Comparison of serum indices results on some biochemical analysers

Pham Viet Tan*, Dinh Thi Thao*,
Nguyen Cam Thach*, Hoang Thu Ha,**
Tran Thi Chi Mai***

**108 Military Central Hospital,*
***Xanh Pon Hospital,*
****National Children's Hospital*

Summary

Objective: To identify hemolysis, icterus, lipemia (HIL) indices measurement on four clinical chemistry analyzers: Abbott Architect C8000 (AA), Roche Cobas C501 (RC), Beckman Coulter AU5800 (BC), Siemens Advia 1800 (SA). *Subject and method:* Plasma of patients were examined at 108 Military Central Hospital (108 MCH) from 12/2020 to 04/2021, comprising of 240ml normal plasma sample, 30ml artificial hemolyzed plasma for H index, 30ml icteric plasma with 360µmol/L total bilirubin, 30ml plasma with 1g/L of Intralipid 20% for lipemia. A cross-sectional study was conducted to compare results of HIL indices on 4 analyzers Abbott Architect C8000 (AA), Roche Cobas c501 (RC), Beckman Coulter AU5800 (BC), Siemens Advia 1800 (SA). *Result:* The agreement of H index among 4 instruments was good, and values of I index on the AA, SA, RC were absolutely suitable (kappa 0.75 - 1.0). Nevertheless, the comparability between results of I index on the BC and 3 others platforms was mediate (kappa 0.53 - 0.55) while I index on the RC, SA, AA was extremely suitable (kappa 1.0). Even though, the agreement of L index between BC and SA was not acceptable (kappa < 0.2), it was comparable on the remaining analyzers (kappa 0.55 - 0.933). *Conclusion:* There was comparability of HIL indices among 4 analyzers except L index between the BC and SA. Specifically, the results of all HIL indices on the SA, RC, AA analyzers were high agreement.

Keywords: Serum indices, 108 Military Central Hospital.

1. Background

To date, clinical chemistry testing plays an important role in diagnosis, treatment, prediction and precaution, therefore the testing quality is considered to improve relentlessly for ensuring accurate, reliable results [1].

Cell-free hemoglobin (i.e., spurious hemolysis), hyperbilirubinemia and hypertriglyceridemia are common interfering substances. The presence of each of these interferences is a potential source of biological and analytical biases. Thus, it is essential to realize and determine blood samples containing interferences in order to eliminate the possibility of pre-analytical errors [2].

Visual assessment of the degree of hemolysis (H), icterus (I) and lipemia (L) is deficient compared to automatic measurement of serum indices [3]. Also, the level of agreement between visual and automatic assessment is poor. Measurement of serum indices, on the other hand, is fast, cheap, objective and reduces the possibility of errors in the pre-analytical phase of laboratory testing [4], [5].

In Vietnam, laboratories currently use different clinical chemistry platforms to measure the same

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Correspondence to: *Nguyen Cam Thach - Department of Biochemistry, 108 Military Central Hospital*
Email: nguyencamthach1973@yahoo.com.

subjects, including serum indices. Utilizing several analyzers in a laboratory has various advantages, however, it is difficult to manage sample quality and identify unreliable outcomes. The variance of HIL indices should be deliberated to minimize effects on a decision as choose or reject testing results.

Even though some aspects of analytical verification have been previously published (precision, comparability or accuracy), data on complete verification protocols for all three serum indices are not available. Therefore, the aim of our study was to perform the identification of serum indices measurement on four clinical chemistry analyzers: Abbott architect C8000 (AA), Roche cobas C501 (RC), Beckman coulter AU5800 (BC), Siemens advia 1800 (SA).

2. Subject and method

2.1. Subject

Plasma of patients examined at 108 Military Central Hospital (108 MCH) from 12/2020 to 04/2021, comprising of 240ml normal plasma sample, 30ml artificial hemolyzed plasma for H index, 30ml icteric plasma with 360µmol/L total bilirubin, 30ml plasma with 1g/L of Intralipid 20% for lipemia.

2.2. Method

The prepration of plasma samples for interferences according to the European Federation of Clinical Chemistry and Laboratory Medicine guidelines [6].

Table 1. Dilution of samples for serum indices

Aliquots	H index		I index		L index	
	Sample (15ml)	Hem (mg/dL)	Sample (15ml)	Bil (mg/dL)	Sample (15ml)	TG (mg/dL)
1	A	600	A1	21.05	A2	1950
1:2	B	300	B1	10.53	B2	975
1:4	C	150	C1	5.26	C2	487
1:8	D	75	D1	2.63	D2	244
1:16	E	37.5	E1	1.32	E2	121
1:32	F	18.75	F1	0.66	F2	60.2

Normal plasma (O): Collection of clear plasma pool having H index < 0.25g/L (25mg/dL), I index < 30.0µmol/L (1.75mg/dL), L index < 0.3mmol/L (26.57mg/dL).

Studied sample for H indice: a whole blood sample stored at -20°C overnight to generate a hemolyzed sample, then hemolyzed plasma was separated by centrifuging at 4000g for 10 minutes at room temperature. 6 samples (A, B, C, D, E, F) were created by diluting consecutively the hemolyzed plasma with O sample.

Icteric sample: 30ml plasma with concentration of bilirubin at 360µmol/l was collected and generated 6 samples (A1, B1, C1, D1, E1, F1) by mixing consecutively the plasma with O sample.

Lipemic sample: A2 sample with TG concentration at ~22mmol/l was generated by adding Intralipid 20% into 30ml O sample, then consecutively diluted 1 volume A2 sample with 2 volume O sample to create other samples B2, C2, D2, E2, F2.

30 studied samples were analysed HIL indices on Abbott Architect c8000, Beckman Coulter AU5800 at 108 MCH and on Siemens Advia 1800, Roche Cobas c501 at Siemens Advia 1800, Roche Cobas c501.

2.3. Statistical analysis

Statistical analysis was performed using Microsoft Excel and MedCalc statistical software 12.7.2.0 (MedCalc software, Ostend, Belgium).

As the values of HIL indices on the BC, SA are qualitative, on the other hand, the values of HIL indexes on the RC, AA are quatitative. Thus, all quatitative results were exchanged into qualitative values based on manufacturer instruction as data shown in Table 2.

Table 2. Analytical specifications of HIL measurement on analyzers

	Abbott Architect	Roche Cobas	Beckman Coulter	Siemens Advia
Reagent	Saline (0.85%-0.90% NaCl) (no specific reagent required)	SI2 (Serum Index Gen.2), REF: 04489365190	LIH reagent, Cat no.OSR62166	Saline (0.90% NaCl) (no specific reagent required)
Wavelengths for H index	500/524nm	570/600nm	410/480nm	571/596nm.
Wavelengths for I index	572/604nm	480/505nm	480/570nm	478/505nm.
Wavelengths for L index	524/804nm	660/700nm	660/800nm	658/694nm
Recommended classifications for hemolysis (mg/dL of free Hb)	0: < 30	Exchangeable data not provided. Analysis range: 5 - 1200	0: < 50	0: < 49.9
	1+: 30 - 100		1+: 50 - 100	1+: 50 - 149.9
	2+: 100 - 200		2+: 100 - 200	2+: 150 - 249,9
	3+: 200 - 500		3+: 200 - 300	3+: 250 - 524.9
	4+: > 500		4+: > 300 - 500	4+: ≥ 525
			5+: > 500	
Recommended classifications for icteria (mg/dL of bilirubin)	0: <2.0	Exchangeable data not provided. Analysis range: 0.5 - 60	0: < 2.5	0: < 1.69
	1+: ≥ 2.0		1+: 2.5 - 4.9	1+: 1.7 - 6.59
	2+: ≥ 4.0		2+: 5.0 - 9.9	2+: 6.6 - 15.9
	3+: ≥ 10.0		3+: 10.0 - 19.9	3+: 16 - 29.9
	4+: ≥ 20.0		4+: 20.0 - 40.0	4+: ≥ 30
			5+: > 40.0	
Recommended classifications for lipemia (mg/dL of Intralipid®)	0: <50	Exchangeable data not provided. Analysis range: 10 - 2000	0: < 40	0: < 124,9
	1+: ≥ 50		1+: 40 - 99	1+: 125 - 249,9
	2+: ≥ 100		2+: 100 - 199	2+: 250 - 499,5
	3+: ≥ 150		3+: 200 - 299	3+: 500 - 999.9
	4+: ≥ 200		4+: 300 - 500	4+: ≥ 1000
			5+: > 500	

The agreement of HIL indices among the different instrumentations was evaluated using Cohen's kappa [7] and the values of Cohen's kappa coefficient were interpreted in the Table 3.

Table 3. Interpretation of Cohen's kappa

Value of kappa	Level of agreement	% of data that are reliable
< 0.2	none	0 - 4
0.21 - 0.39	minimal	4 - 15
0.4 - 0.59	weak	15 - 35
0.6 - 0.79	mediate	35 - 63

0.8 - 0.9	strong	64 - 81
Above 0.9	almost perfect	82-100

3. Result

Table 4. Comparability of HIL index between Beckman Coulter and 3 others analyzers

	Beckman Coulter		
	H index kappa (95% CI)	I index kappa (95% CI)	L index kappa (95% CI)
Siemens advia	0.797 (0.617 - 0.976)	0.538 (0.305 - 0.772)	< 0.2
Abbott architect	0.797 (0.617 - 0.976)	0.55 (0.315 - 0.785)	0.832 (0.651 - 1.00)
Roche cobas	0.95 (0.854 - 1.00)	0.55 (0.315 - 0.785)	0.887 (0.738 - 1.00)

Comment: The agreement of H index between BC and the remaining platforms and the agreement of L index between BC and AA, RC were strong. However, the agreement of I index among intruments was weak. Additionally, there was no comparability between L index of BC and SA.

Table 5. Comparability of HIL index between Siemens advia and 3 others analyzers

	Siemens advia		
	H index kappa (95% CI)	I index kappa (95% CI)	L index kappa (95% CI)
Beckman coulter	0.797 (0.617 - 0.976)	0.538 (0.305 - 0.772)	< 0.2
Abbott architect	0.75 (0.559 - 0.941)	1.00 (1.00 - 1.00)	0.727 (0.488 - 0.967)
Roche cobas	0.75 (0.559 - 0.941)	1.00 (1.00 - 1.00)	0.933 (0.805 - 1.00)

Comment: The comparability of HIL indexes among SA, AA, RC were almost prefect, nevertheless, the agreement of I indice between SA and BC was only weak.

Table 6. Comparability of HIL index between Abbott architect and 3 others analyzers

	Abbott architect		
	H index kappa (95% CI)	I index kappa (95% CI)	L index kappa (95% CI)
Beckman coulter	0.797 (0.617 - 0.976)	0.55 (0.315 - 0.785)	0.832 (0.651 - 1.00)
Siemens advia	0.75 (0.559 - 0.941)	1.00 (1.00 - 1.00)	0.727 (0.488 - 0.967)
Roche cobas	1.00 (1.00 - 1.00)	1.00 (1.00 - 1.00)	0.55 (0.315 - 0.785)

Comment: The value of HIL indices on AA was agreement with the others analysers. On the other hand, the comparability of L index between AA and RC was weak. The result of L index on AA and RC was slight suitability.

Table 7. Comparability of HIL index between Roche cobas and 3 others analyzers

	Roche cobas		
	H index kappa (95% CI)	I index kappa (95% CI)	L index kappa (95% CI)
Beckman coulter	0.95 (0.854 - 1.00)	0.55 (0.315 - 0.785)	0.887 (0.738 - 1.00)
Abbott architect	1.00 (1.00 - 1.00)	1.00 (1.00 - 1.00)	0.55 (0.315 - 0.785)
Siemens advia	0.75 (0.559 - 0.941)	1.00 (1.00 - 1.00)	0.933 (0.805 - 1.00)

Comment: The values of HIL indices among 4 instruments were strong agreement. However, I index on RC and BC, L index on RC and AA were only weak.

4. Discussion

The main finding of our study was that a comparability in the quality performance of HIL indices between the manufacturers (Beckman coulter, Siemens advia, Abbott architect, Roche cobas) was different. The agreement of H index among 4 instruments was good as results in Table 4, 5, 6, 7 and values of I index on the AA, SA, RC were absolutely suitable (kappa 0.75 - 1.0). Nevertheless, the comparability between results of I index on the BC and 3 others platfroms was mediate (kappa 0.53 - 0.55) while I index on the RC, SA, AA was extremely suitable (kappa 1.0). Even though, the agreement of L index between BC and SA was not acceptable (kappa < 0.2) as results in Table 4 and 5, it was comparable on the remaning analyzers (kappa 0.55 - 0.933). On top of that, the finding shown that the comparability between the SA and the AA, RC were very good for all HIL indices.

There is heterogeneity between analyzers in the hemolysis, icterus, lipemia (HIL) quality performance due to HIL indices on clinical chemistry analyzers measure spectra on several different wavelengths and provide approximate concentrations of Hb, bilirubin and lipids in the sample, as a result. Furthermore, some manufacturers require a specific reagent to measure HIL indices, while others use only saline solution or water. Most laboratories therefore do not consider HIL measurement a "real laboratory method"; and serum indices are only used to evaluate the degree of interference [8].

Previous studies reported that the agreement of HIL indices between biochemical instruments was still controversial. Nora Nikolac Gabaj et al (2018) assessed HIL indices on 3 analysers Abbott architect c8000, Beckman coulter AU5800 and Roche cobas 6000 c501, the measurement of L index on all 3 platforms was comparable and the value of H index was suitable between BC and AA, RC (Cohen's κ [95% CI] = 0.795 [0.692 - 0.898]; Cohen's κ [95% CI] = 0.825 [0.729 - 0.922]), whilst the comparability of I indice was not acceptable among 3 analyzers [8].

Another evaluation of Lippi G et al (2013) in Italy on 5 analyzers (Beckman coulter AU5800, roche cobas 6000, Siemens dimension vista 1500, Abbott architect C 16000 and Ortho vitros 5.1/FS) found that there was an agreement of H index among the AA, BC, RC with Cohen's kappa from 0.62 to 1.0. However, the finding had no data about I and L indexes on these analysis systems.

Until now, our study was the first assessment of comparability of HIL indices on 4 different clinical chemistry platforms. We performed on 4 common analyzers in laboratories in Vietnam. In contrast, this research has several limitations as the difference in interpretation of HIL results on analyzers, including qualitative analysis and quatitative analysis, so it is nessesary to verify the comparability of HIL on different ranges of quatitative levels. The lack of data references is also a disadvantage of our study.

5. Conclusion

The agreement of HIL indices among 4 analyzers was acceptable except results of L index on the BC was not comparable with that on the SA. Specifically, the results of all HIL indices on the SA, RC, AA analyzers were high agreement.

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