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Original Article

Pathology Section

The Effects of Plasma Prothrombin Time and Activated Partial Thromboplastin Time Based on Different Instruments and Methods

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ABSTRACT

Introduction: Many laboratories have more than one coagulometer with different types and methods that are used simultaneously. In patients requiring Plasma Prothrombine Time (PPT) and Activated Partial Thromboplastin Time (APTT), follow-up treatments may be performed on different instruments.

Aim: To analyse whether there are differences in the value of PPT and APTT between 3 instruments with different methods.

Materials and Methods: This study took 64 samples of patients with End Stage Renal Disease (ESRD) who underwent haemodialysis in Haemodialysis Centre of Dr. Soetomo General Hospital Surabaya between April 2017 and October 2017. All samples were carried out for examination of PPT and APTT on three instruments: CoaDATA 501 with one wavelength optical detection, Sysmex CS2100i with three wavelengths optical detection, and STA Compact using electromechanical methods.

Results: Significantly different results were obtained in the PPT comparison between the group of CoaData with Sysmex CS2100i (p≤0.001) and CoaData with STA Compact (p≤0.001). While in the intergroup APTT, all gave significantly different test results (p<0.001).

Conclusion: Because of difference value of PPT and APTT in difference instrument and method, therefore serial tests should be performed in the same instrument to obtain valid and reliable results.

Keywords: CoaDATA 501, Sysmex CS2100i, STA compact, Optical method, Electromechanical method

INTRODUCTION

The coagulometer for the examination of PPT and APTT available today has a variety of detection methods. The coagulation laboratory has changed dramatically over the last 30 years, and so has coagulation methodology. It has seen a move from manual tests, to semi-automated tests and currently to fully automated machines. Fully automated systems, when compared with manual methods, are efficient in terms of time and labour, as well as being economical in sample and reagent used. The manual tilt-tube test is the gold standard method for the determination of prothrombin time using international reference preparations of thromboplastin [1]. New detection methods are emerging to eliminate the weakness of the previous method. The principle of the method of the coagulometer instrument is divided into electromechanical and photo-optical. Electromechanical include impedance-steel ballrotating cuvette; and impedance- steel ball-rotating steel ball. Photo-optical include scatter light detection for clotting assays, transmitted light detection for chromogenic assay, transmitted light detection for immunoassay, nephelometry, photo-optical end point determination and analysis, percentage detection method and rate method [2].

Many laboratories, especially in hospitals, have more than one coagulometer with different methods. One coagulometer is usually the main instrument, and the other used as a backup as well as a comparison instrument if the tests done by a certain instrument cannot produce valid results. This kind of result often needs confirmations as certain methods have a limited detection time. It occurs becuase of lysis or in lipemic and jaundice samples [3]. So, many labratories need to keep backup coagulometers that uses non photo-optical detection systems like electromechanical detection system. In cases, a laboratory has a lot of work load, both set of instruments are put to work. Patients requiring elective surgeries, certain laboratory test such as, PPT or APTT are done only once. This does not cause a problem, since a repeat is not required and the value is compared with the standard reference, either of the manufacturer or the specific population standard. However, in test for patients who require follow-up, test are repeated, example, a follow-up examination for PPT or APTT is required in patients needing massive transfusions, pre and post-haemodialysis patients with renal failure, monitoring anticoagulant treatment, recombinant factor therapy, heart surgery and other surgeries. In fact, there are still many laboratories that donot pay attention which instrument was used for the first examination of a certain patient, which was then used for the second and so on. Yet some laboratories donot keep a note of which specific instrument was used for each patient the first time, specially those requiring follow-ups.

All coagulation examinations by automatic or semi-automatic instrument using the principle of making plasma becomes turbid or opaque because of fibrin formation. This is because of the induction of thromboplastin and calcium in the added reagents. Then turbidity is detected by optical-based method (optical and photometric) or the occurrence of the clot is detected by mechanical-based method (electromechanical and electromagnetic) [4].

This study aims to compare three instruments, i.e., CoaDATA 501 (LABitec, Germany), which uses turbodensitometric measuring principle with optical detection method at one wavelength, Sysmex CS2100i (Siemens, Kobe, Japan), which uses optics at three wavelengths to overcome the interferences of colour and turbidity, and STA Compact (Diagnostica Stago, Inc., Asni eres sur Seine, France), which uses electromechanical detection based methods. There is no study which compares these instruments previously. If there is no difference in the results of detection on each instrument, then running on any instrument on the PPT and APTT serial tests is not a problem. On the contrary, if there is a difference, then it is necessary to make PPT and APTT examination policies that require a follow-up. Otherwise, serial data is run on the same instrument to provide reliable results in order not to harm the patient. This is also certainly very helpful for clinician to decide the next action for the patient.

MATERIALS AND METHODS

Patients

This study was an observational analytic design. Samples were obtained from End State Renal Disease (ESRD) patients undergoing a scheduled haemodialysis (twice a week) at Haemodialysis Centre of Dr. Soetomo General Academic Hospital in Surabaya, Indonesia between April 2017 and October 2017. The patients have given us the consent. Ethical clearance approval has also been obtained from Health Research Ethics Committee of Dr. Soetomo Hospital Surabaya. Seventy-six samples were obtained in this study. The samples were taken just before the patient underwent haemodialysis, and or five minutes after haemodialysis ended. During the course of the haemodialysis, the patient received heparin 2500 U. Samples were taken in patients undergoing haemodialysis because it was expected that there would be a variation of the result, which was normal for pre haemodialysis taking and extended post haemodialysis [5]. A total of 12 samples were excluded because the result of the examination did not give a value, due to no coagulation up to the time limit of detection, either on one or more instruments. In the end, it was only the results obtained from 64 samples that were processed statistically. Sixty-four samples consist of 20 patients each who were taking pre- and post-haemodialysis respectively, one patient who was taking pre-haemodialysis only and 23 patients who were taking post haemodialysis only.

The same samples were tested in three instruments, therefore there were 3 groups in this study. The samples which were examined with CoaDATA 501 was stated as Group 1, Sysmex CS 2100i as Group 2 and STA Compact as Group 3.

The peripheral blood of the patient was inserted to sodium citrate tube 0.109 mol/L (3.2%) (BD Vacancies Plus, Becton Dickinson, Franklin Lakes, NJ, USA) with a proportion of 1 volume of citrate to 9 volumes of blood, then centrifuged at a rate of 2000 g for 15 minutes at room temperature to obtain a Poor Platelet Plasma (PPP) according to CLSI Guideline H03-A5 'Procedures for the collection of diagnostic blood specimens by venipuncture' and with the CLSI guideline H21-A5' Collection, transport, and processing of blood specimens for testing plasma-based coagulation assays and molecular haemostasis assays [6,7]. Plasma was then further divided into three aliquots and checked on three instruments. Blood samples were processed no more than one hour since the sampling, performed in laboratory of Clinical Pathology Dr. Soetomo General Hospital and General Hospital of Universitas Airlangga, Surabaya.

Instruments and Reagents

Instruments: CoaDATA 501 is a semi-automatic analyser operating in opto-mechanical method. The light goes through a cuvette containing a plasma test onto a photo-detector. The changes in the intensity of light transmission, which might be increased or decreased, are converted into electrical signals. The detection uses a single wave length of 405 nm. The reduction or alteration of light in the plasma, which is considered as the endpoint, is converted digitally by each optical instrument [8].

Sysmex CS2100i is a fully automated blood coagulation analyser with multi-wavelength detection (using multi-wavelengths of 405, 575, 660 nm) and four analysis methods (coagulation, chromogenic, immunoassay and aggregation). The system uses photo-optical detection, measuring light transmittance over the entire course of clot formation, not just the end [9].

STA Compact is a fully automated electromechanical coagulation analyzer. In principle, a steel ball undergoes an oscillation in the cuvette under the electromagnetic force generated by two electrode coils, each passing through an electric current, producing a spherical movement of the ball. The movement of the sphere produces fixed amplitude if the plasma viscosity in the cuvette remains fixed; and decreases if the plasma viscosity in the cuvette increases. The clot on the plasma sample will decrease the movement of the sphere and form the endpoint. The emission coefficient detection system emits an electromagnetic field and the signal is received by the coil based on the ball position in the cuvette. An algorithm is used against the variation of the resulting electromagnetic field to calculate the amplitude and then determine the clotting time [10].

Quality Control

All three instruments have been calibrated and quality control for normal and abnormal category between days before running the sample according to the instructions on the control kit on each instrument. Accuracy controls are ensured within the normal range, and precision control results are fulfilled according to the requirements of each manufacturer.

Reagents

The list of reagents which were used in the study are tabulated in [Table/Fig-1].

Instrument	Manufacture	Parameter	Name of reagent	Reference number	Lot number
CoaDATA 501	TECO Gmbh, Neufahm, Germany	PPT	Uniplastin [11]	10620125	352702
		APTT	TEClot APTT-S [12]	A0320-050	10322494
		$CaCl_2$	Calcium Chloride ($CaCl_2$) 0.025M [13]	A0350-002	10352449
Sysmex CS2100i	Siemens Healthcare Diagnostics, Marburg, Germany	PPT	Innovin [14]	B4212-40	549713B
		APTT	Actin FSL [15]	B4219-1	556917A
		$CaCl_2$	$CaCl_2$ 0.025M [16]	BT-565-104	A7023
STA Compact	Diagnostica Stago SAS, Seie, France	PPT	Neoplastine CI Plus 5 [17]	00606	250077
		APTT	Cephascreen 4 [18]	00308	251315
		$CaCl_2$	$CaCl_2$ 0.025 M [19]	00367	250643

[Table/Fig-1]: The list of reagents which were used.
PPT: Plasma prothrombin time; APTT: Activated partial thromboplastin time; $CaCl_2$: Calcium chloride

STATISTICAL ANALYSIS

The analysis to determine the difference between the groups used Friedman test with post-hoc Wilcoxon signed rank test because the sample data is abnormally distributed. The normality test used was Kolmogorov-Smirnov test. Test of paired sample pre and post haemodialysis used paired t-test when the data were normally distributed. The statistical analysis used IBM SPSS Statistics for Windows software, Version 22.0. Armonk, NY: IBM Corp. The interpretation of the test results was indicated significant if $p<0.05$.

RESULTS

Male dominates the samples, and the most cause of ESRD was hypertension [Table/Fig-2]. The highest mean results of PPT and APTT were detected in the STA Compact (Group 3), whereas the lowest mean PPT and APTT were detected in the Sysmex CS2100i (Group 2). The different tests between Group 1, 2 and 3 show that the differences between groups are significant ($p<0.001$) in both PPT and APTT. Significant differences for PTT are shown between Groups 1 and 2, and also 2 and 3. While in APTT, all tests show significant differences [Table/Fig-3].

The reference value of PPT for CoaDATA 501 is 10-15 seconds; Sysmex CS2100i goes 9-12 seconds; STA Compact goes 11.5-15.5 seconds, and as well as APTT reference value for CoaDATA 501 was 27-42 seconds; Sysmex CS2100i 23-33 was seconds; STA Compact was 26-37 seconds. This reference value was

Variables	Numbers
Age (years)	
Median (minimum-maximum)	52 (27-66)
Gender	
Men	43 (67%)
Women	21 (33%)
Primary diagnosis	
Diabetes melitus	22 (35%)
Hypertension	42 (65%)
Pre haemodialysis	21 (33%)
Post haemodialysis	43 (67%)

[Table/Fig-2]: Characteristics of patients.

obtained from the inserted kit for CoaDATA 501 and STA Compact, while for Sysmex CS2100i was obtained from previous local studies on healthy populations. Twelve samples which dropped due to no coagulation on the results, they did not provide information of a tendency to a particular method.

Data from 20 patients with pre and post haemodialysis also were tested with paired t-test or Wilcoxon signed rank test depending on the data distribution, indicating the result that the mean PPT Pre haemodialysis was significantly higher in all three instruments with significance for CoaDATA 501, Sysmex CS2100i, STA Compact respectively: p=0.046, p=0.046, p=0.005. While for APTT pre haemodialysis results did not differ significantly with post haemodialysis on the three instruments for CoaDATA 501, Sysmex CS2100i and STA Compact respectively: p=0.940, p=0.955, p=0.370 [Table/Fig-4].

DISCUSSION

The results of this study differ from previous studies showing that there is good conformity between the results of PPT and APTT of normal, abnormal, partial lyses between the three coagulometers with different methods of STA Compact Max, CS2000i, ACL Top (nephelometric principle) [4]. There is a good correlation between photo-optical (MTX II) and photo-mechanical analyser (AMAX 200) for PPT and APTT [20], and a strong correlation between photo-optical clot detection method Sysmex CA-1500 and electromechanical detection STA though on a cloudy sample [21]. Meanwhile, the cases of lipemia samples reported by Aggarwal S et al., obtained different PPT and APTT measurement results between the cogulometer with photo-optical and mechanical methods [22]. Geens T et al., in his study gave significantly different results for all parameters including PPT and APTT between Sysmex CS5100 using optical methods and STA-R Evolution using mechanical methods, this difference was probably due to differences in methods and reagents [23]. Nayak MD et al., indicated that in the Amax Destiny Plus™- Trinity Biotech semi-automatic instrument with optic-based method is better than the mechanic on prothrombin time examination [24]. Twelve samples were dropped because no coagulation results were obtained by the three instruments, indicating that no one method was found to be superior to others in the study. Hill M and O'Toole R, showed results that Start Max, a semi-automatic analyser using a mechanic detection system, was able to address the early reaction error sample in the fully automated Sysmex 2100i analyser [25].

Haemostasis testing is subject to inter-laboratory distortion due to pre-analytical and analytical variables, including differences in method and endpoint detection technologies such as photo-optical vs. mechanical clot detection. Fully automated vs. semi-automated equipment and reagent variables can influence the results [2,26].

Differences in results can be caused by different methods or working principles on all three instruments, as mentioned in CLSI H47-A2 2008 (One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (APTT) Test; Approved Guideline -Second Edition) on the effect of different methods on the coagulometer instrument, which will have an impact on the output or different measurement results [27]. In this study CoaDATA 501 uses a turbodensitometric principle with photo-optical clot detection with a one-wavelength method (405 nm) [8], Sysmex CS 2100i uses the principle of photo-optical clot detection with multi-wavelength (340, 405, 575, 660, 800 nm) [9], STA Compact uses viscosity-based detection with electro-mechanical detection-based [10].

In addition to the differences in method as an instrument, CLSI H47-A2 2008 also mentions that the presence of different thromboplastin dosage forms (commercially available PPT reagents according to the its instrument) may provide varied responses in terms of value or PPT levels [27].

As mentioned before, the PPT reagent differs across the three instruments, shown by the different compositions in each of the PPT and APTT reagents, the reagents on CoaDATA 501 for PPT using Uniplastin, is a calcium thromboplastin derived from animals accompanied by 0.01% Thimerosal (preservative), APTT uses TEClot APTT-S containing sodium chloride, polyethylene glycol 2000, sucrose and sodium azide (preservative) and 11 calcium chloride ($CaCl_2$) 0.025M [11-13]. Reagents in Sysmex CS2100i, PPT using Innovin, are thromboplastin tissue contains calcium, standardised with ISI; APTT reagents use Actin FSL containing purified soy phosphatides, rabbit brain phosphatide, ellagic acid,

Parameter	Group1	p-value between group	Group 2	p-value between group	Group 3	p-value between group*	p-value intergroup
PPT							
Mean±SD	13.24±2.24	≤0.001	10.56±0.89	≤0.001	13.33±1.32	0.488	<0.001
(Min-Max)	(10.1-20.9)		(8.8-13)		(10.4-17)		
APTT							
Mean±SD	35.13±22.07	0.002	32.32±19.54	≤0.001	42.83±21.23	≤0.001	<0.001
(Min-Max)	(19.5-135)		(19.3-130.4)		(26.1-136)		

[Table/Fig-3]: Mean±SD and level of significance of PPT and APTT in groups 1, 2 and 3.
*P between group 3 and 1; PPT: Plasma prothrombin time; APTT: Activated plasma thromboplastin time; SD: Standard deviation; min: minimum; max: maximum;
The samples that were examined with the CoaDATA 501 was categorised as group 1, Sysmex CS 2100i was categorised as group 2, and with STA Compact was categorised as group 3

Parameter	PPT Mean±SD Pre-haemodialysis	PPT Mean±SD Post-haemodialysis	p-value	APTT Mean±SD Pre-haemodialysis	APTT Mean±SD Post-haemodialysis	p-value
CoaDATA 501	14.27±2.79	13.20±1.28	0.046	38.12±25.90	32.45±8.15	0.940
Sysmex CS2100i	10.91±1.01	10.65±1.08	0.046	34.54±20.60	31.45±8.81	0.955
STA Compact	13.84±1.57	13.03±0.80	0.005	45.94±25.16	44.41±11.13	0.370

[Table/Fig-4]: Mean±SD and level of significance of PPT and APTT between pro and post haemodialysis.

buffer and calcium chloride solution containing calcium chloride ($CaCl_2$) 0.025 mol/L [14-16,28]. Reagents in STA Compact, PPT using Neoplastine CI Plus 5, is an ISI standard lyophilized thromboplastin, standardised rabbit brain network with a solvent in the form of calcium; APTT reagents using Cephascreen 4 are made of cephaline (platelet substitute) from rabbit brain tissue, polyphenolic activator on buffer medium and CaCl2 0.025 M [17-19]. Differences in the composition of each reagent are thought to be important factors causing variation in the results of the three instruments, but this has not been explained the direct relationship between the composition of the reagent with the rapid or slow activation of coagulation.

Differences in the results of the examination of PPT and APTT are due to factors of analytic and biologic variability. Nagler M et al., have found variability in the results of interagency coagulation tests in general and between instruments in particular. Variability influenced by variation of component (technician, assay design, laboratory procedure in determining reagent and calibrator to be used), level of standardisation in each laboratory including the different reference value standards in each instrument, as well as compliance with the guidelines for the conduct of the examination, are expressed as causal sources of variability in the results of examinations from different laboratories [29].

Biologic variability for coagulation screening tests is generally low. The two components of biological variability are inter-individual variability, that is variability due to the heterogeneity of the influence of physiology among individuals, and inter-individual variability, due to the same individual variability over time. However, the index of individuality (the ratio between intra-individual and inter-individual variability) in routine preoperative screening for coagulation abnormalities may be influenced by variability between subjects [30].

The difference in outcomes caused by differences in instruments, reagents and methods is also corroborated by different reference values on the instrument set. This reference value is obtained from manufacture except Sysmex CS2100i, where the value of PPT and APTT of Sysmex CS 2100i is the smallest compared to CoaDATA 501 and STA Compact, this is in accordance with the results of this study where the mean PPT and APTT patients obtained from Sysmex CS2100i also show smallest results among others. Differences in reference values are also found in Geens research (2014) for APTT between Sysmex CS2100i with a reference value of 23-31 seconds and STA-R Evolution 30-42 seconds. Significant differences were also obtained on the validation and verification of the Sysmex CS5100 referral value for APTT, between the manufacturer reference values and those obtained by the laboratory itself from 40 healthy individuals [23].

LIMITATION

The limitations of this study were not to compare between healthy people, patients with tendency of shortening and lengthening PPT and APTT results, so it is difficult to tell which groups actually made a difference.

CONCLUSION

In conclusion, the instrument of CoaDATA 501, Sysmex CS2100i and STA Compact provide different results in both PPT and APTT intergroup. These difference due to differences in method and reagents. Therefore, the recommendation for serial or follow-up tests should use the same instruments to obtain valid and reliable results.

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REFERENCES

[1] Crighton G. Methods of Coagulation. Methods Mol Biol. 2013;992:73-83.
[2] Laffan MA, Manning RA. Investigation of Haemostasis. In: Bain BJ, Bates I, Laffan MA, Lewis SM (eds). Dacie and Lewis Practical Haematology. 12th ed. China: Elsevier, 2017:377-78.
[3] Woolley A, Goldmard JL, Kitchen S. Effects of haemolysis, icterus and lipaemia on coagulation tests as performed on Stago STA-Compact-Max analyser. International Journal of Laboratory Hematology. 2016;38(4):375-88. doi: 10.1111/ijlh.12498. Epub 2016 Jun 16.
[4] Rathod NN, Nair SC, Mammen J, Singh S. A comparison study of routine coagulation screening tests (PT and APTT) by three automated coagulation analyzers. Int J Med Sci Public Health. 2016;5(8):1563-68.
[5] Khalid A, Zafar L. Effect of haemodialysis on mean prothrombin time and activated partial thromboplastin time in patients of end stage renal disease. Journal of Rawalpindi Medical College (JRMC). 2015;19(3):247-49.
[6] Clinical and Laboratory Standards Institute (CLSI). Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard-Fifth Edition. CLSI: document H03-A5. Wayne (PA): Clinical and Laboratory Standards Institute, 2003.
[7] Clinical and Laboratory Standards Institute (CLSI). Collection, Transport, and Processing of Blood Specimen for Testing Plasma-Based Coagulation Assays and 14 Molecular Hemostasis Assays: Approved Guideline- Fifth Edition. CLSI: document H21-A5. Wayne (PA): Clinical and Laboratory Standards Institute, 2008.
[8] CoaDATA 501. Manual Operator; Version Manual 2.1, 1-54, (Accessed on 2 March 2018). http://peramed.com/peramed/docs/90.200.0006_5060169855687_EN.pdf.
[9] Sysmex. CS2100i-Advanced coagulation testing designed with you in mind. (Accessed on 2 March 2018. https://www.sysmex-europe.com/products/cs-2100i-17.html.
[10] Diagnostica Stago. STA Compact® The reliable analysis (Accessed on 2 March 2018). https://www.ssllc.com/images/uploads/STA%20Compact%20 Brochure.pdf.
[11] Tulip Diagnostics (P) Ltd., Material Safety Data Sheet: Uniplastin, India, 2001:1-5. (Accessed on 2 March 2018). www.tulipgroup.com/Tulip_New/msds/.../ uniplastin.pdf.
[12] TECO. Material Safety Data Sheet: TEClot APTT-S, TECO GmbH, Neufahrn NB Germany.
[13] TECO. Material Safety Data Sheet: Calcium Chloride 0.025 M, TECO GmbH, Neufahrn.
[14] Sysmex Corporation. Application sheet for PT (INR calibrated) with Dade® Innovin® . CS-200i/2100i System Application Guide 1.5. Valid from software version: 00-61, 1-7.
[15] Sysmex Corporation. Application Sheet for aPTT with Dade®Actin® FSL activated PTT reagent. CS-200i/2100i System Application Guide 1.5. Valid from software version: 00- 61,01-14.
[16] Siemens. Calcium Chloride Solution. Marburg: Siemens Healthcare Diagnostica Product GmbH. April 2010.
[17] Diagnostica Stago. Material Safety Data Sheet: STA-Neoplastine CI Plus 5, Asnières sur Seine, 2013. http://www.annardx.com/productos/images/ productos/diagnostica/coagulacion/00667- pt-sta-neoplastine-ci-plus-10-isi-13-octubre-2013-ingle701387819.pdf (Updated on October 2013).
[18] Diagnostica Stago. Material Safety Data Sheet: STA-Cephascreen, Asnières sur Seine, 2013. http://www.annardx.com/productos/images/productos/ diagnostica/coagulacion/00308.pd f. (Updated on February 2013).
[19] Diagnostica Stago. Material Safety Data Sheet: CaCl2 0.0025 M, Asnières sur Seine, 2013. http://www.annardx.com/productos/images/ productos/diagnostica/coagulacion/00367- sta-cacl2-0025-m-06042013-ingle1864469548.pdf (Updated on April 2013).
[20] Tekkesin N, Kilinc C. Optical and mechanical clot detection methodologies: A comparison study for routine coagulation testing. J Clin Lab Anal. 2012;26:125-29.
[21] Bai B, Christie DJ, Goman RT, Wu JR. Comparison of optical and mechanical clot detection for routine coagulation testing in a large volume clinical laboratory. Blood Coagul Fibrinolysis. 2008;19(6):569-76.
[22] Aggarwal S, Nayak DM, Manohar C. Discrepancy in optical & mechanical method in coagulation tests in turbid sample. Indian J Haematol Blood Transfus. 2014;30(S1):402-04.
[23] Geens T, Vertessen F, Malfait R, Deiteren K, Maes MB. Validation of the Sysmex CS5100 coagulation analyzer and comparison to the Stago STA-R analyzer for routine coagulation parameters. Int Jnl Lab Hem. 2015;37:372-81.
[24] Nayak MD, Manohar C, Saroja, Patil A. Comparison of photo-optical and mechanical methods for prothrombin time test. Indian J Appl. 2013; Res 3:457-58.
[25] Hill M, O'Toole R. Kendrick C. Stago Start Max analyser validation and early reactions error (ERE) in haemostasis testing at Wellington SC. N Z J Sci. 2017;71:129-35.
[26] Adcock DM, Brien WF, Duff SL, Johnston M, Kitchen S, Marlar RA, et al. Procedure for validation of INR and local calibration of PT/INR systems. In: Approved Guideline, 16 Clinical and Laboratory Standards Institute. 2005;25:23.
[27] Clinical and Laboratory Standard Institute. CLSI-H57A Protocol for the Evaluation, Validation, and Implementation of Coagulometers: Approved Guideline. Wayne, PA: Clinical and Laboratory Standard Institute; 2007.
[28] Flieder T, Gripp T, Knabbe C, Birschmann. The Sysmex CS-5100 coagulation analyzer offers comparable analytical performance and excellent throughput capabilities. Practical Laboratory Medicine. 2016;6:38-47.

[29] Nagler M, Bachmann L M, Alberio L, Angelillo-Scherrer A, Asmis LM, Korte W, et al. Variability between laboratories performing coagulation tests with identical platforms: a nationwide evaluation study. Thrombosis Journal. 2013;11:6.

[30] Banfi G, Del Fabbro M. Biological variation in tests of hemostasis. Semin Thromb Hemost. 2009;35:119-26.

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