be concluded that homemade lyophilized serum can be used as an option for daily quality control materials and replace commercial controls. In the future, this research is expected to be a reference for the next researcher regarding the understanding of quality control in laboratory quality assurance and can be a benefit for laboratory installations in utilizing the remaining patient serum collected as an alternative control material in quality assurance, especially in the parameters of SGOT, SGPT, creatinine, BUN, glucose, uric acid, triglycerides, and cholesterol to reduce costs incurred in buying control materials but still able to carry out quality assurance routinely and continuously to provide optimal quality assurance results.

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