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CAN A SEMIAUTOMATIC ANALYZER BE A STAND BY FOR THE FULLY AUTOMATIC BIOCHEMISTRY ANALYZER?

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ABSTRACT

The laboratory accreditation has revolutionized the concept of quality in laboratory sciences. One of laboratory quality indicators is the delivery of results at the right time. This is labeled as the turnaround time (TAT)of the results. To prevent the TAT failure the requirement of the alternatives at the time of Breakdown comes into play. Most common rescue that are proposed are: one is to outsource the test at the time of breakdown, other is to have a standby machine in hand. In the developing countries, where the private laboratories are willing to go for accreditation, certain financial constraints are experienced. Keeping this limitation in the background, the present study is conducted .This one time study was done to test the capacity of the semiautomatic biochemistry analyzer as a standby for the fully automatic biochemistry analyzer to achieve the Quality results in time. Both the machines are checked for the precession and the accuracy by IQC and EQAS. The Total Allowable Error for each analyte on both the analyzer is calculated and checked against the guidelines laid down under the CLSI guidelines. Once the allowable error is within the limits, an exercise is done running both levels normal and pathological of the IQC of Bio Rad as samples on the two analyzers. Twenty readings for each analyte are taken. The results are calculated using the correlation coefficient and t test. Although both the machines are precise and accurate when compared with the peer references (EQAS –Bio Rad), the semi automatic analyzer cannot act as a standby for the following analytes when run on the fully automatic analyzer.

KEY WORDS; Accreditation, Breakdown, Correlation coefficient, Total Allowable Error.

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INTRODUCTION

The objective of this study is to present the model for Inter Instrument validation between two different types of automated biochemistry analyzers, this validation established with calculating the correlation coefficient that is helpful in clinical laboratory breakdown condition. This correlation is also required for the same biochemistry analyzer that is used as reference and backup system analyzer.

Since we know that the correlation depends upon environmental factor (eg. room temperature, humidity), reagent condition, machine maintenance, calibration and purity of water.

In a bivariate distribution, correlation between the variables are established, if the change in one variable affects a change in the other variable, the variables are said to be correlated. If the two variables deviate in the same direction, i.e., if the increase (or decrease) in one results in a corresponding increase (or decrease) in the other, correlation is said to be direct or positive. But if they constantly deviate in the opposite directions i.e., if increase (or decrease) in one result in corresponding decrease (or increase) in the other, correlation is said to be diverse or negative. Correlation is said to be perfect if the deviation in one variable is followed by a corresponding and proportional deviation in the other.The quantity r, called the linear correlation coefficient which measures the strength and the direction of a linear relationship between two variables.

The mathematical formula for computing ***r*** is:

$$r = \frac{n\sum xy - (\sum x)(\sum y)}{\sqrt{n(\sum x^2) - (\sum x)^2}\sqrt{n(\sum y^2) - (\sum y)^2}}$$

Where *n* is the number of pairs of data. The value of *r* is such that $-1 \leq r \leq +1$. The + and – signs are used for positive linear correlations and negative linear correlations, respectively.

Positive correlation: If x and y have a strong positive linear correlation, r is close to +1. An r value of exactly +1 indicates a perfect positive fit. Positive values indicate a relationship between x and y variables such that as values for x increases, values for y also increase. Negative correlation: If x and y have a strong negative linear correlation, r is close to -1. An r value of exactly -1 indicates a perfect negative fit. Negative values indicate a relationship between x and y such that as values for x increase, values for y decrease. No correlation: If there is no linear correlation or a weak linear correlation, r is close to 0. A value near zero means that there is a random, nonlinear relationship between the two variables. **A perfect correlation** of ± 1 occurs only when the data points all lie exactly on a straight line. If r = +1, the slope of this line is positive. If r = -1, the slope of this line is negative. A correlation greater than 0.8 is generally described as strong, whereas a correlation less than 0.5 is generally described as weak and correlation between the 0.5 to 0.8 is generally described as intermediate. The *coefficient of determination,* r^2, is useful because it gives the proportion of the variance of one variable that is predictable from the other variable. The *coefficient of determination* is the ratio of the explained variation to the total variation.

The coefficient of determination is such that $0 \leq r^2 \leq 1$, and denotes the strength of the linear association-between *x* and *y.* The *coefficient of determination* represents the percent of the data that is the closest to the line of best fit. For example, if $r = 0.922$, then $r^2 = 0.850$, which means that 85% of the total variation in *y* can be explained by the linear relationship between *x* and *y* (as described by the regression equation). The other 15% of the total variation in *y* remains unexplained. The *coefficient of determination* is a measure of how well the regression line represents the data. If the

regression line passes exactly through every point on the scatter plot, it would be able to explain all of the variations. Further the line is away from the points, the less it is able to explain. The correlation feature uses simple linear regression to calculate the correlation curve y = mx + b where x is the expected result and y is the observed result. In the correlation curve, the applied slope (mA) and intercept (bA) are calculated as mA = 1/m and bA = -b/m. This instrument is intended to be used to read and calculate the results of *in vitro* clinical diagnosis assay, as well as any other application requiring absorbance or concentration readings at or near the available wavelengths. This general purpose principle is intended to be used by laboratory professional capable of selecting the appropriate features and options for each specific clinical application.

MATERIALS AND METHODS

General biochemistry tests were measured using control sample (Bio-Rad assayed chemistry control) of both levels (normal and pathological) in two automated analyzers, fully automated (Dimension X pand plus) and semi automated (Stat fax 3300) during 20 days. Dimension X pand plus was used as the reference analyzer and Stat fax 3300 as a backup system. Method and chemical used in fully and semi automated analyzer is shown in table 1.

RESULTS

Instrument validation between fully and semi automated analyzer indicates intermediate correlation and other shows no correlation (Table 3). During this study none of the biochemistry test parameter showed maximum correlation of the total parameter analyzed Total bilirubin, calcium and glucose showed intermediate correlation. There correlation coefficient and coefficient of determination were measured as total bilirubin (0.62, 38.44), calcium (0.53, 28.04) and glucose (0.52, 27.04) where as no correlation were found in creatinine (0.02, 0.04). Daily IQC data values (Table 2) suggest that both the machines are precise and accurate when compared with the peer references (EQAS –Bio Rad) but the semi automatic analyzer cannot act as a standby for the
following analytes when run on the fully automatic analyzer.

Table-1
Method and chemicals used in fully and semi automated analyzer

S.N.	Name of Test	Fully automated (Dimension X pand)			Semi automated			
		Method	Chemical	Enzyme used/ medium	Method	Chemical	Enzyme used/mediu m	Company na
1	Total Protein	Biuret	$CuSo_4$, NaOH, Na-K- tartarate	NA	Biuret	$CuSo_4$, NaI/ KI, Na-K- tartarte	NA	SPINREAC
2	Albumin	BCP dye binding	BCP dye purple	Acidic (pH 4.2)	BCP dye binding	BC green	Acidic	SPINREACT
3	ALP	Procedure Bowers & Mc Comb	PNPP +AMP	Alkaline phosphatase , alkaline (pH 10.35), Mg^{2+}	DGKC and SCE method (enzyme kinetic)	PNPP + H_2O	Alkaline phosphatas e, alkaline (pH 10.35), $Mgcl_2$, diethnol amine	MERCK
4	TBI	Diazomethod (Jendrssik and Grof, 1938)	Diazotized Sulphanilic acid	Low pH, caffeine/Ben zoate/acetat e/EDTA	Diazometh od (Jendrssik and Grof, 1938)	Sulphanilic acid DMSO, HCl, $NaNO_2$	Low pH	SPINREACT
5	DBI	Diazomethod (Jendrssik and Grof, 1938)	Diazotized Sulphanilic acid	Low pH, caffeine/Ben zoate/acetat e/EDT	Diazometh od (Jendrssik and Grof, 1938)	Sulphanilic acid, HCl, $NaNO_2$	Low pH	SPINREACT
6	Calcium	OCPC method(Schwar tzenbach et al.,)	OCPC + 8 quinolinol	Mg^{2+} , pH 9.7	OCPC method(Sc hwartzenba ch et al.,)	OCPC	NA	ACCUREX
7	SGOT	NADH, Kinetic UV , IFCC reaction	L- Aspartate & α- ketoglutarate, NADH	Alkaline (pH 7.8) Coenzyme Pyridoxal-5- Phosphate, MDH, LDH	NADH, Kinetic UV , IFCC reaction	L- Aspartate & α- ketoglutara te, NADH	Alkaline (pH 7.8) Coenzyme Pyridoxal- 5- Phosphate, MDH, LDH	SPINREACT
8	SGPT	NADH, Kinetic UV , IFCC reaction	Alanine, NADH, LDH	Alkaline (pH 7.4) Coenzyme Pyridoxal-5-	NADH, Kinetic UV , IFCC reaction	Alanine, NADH, LDH	Alkaline (pH 7.4) Coenzyme Pyridoxal-	SPINREACT

				Phosphate, LDH			5-Phosphate, LDH	
9	Creatinine	Jaffe's kinetic method	Picrate, NaOH, $K_3Fe(CN)_6$,	NA	Jaffe's kinetic method	Picrate, NaOH, Po_4^{2-},	NA	MERCK
10	BUN	Urea nitrogen method	α-KG, NADH	Urease, GLDH	Urea enzymatic method	Phosphate Buffer(pH 7.0), Phenolic Chromogen, Hypochlorite	Urease	ACCUREX
11	Glucose	Hexokinase – glucose-6phosphate dehydrogenase	ATP, NADP, Buffers, Activators	Hexokinase, G-6-PDH, Mg^{2+},	Glucose oxidase method	Phosphate Buffer, 4-amino antipyrine, Phenol	Glucose-oxidase, Peroxidase	ACCUREX

Table-2
Internal Quality Control data of Test analytes

	ALP				ALT/SGPT				AST/SGOT				DBI				TBI				BUN			
S.N.	Normal		Pathological		Normal		Pathological		L1		L2		L1		L2		L1		L2		L1		L2	
	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F
1	135.2	110.1	393.7	439.1	25.5	40.0	64.6	88.0	17.0	40.0	110.6	172.0	0.3	0.3	1.6	1.4	**0.2**	**1.1**	3.9	4.7	34.5	34.4	86.8	101.2
2	104.9	81.1	291.4	348.2	26.0	41.0	60.5	96.0	29.5	38.0	102.4	177.0	0.3	0.3	1.3	1.4	**1.0**	**1.0**	3.9	4.7	33.2	31.1	89.6	99.1
3	100.6	83.0	313.0	372.2	23.9	42.0	50.3	95.0	27.1	41.0	94.0	178.0	0.4	0.3	1.4	1.3	**1.2**	**1.0**	3.6	4.7	33.7	31.1	89.9	100.9
4	108.8	79.7	348.9	379.1	24.0	40.0	60.7	96.0	26.4	40.0	104.7	185.0	0.5	0.3	1.4	1.4	**1.3**	**0.9**	3.9	4.9	39.4	31.6	91.4	106.5
5	119.0	83.2	315.5	363.6	24.1	41.0	50.1	95.0	26.1	37.0	80.4	177.0	0.3	0.3	1.3	1.3	**0.7**	**1.0**	4.1	5.0	34.0	32.9	88.4	102.9
6	104.9	80.6	310.0	332.2	16.2	41.0	45.4	94.0	24.2	39.0	57.6	174.0	0.3	0.2	1.4	1.3	**1.1**	**0.9**	4.2	4.8	33.6	33.0	85.7	104.0
7	101.7	114.1	424.0	352.9	21.8	42.0	50.0	99.0	19.8	38.0	75.0	192.0	0.4	0.3	1.2	1.5	**1.0**	**1.0**	4.7	5.3	35.4	32.4	84.0	106.1
8	105.1	86.1	349.9	361.2	24.2	41.0	61.5	95.0	26.1	37.0	105.9	187.0	0.3	0.2	1.4	1.3	**0.8**	**1.0**	3.7	4.7	34.7	33.5	97.9	102.2
9	134.0	111.8	380.2	350.7	23.0	42.0	66.0	97.0	21.0	36.0	130.0	190.0	0.0	0.3	1.0	1.4	**1.0**	**1.0**	4.0	5.0	41.0	31.1	92.0	103.1
10	114.6	115.7	446.5	409.2	27.0	41.0	69.9	96.0	30.3	37.0	122.6	183.0	0.4	0.3	1.0	1.3	**1.0**	**1.0**	4.4	4.9	30.5	32.4	86.0	100.9
11	154.1	111.1	385.9	415.6	31.6	42.0	76.0	99.0	33.5	37.0	129.9	184.0	0.4	0.3	1.3	1.3	**1.0**	**0.9**	3.9	4.8	33.8	32.6	90.7	101.1
12	127.6	112.7	357.1	438.3	32.0	42.0	77.5	97.0	24.9	36.0	128.8	182.0	0.4	0.3	1.5	1.3	**0.9**	**1.0**	0.9	4.9	28.6	30.7	101.5	100.1
13	149.4	107.4	421.8	422.0	33.6	41.0	72.9	96.0	33.5	42.0	126.8	179.0	0.3	0.2	1.4	1.3	**1.0**	**1.0**	4.0	4.9	30.4	33.6	92.0	99.1
14	143.1	116.9	382.4	413.0	33.6	41.0	75.9	95.0	34.8	45.0	126.9	181.0	0.4	0.3	1.6	1.3	**0.9**	**1.0**	4.3	4.8	33.0	33.7	91.2	100.1
15	110.4	108.4	398.0	461.8	27.9	39.0	62.8	96.0	22.9	38.0	102.2	192.0	0.4	0.3	1.2	1.3	**0.8**	**1.0**	3.5	5.1	24.1	31.2	91.4	100.2
16	126.1	117.3	344.1	447.9	33.0	39.0	52.0	100.0	36.4	37.0	84.2	189.0	0.4	0.3	1.1	1.4	**1.0**	**1.0**	4.3	4.9	33.4	34.1	96.4	99.7
17	118.0	123.5	353.0	468.9	35.1	39.0	55.0	97.0	32.8	43.0	85.6	196.0	0.4	0.2	1.2	1.3	**0.9**	**1.0**	4.2	5.1	33.8	34.8	100.8	100.9
18	116.6	122.6	349.0	493.3	26.7	38.0	58.5	99.0	27.8	38.0	87.6	206.0	0.3	0.3	1.2	1.3	**1.0**	**1.0**	4.8	5.0	39.0	33.5	114.0	101.3
19	118.7	116.3	333.8	487.7	33.0	38.0	64.1	94.0	32.0	37.0	99.0	94.0	0.4	0.3	1.1	1.4	**0.9**	**1.0**	4.0	5.0	35.5	32.2	110.0	102.4
20	117.6	115.5	380.2	491.3	32.0	41.0	52. 0	95.0	32.0	33.0	84.0	94.0	0.4	0.3	1.2	1.4	**0.9**	**1.0**	4.0	5.0	35.5	33.5	96.4	101.1

	CREA				ALB				TP				GLU				CA			
S.N.	Normal		Pathological		Normal		Pathological		L1		L2		L1		L2		L1		L2	
	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F	S	F
1	1.2	2.2	4.2	6.0	4.9	4.2	3.4	2.4	6.9	7.4	4.3	4.3	**72.5**	**94.0**	262.5	279.0	**10.1**	**9.6**	11.9	11.3
2	1.4	2.1	4.3	6.1	4.6	3.8	3.3	2.4	5.8	6.9	4.1	4.4	**87.3**	**90.0**	253.7	279.0	**8.8**	**8.7**	10.8	11.7
3	1.3	2.1	4.3	6.3	4.5	3.9	2.9	2.5	5.7	7.0	4.3	4.4	**82.9**	**90.0**	273.0	275.0	**8.4**	**9.1**	11.1	11.6
4	1.3	2.0	4.7	6.3	4.7	3.8	3.3	2.6	6.1	6.6	3.9	4.6	**84.8**	**87.0**	267.5	285.0	**8.5**	**8.8**	10.8	12.2
5	1.3	2.1	4.4	6.1	4.8	3.9	3.0	2.5	6.1	7.0	3.5	4.6	**88.4**	**88.0**	247.5	280.0	**7.0**	**8.9**	12.0	11.8
6	1.3	2.0	4.3	6.2	3.9	3.9	3.5	2.5	6.5	6.9	5.5	4.4	**90.1**	**87.0**	215.6	279.0	**8.3**	**8.9**	11.8	11.9
7	1.2	2.0	3.7	6.4	4.1	4.0	2.7	2.7	5.8	7.1	3.5	4.9	**81.5**	**88.0**	146.0	294.0	**9.2**	**9.1**	13.5	12.9
8	1.2	2.1	4.6	6.0	4.5	4.0	3.9	2.5	5.7	7.3	4.8	4.5	**81.7**	**90.0**	218.1	274.0	**8.9**	**9.2**	10.9	11.7
9	1.0	2.1	4.0	6.1	4.0	3.9	3.0	2.5	6.0	6.8	3.0	4.5	**80.0**	**90.0**	167.0	281.0	**8.0**	**8.9**	12.0	11.9
10	1.4	2.1	4.4	6.3	4.4	3.9	4.3	2.5	6.5	7.1	5.9	4.6	**81.5**	**90.0**	280.9	283.0	**8.3**	**9.0**	12.7	12.0
11	1.1	2.0	4.3	6.0	4.7	3.8	3.9	2.5	6.1	7.0	3.3	4.6	**82.8**	**89.0**	237.0	279.0	**8.5**	**8.9**	10.3	12.0
12	1.2	2.1	5.6	6.2	4.9	3.8	3.7	2.5	6.0	6.9	4.7	4.7	**75.7**	**88.0**	224.8	280.0	**9.1**	**8.9**	12.8	12.2
13	1.4	2.0	4.2	6.1	4.4	3.9	3.4	2.5	5.7	6.9	3.9	4.5	**95.0**	**89.0**	244.6	275.0	**9.4**	**9.2**	13.8	6.1
14	1.4	2.1	4.2	6.0	4.5	4.0	3.5	2.5	6.2	7.2	4.1	4.5	**92.9**	**89.0**	270.0	278.0	**8.8**	**9.3**	11.3	12.1
15	1.3	2.1	4.5	6.3	4.8	3.8	3.0	2.6	6.5	6.9	5.5	4.7	**79.3**	**91.0**	206.0	286.0	**10.2**	**9.0**	12.8	12.1
16	1.2	2.1	3.9	6.3	4.4	3.8	3.1	2.5	7.6	7.1	4.7	4.6	**84.0**	**90.0**	210.0	278.0	**10.0**	**9.1**	12.6	11.9
17	1.2	2.1	4.6	6.4	4.4	4.0	3.2	2.6	6.0	7.1	4.9	4.7	**78.3**	**91.0**	255.0	272.0	**10.0**	**9.2**	10.8	12.5
18	1.3	2.1	4.5	6.4	4.5	3.9	3.3	2.6	6.8	7.0	4.8	4.7	**85.0**	**90.0**	248.0	273.0	**10.1**	**9.2**	11.0	273.0
19	1.3	2.1	4.3	6.3	4.8	3.8	3.8	2.6	5.3	7.0	4.7	4.7	**79.0**	**91.0**	228.0	275.0	**8.7**	**9.0**	10.8	12.5
20	1.3	2.1	1.3	6.3	4.8	3.8	3.8	2.6	7.6	7.1	4.8	4.5	**79.**	**91.**	228.0	275.0	**8.9**	**9.0**	10.8	12.4

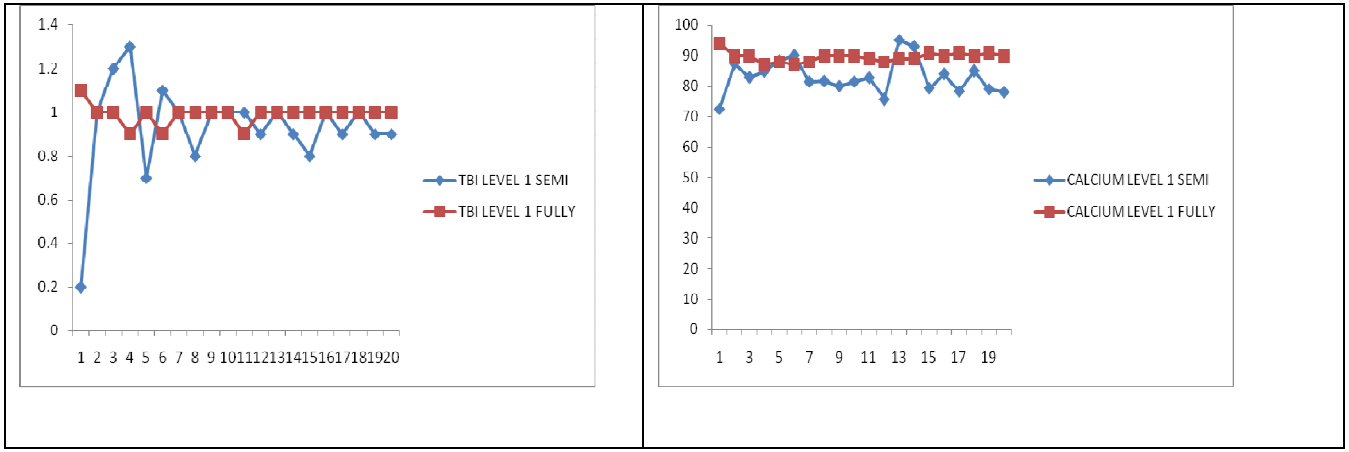
Table 3
Karl Pearson's Correlation Coefficient

S. N.	Parameter	Biological reference range Semi automated analyzer	Biological reference range Fully automated analyzer	Correlation Coefficient Normal level		Correlation Coefficient Pathological level		Correlation
				r	r^2	r	r^2	
1.	ALP	M<270,F<240	50-136 U/L	-2.43	No	0.21	4.41	No
2.	ALT	M<40,F<32	30-65 U/L	-0.31	9.6	-0.02	0.00	No
3.	AST	M<38,F<31	15-37 U/L	0.27	7.29	-0.003	0.00	No
4.	DBI	0.0-0.6 mg/dl	0.0-0.6 mg/dl	-0.12	1.44	-0.18	3.24	No
5.	TBI	0.2-1.0 mg/dl	0.2-1.0 mg/dl	-0.62	38.44	0.18	3.24	Intermediate
6.	UREA	10-50 mg/dl	15-38.5 mg/dl	0.10	1	-0.19	3.61	No
7.	CREATININE	M 0.8-1.3 mg/dl F 0.6-1.2 mg/dl	M 0.8-1.3 mg/dl F 0.6-1.2 mg/dl	0.02	0.04	-0.05	0.25	No
8.	ALBUMIN	3.5-5.0 g/dl	3.5-5.0 g/dl	-0.12	1.44	-0.28	7.84	No
9.	TOTAL PROTEIN	6-8 g/dl	6-8 g/dl	0.20	4	0.02	0.04	No
10.	GLUCOSE	Fasting 70-110 6-8 mg/dl PP 80-120 mg/dl Random 70-120 mg/dl	Fasting 70-110 6-8 mg/dl PP 80-120 mg/dl Random 70-120 mg/dl	-0.52	27.04	-0.45	20.25	Intermediate
11.	CALCIUM	8.5-11 mg/dl	8-11 mg/dl	0.53	28.09	-0.18	3.24	Intermediate

r = Correlation Coefficient, r^2 = Coefficient of Determination

Graph 1

Graphical representation of comparison of control values recorded by fully and semi automated analyzer for test parameters



DISCUSSION

The present study aims to establish Correlation Coefficient between fully automated and Semi automated analyzer that is used in clinical biochemistry laboratory. This study will be an efficient, economical and reliable protocol which can be used to prepare the laboratory before case of machine breakdown.

Laboratories accredited according to ISO 15189 standards have to provide quality test results and also test reports in assigned turn-around time (TAT) which is 1 hour for emergency tests. This TAT could be accomplished by the two analyzers both available and functional with comparable results between themselves. The aim of this study is to describe the model implemented in laboratory which is a mechanism or continuous verification of results comparability on two different automated analyzers. This verification is performed on daily basis, defined due to characteristics of the test procedure. This model ensures the comparability of two automated analytical systems. For allowable biases of backup toward reference analyzer, CVs defined criteria include biological variation and represent the total allowed bias from the mean value (1). The key finding of this study is that a simple algorithm could ensure continuous comparability and reliability of test results and constant preparedness of two analyzers. The presented model provides fast switch from one to another analytical system due to possible turndown episode of reference analyzer. One of the principal quality indicators in accredited laboratory is ensuring reliable and accurate results from the samples with appropriate interpretation. This model could measure laboratory performance and also provide the most accurate results (2), regardless on which automated system samples are determined. In this way, laboratory can greatly contribute to patient diagnosis and provide the important part of the patients' best health care. If laboratory results are not comparable from different analytical systems, possibility for incorrect diagnosis and poor quality of patient care is increased (3, 4). This model also provides a trustful basis for ensuring longitudinal patients follow up thereby, model is one of the way for laboratory process and emergency test reports standardization (5). Although the most laboratory errors are pre analytical or post analytical phase (6), analytical errors due to system failure could be avoided with two equally ready and functional analyzers. The described model for comparability could reduce analytical phase errors occurred due to some failure of the reference analyzer. This model of results comparison ensures continuous analytical quality of laboratory reports and improves overall efficiency of laboratory services. Reliable and comparable results on daily basis provide high quality of examination procedures and reporting of results in recommended and appropriate time to the best of the patient care.

Limitations of the study: Since this was the one time data of the laboratory 'may be a series of observations regarding the comparability of the analyzer could change the position of the analyte from no or intermediate to maximum correlation.

CONCLUSIONS

This model of instrument validation establishes correlation between two laboratory analyzer that are helpful to choose test parameter that not deviate in case of test done on backup system and maintain continuous analytical quality of laboratory reports and improves overall efficiency of laboratory ser**vi**ces.

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