AMLR Asociația de Medicină de Laborator din România

Romanian Journal of Laboratory Medicine 2026;34(1):55–60

RESEARCH ARTICLE

DOI:10.2478/rrlm-2026-0008

Establishment of intra- and inter-laboratory reference change values for coagulation tests: PT, INR, and aPTT

Mehmet Akif Bildirici*, Sedat Gülten

Department of Medical Biochemistry, Faculty of Medicine, Kastamonu University, Türkiye

ABSTRACT

Background: Coagulation assays such as prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT) are widely used for patient monitoring. Accurate interpretation of sequential test results requires consideration of both biological and analytical variation. The reference change value (RCV) is a statistical tool that determines whether changes in serial results are clinically significant. While RCVs are typically calculated using intra-laboratory data, inter-laboratory variability remains largely unexplored for coagulation parameters. This observational study aimed to calculate intra- and inter-laboratory RCVs for PT, INR, and aPTT.

Methods: Internal quality control (IQC) data and external quality assessment (EQA) results were collected monthly throughout 2024. Intra-laboratory analytical imprecision (CV_A) was derived from IQC data, while inter-laboratory CV_A was estimated using EQA results. RCVs were calculated using an asymmetric log-normal model incorporating within-subject biological variation (CV_I) and a Z-score of 1.64.

Results: Intra-laboratory CV_A values were 5.1% (PT), 5.3% (INR), and 3.5% (aPTT), whereas inter-laboratory CV_A values were substantially higher: 21.1%, 18.1%, and 13.6%, respectively. Corresponding intra-laboratory RCV increase values were 14.2% (PT), 14.6% (INR), and 11.0% (aPTT), while inter-laboratory RCV increase values reached 63.1%, 52.5%, and 37.9%. Individuality index values were <0.6 for all tests, highlighting the limited value of reference intervals and the clinical utility of RCVs.

Conclusions: The findings demonstrate that inter-laboratory RCVs for PT, INR, and aPTT are substantially wider than intra-laboratory RCVs, reflecting the impact of between-laboratory analytical variability. These results emphasize the need for context-specific RCV thresholds, particularly when interpreting serial coagulation test results across different laboratories.

Keywords: analytical imprecision, biological variation, coagulation, external quality assessment, reference change value

Received: 17 November 2025; Accepted: 18 January 2026; Published: 27 January 2026.

INTRODUCTION

Clinical laboratory testing plays a pivotal role in diagnosing, treating, and monitoring numerous medical conditions. Among these, coagulation assays such as prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT) are essential for evaluating hemostatic function, especially in patients with suspected bleeding disorders or those receiving anticoagulant medication [1].

Coagulation tests evaluate the efficiency of clot formation by activating the coagulation cascade, and PT/INR and aPTT are among the most commonly used routine tests in clinical practice. PT assesses the function of the extrinsic and common coagulation pathways, while aPTT evaluates the intrinsic and common pathways. INR was developed to standardize PT reporting globally by correcting for differences in reagents and instruments used in various laboratories [1]. PT/INR is primarily used to monitor warfarin therapy, whereas aPTT is employed for screening hereditary or acquired factor deficiencies and for monitoring unfractionated heparin therapy. These assays are also routinely requested for preoperative patient evaluations [1,2]. Despite their widespread application, clinical laboratory tests are susceptible to biological and analytical variability. In particular, the within-subject biological variation (CV_I) of most laboratory tests is significantly smaller than the between-subject variation (CV_G); this high individuality also limits the utility of population-based reference intervals for clinical interpretation in patients [3].

Variability from both analytical and biological sources makes it difficult to interpret sequential laboratory test results, especially across different laboratories [4]. The reference change value (RCV) is a statistical tool that

* Corresponding author: Mehmet Akif Bildirici, Department of Medical Biochemistry, Faculty of Medicine, Kastamonu University, Türkiye. E-mail: bildiriciakif@gmail.com

integrates analytical imprecision (CV_A) and CV_I to determine whether a difference between two consecutive test results represents a clinically meaningful change rather than random variation [5]. While RCV is traditionally applied under the assumption of stable analytical conditions within a single laboratory, this assumption may not hold in real-world clinical practice, where patients are frequently followed across multiple healthcare institutions [6,7]. In such settings, external quality assessment (EQA) data, which are evaluations of a laboratory's performance conducted by an external agency, become valuable, as they enable the estimation of inter-laboratory CV_A and, consequently, the calculation of inter-laboratory RCVs [4].

Given the clinical importance of coagulation tests in managing bleeding disorders and anticoagulant therapy, and the increasing frequency of patient follow-up across different laboratories, it is crucial to define both intra-laboratory and inter-laboratory RCVs for PT, INR, and aPTT. This study aimed to determine intra-laboratory and inter-laboratory CV_A values and to calculate corresponding RCVs using IQC and EQA data. These RCVs, once established, could significantly improve the accuracy of serial coagulation test interpretation, thereby enhancing patient care and outcomes in our clinical practice.

METHODS

This study used de-identified quality control and EQA data without patient-level information, so local regulations did not require ethical approval.

Study design

This observational analytical study was conducted at the Medical Biochemistry Laboratory of Kastamonu Training and Research Hospital (Türkiye). Intra-laboratory CV_A for three commonly used coagulation tests (PT, INR, and aPTT) was calculated using IQC data collected from the laboratory information management system throughout 2024. In contrast, inter-laboratory CV_A was determined based on EQA results obtained during the same period.

Data sources and quality control

All measurements were performed on the Sysmex® CS-2500 System (Sysmex Corporation, Kobe, Japan), a fully automated coagulation analyser that utilizes optical clot detection methodology. PT and INR were measured using Thromborel® S reagent, and aPTT was measured using Dade® Actin® FS reagent (both Siemens Healthineers, Marburg, Germany).

The IQC materials were run at two daily levels for each test (from lyophilized Siemens Control Plasma N and Control Plasma P [Siemens Healthineers, Marburg, Germany]), covering normal and pathological control levels. IQC results were evaluated according to Westgard rules and accepted or rejected [8]. Control material lot numbers varied by month:

- For Control N: January–February: lot 507934; March–June: 507938; July–September: 507941; October–December: 556745.
- For Control P: January–February: lot 556746; March–June: 556747; July–September: 556749; October–December: 556754.

Monthly, the mean (μ) and standard deviation (σ) values were calculated for the two control levels of each test. Coefficients of variation (CVs) for these control levels were computed using the formula:

$$CV_A\,(\%) = (\sigma / \mu) \times 100$$

The monthly CV_A values from normal and pathological IQC levels were averaged to reflect routine laboratory performance across clinically relevant concentration ranges. Subsequently, the mean intra-laboratory CV_A across all 12 months of 2024 was determined for each test.

Inter-laboratory CV_A values were derived from the EQA data obtained from the KBUDEK coagulation program (Turkish Society of Clinical Biochemistry Specialists, İstanbul, Türkiye), which is conducted in accordance with ISO/IEC 17043:2010 standards. Monthly CV_A values from all participating laboratories were averaged to estimate inter-laboratory analytical variation over the same twelve-month study period.

Statistical analysis, RCV calculation

The RCVs were calculated to determine whether a difference between two consecutive test results for the same patient represents a statistically and clinically significant change. Calculations were performed separately within the same laboratory (intra-laboratory) and between different laboratories (inter-laboratory) scenarios.

For this purpose, the so-called asymmetric RCV formula, which gives different RCVs for increase and decrease (RCV_inc and RCV_dec), was applied [9]:

$$RCV\_inc/dec = 100\% \times \left(\exp\left(\pm Z \times 2^{1/2} \left(\ln\left(CV_A^2 + 1\right) + \ln\left(CV_I^2 + 1\right)\right)^{1/2} - 1\right)\right)$$

where: Z is the z-score for the desired confidence interval (CI), CV_A is the coefficient of analytical variation (intra or inter), and CV_I is the within-subject biological variation. A one-sided z-score of 1.64 was applied to calculate asymmetric RCVs at the 95% CI, as recommended for clinical interpretation of serial results [3].

Biological variation data (CV_I and CV_G) for PT, INR, and aPTT were obtained from the highly reliable EFLM biological variation database [10], which applies the Biological Variation Data Critical Appraisal Checklist (BIVAC) for data reliability.

The individuality index (II) was also calculated for each test to evaluate whether population-based reference intervals are sufficient for interpreting serial results [11]:

$$II = CV_I / CV_G$$

An II < 0.6 indicates high individuality; in this case, population-based reference intervals are less valuable, making RCVs critical for patient monitoring [12].

Microsoft Excel 2013 (Microsoft Corporation, Redmond, WA, USA) was used for all data analyses.

RESULTS

Intra-laboratory QC and imprecision analysis

A total of 2646 IQC measurements were obtained for PT, INR, and aPTT assays over the 12-month period. Outliers identified according to Westgard rules were more frequent in PT and INR assays than in aPTT, indicating greater intra-laboratory consistency for aPTT. Overall, monthly analytical imprecision was higher for PT and INR than for aPTT, with increased variability particularly at pathological control levels. When averaged across control levels, intra-laboratory CVs were lowest for aPTT and highest for INR and PT (aPTT: 3.5%, PT: 5.1%, INR: 5.3%). Notably, for all three assays, intra-laboratory CVs exceeded the desirable analytical performance goals derived from the EFLM biological variation database, with PT and INR showing relatively greater imprecision compared with aPTT. Detailed numerical results are provided in Table 1.

Inter-laboratory analytical imprecision based on EQA data

Inter-laboratory analytical imprecision for PT, INR, and aPTT was evaluated using EQA data, which reflected substantial methodological heterogeneity across participating laboratories. Most laboratories employed Sysmex coagulation analyzers with Siemens reagents, alongside several other commonly used instrument–reagent combinations. Within this heterogeneous analytical environment, PT and INR exhibited pronounced inter-laboratory variability throughout the study period. In contrast, aPTT consistently demonstrated lower CV_A values, indicating comparatively greater analytical concordance across laboratories (Table 2).

Biological variation, individuality, and reference change values

Table 3 summarizes the biological variation parameters, the individuality index (II), CV_A, and calculated reference change values (RCVs) for PT, INR, and aPTT. All three parameters showed low II values (<0.6), indicating marked individuality and supporting the use of RCV rather than population-based reference intervals for clinical interpretation [12]. Notably, inter-laboratory analytical imprecision markedly widened the RCVs; for example, the positive RCV for INR increased from 14.6% in the intra-laboratory setting to 52.5% in the inter-laboratory setting, highlighting the substantial impact of between-laboratory variability on serial result interpretation.

Table 1. Intra-laboratory quality-control measurements, outliers, analytical imprecision, and desirable CV data of coagulation parameters

		PT		INR		aPTT	
Control Level		**Normal**	**Pathological**	**Normal**	**Pathological**	**Normal**	**Pathological**
Measurement, n		513	489	513	488	340	303
Outliers*, n (%)		43 (8)	37 (8)	43 (8)	36 (7)	11 (3)	7 (2)
CV (%)	January	7.3	6.2	8.5	6.3	2.4	2.8
	February	6.9	6.0	8.3	6.1	2.4	2.6
	March	5.3	5.2	5.3	5.9	1.6	3.4
	April	5.4	5.3	5.4	6.0	1.5	3.5
	May	5.1	5.0	5.1	5.8	1.6	3.3
	June	5.4	5.3	5.4	5.9	1.7	3.4
	July	3.0	4.7	3.5	4.2	1.5	8.6
	August	3.2	4.9	3.7	4.4	1.7	8.7
	September	3.1	4.8	3.6	4.3	1.6	8.5
	October	4.6	5.1	4.6	4.9	3.3	4.8
	November	4.8	4.9	4.4	4.7	3.1	4.6
	December	4.7	5.0	4.5	4.8	3.2	4.7
$CV_{Average}$ (%)		4.9	5.2	5.2	5.3	2.1	4.9
CV_A (%)		5.1		5.3		3.5	
$CV_{Desirable}$ (%)		1.3		1.3		1.4	

The EFLM BV database was the source of desirable CV data [10]. * Outlier is the number of samples rejected according to Westgard rules [8]. Abbreviations: aPTT – activated partial thromboplastin time, CV – coefficient of variation, CV_A – analytical imprecision, INR – International Normalized Ratio, PT – prothrombin time.

Table 2. Inter-laboratory analytical imprecision values for coagulation parameters

	PT			INR			APTT		
	Number of EQA participants	Mean of results	Inter-lab CV_A * (%)	Number of EQA participants	Mean of results	Inter-lab CV_A * (%)	Number of EQA participants	Mean of results	Inter-lab CV_A * (%)
January	286	20.7	32.6	355	1.7	28.9	343	65.6	16.8
February	342	16.3	21.3	383	1.4	18.9	373	51.5	14.6
March	360	12.7	12.2	395	1.1	8.9	387	45.3	10.9
April	366	12.6	11.6	395	1.1	9.6	389	43.9	10.6
May	376	16.2	17.8	406	1.4	15.7	397	61.0	12.9
June	370	23.0	28.3	400	1.9	24.6	380	59.8	16.9
July	350	16.1	20.8	380	1.4	18.1	372	52.8	14.0
August	362	12.7	12.7	392	1.1	8.9	385	45.9	10.7
September	362	21.0	33.6	393	1.7	28.0	375	66.3	14.7
October	372	20.9	31.9	402	1.7	27.7	387	66.3	14.6
November	369	12.7	11.9	399	1.1	9.7	389	45.7	11.5
December	375	16.2	19.0	405	1.4	18.6	396	52.0	15.0

* Inter-laboratory CV_A values were calculated using EQA data obtained from laboratories employing various coagulation platforms, predominantly Sysmex CA/CS/CN series (with Siemens reagents), STA Compact (Stago), ACL TOP series (Werfen), and Rayto systems, as well as several other commonly used automated systems. Abbreviations: aPTT – activated partial thromboplastin time, CV_A – analytical imprecision, EQA – external quality assessment, INR – International Normalized Ratio, PT – prothrombin time.

Table 3. Biological variation, individuality index, analytical imprecision, and RCVs for coagulation parameters

		PT	INR	APTT
Within-subject biological variation (CV_I), % [95% CI]		2.6 [2.4 — 5.8]	2.5 [2.3 — 3.0]	2.8 [1.7 — 6.8]
Between-subject biological variation (CV_G), % [95% CI]		5.1 [2.8 — 5.7]	4.6 [2.9 — 6.8]	7.2 [4.9 — 8.9]
Individuality index (II)		0.5	0.5	0.4
Analytical imprecision (CV_A), %	Intra-laboratory	5.1	5.3	3.5
	Inter-laboratory	21.1	18.1	13.6
RCV increase, % [95% CI]	Intra-laboratory	14.2 [14.0 — 19.7]	14.6 [14.4 — 15.2]	11 [9.5 — 19.5]
	Inter-laboratory	63.1 [63.0 — 65.5]	52.5 [52.4 — 52.7]	37.9 [37.4 — 42.2]
RCV decrease, % [95% CI]	Intra-laboratory	-12.5 [-16.4 to -12.3]	-12.7 [-13.2 to -12.6]	-9.9 [-16.3 to -8.7]
	Inter-laboratory	-38.7 [-39.6 to -38.7]	-34.4 [-35.5 to -34.4]	-27.5 [-29.7 to -27.2]

Abbreviations: aPTT – activated partial thromboplastin time, CI confidence interval, INR – International Normalized Ratio, PT – Prothrombin time, RCV – reference change value.

DISCUSSION

Accurate interpretation of sequential coagulation test results is crucial for clinical decision-making, particularly in patients receiving anticoagulation therapy or undergoing surgical interventions. The use of reference change values (RCVs), which integrate both analytical and within-subject biological variation, provides an objective framework for distinguishing clinically meaningful changes from analytical noise. In this study, we evaluated both intra- and inter-laboratory RCVs for routine coagulation tests (PT, INR, and aPTT) using one-year IQC data and EQA results. The principal finding is that inter-laboratory RCVs were markedly wider than intra-laboratory RCVs for all three parameters, exceeding them by approximately three- to four-fold. This highlights the substantial contribution of between-laboratory analytical variability to the interpretation of serial coagulation test results. To our knowledge, this is the first study to report inter-laboratory RCVs for coagulation parameters, thereby offering a novel and clinically relevant perspective for interpreting results obtained across different laboratory settings.

The pronounced differences between intra- and inter-laboratory RCVs underscore the limitations of applying intra-laboratory thresholds when serial PT, INR, and aPTT measurements are obtained from different laboratories. Analytical variability arising from differences in instruments, reagents, calibration procedures, and measurement principles may falsely suggest clinically meaningful change when intra-laboratory RCVs are used across laboratory settings. Consequently, relying solely on intra-laboratory RCVs in such scenarios may increase the risk of false-positive interpretations and inappropriate clinical decisions. Therefore, when patient monitoring involves measurements performed across different laboratory settings, inter-laboratory RCVs should be considered.

Previous studies on coagulation testing have predominantly focused on intra-laboratory RCV estimation, most often using classical symmetric approaches derived from biological variation data. These investigations, conducted in controlled single-laboratory settings, generally reported relatively narrow RCVs, particularly when analytical imprecision was low and healthy populations were studied [13–18]. Similar to the approach in the present study, more recent studies applying asymmetric, log-

normal RCV models—such as those by Zengi and Uçar [19] and Kristoffersen et al. [20]—have confirmed the high individuality of coagulation tests (II < 0.6) and the limited utility of population-based reference intervals for serial monitoring. In these studies, the reported intra-laboratory RCV increases and decreases ranged approximately from +8% to-7% for PT and from +15% to-13% for aPTT, reflecting relatively narrow threshold values under single-laboratory conditions. However, all previously published reports remain confined to intra-laboratory contexts. None have addressed the impact of inter-laboratory analytical variability on RCV estimates. By incorporating inter-laboratory CV_A derived from EQA data, our study extends the existing literature and provides RCV estimates that are more representative of real-world clinical practice. A similar EQA-based approach has previously been applied to other analyte classes, such as hemoglobin A1c and thyroid function tests [7,21], but not to routine coagulation assays.

From a clinical perspective, these findings have direct implications for patient monitoring, particularly in settings such as anticoagulation management, perioperative assessment, and multicenter clinical studies. Comparing serial PT, INR, or aPTT results obtained from different laboratories using intra-laboratory RCVs alone may lead to false-positive interpretations of clinically significant change. Whenever feasible, serial measurements should be performed in the same laboratory; when this is not possible, the use of inter-laboratory RCVs—such as those proposed in the present study—may provide a more appropriate interpretative framework. For example, a patient receiving vitamin K antagonist therapy may show an apparent INR increase of 20–25% when follow-up testing is performed in a different laboratory. While such a change would exceed the intra-laboratory RCV and potentially prompt unnecessary dose adjustment, it may remain within the inter-laboratory RCV range, indicating that the observed difference is more likely attributable to analytical variability rather than a true biological change.

While our study provides valuable insights, it also has several limitations that warrant consideration. First, the estimation of inter-laboratory analytical variation was based on EQA data derived from lyophilized and pooled materials rather than native patient samples. Such materials may not fully reflect the commutability characteristics of clinical specimens, potentially leading to over- or underestimation of inter-laboratory CV_A and, consequently, the derived RCVs. Second, inter-laboratory RCVs were derived from aggregated EQA data obtained from laboratories using diverse analytical platforms and reagent systems. This methodological heterogeneity may have contributed to higher analytical variation estimates due to inter-method differences and may also limit the generalizability of our findings to laboratories employing alternative platforms or operating under different regulatory frameworks. Platform-specific inter-laboratory RCVs were not evaluated and warrant further investigation. Lastly, this study was based on quality control materials rather than patient-derived samples; thus, the applicability of the proposed RCVs to patient populations with coagulopathies or under anticoagulant therapy remains to be validated in future clinical studies.

CONCLUSIONS

The findings of this study have important implications for both clinical practice and laboratory medicine. Inter-laboratory RCVs for commonly used coagulation parameters—PT, INR, and aPTT—were found to be substantially wider than intra-laboratory RCVs, reflecting the considerable analytical variability that exists between laboratories. These results highlight the need for cautious interpretation of serial coagulation test results, particularly in clinical scenarios where patient follow-up involves different laboratories or healthcare institutions. Adoption of setting-specific RCV thresholds may improve the clinical utility and interpretability of coagulation tests in longitudinal patient monitoring and reduce the risk of misclassification due to analytical variability.

ABBREVIATIONS

aPTT – activated partial thromboplastin time

BIVAC – Biological Variation Data Critical Appraisal Checklist

CI – confidence interval

CV – coefficient of variation

CV_A – analytical imprecision

CV_G – between-subject variation

CV_I – within-subject biological variation

EFLM – European Federation of Clinical Chemistry and Laboratory Medicine

EQA – external quality assessment

II – individuality index

INR – international normalized ratio

IQC – internal quality control

PT – prothrombin time

RCV – reference change value

RCV_inc – reference change value for increase

RCV_dec – reference change value for decrease

μ – mean

σ – standard deviation

ACKNOWLEDGEMENT

None.

AUTHORS' CONTRIBUTION

MAB: conceptualization, methodology, investigation, formal analysis, visualization, writing – original draft, writing – review & editing.

SG: conceptualization, investigation, data curation, supervision, writing – review & editing.

All authors have read and approved the final version of the manuscript.

CONFLICT OF INTEREST

None to declare.

Publisher's Note: The Editorial Office stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

REFERENCES

1. Winter WE, Flax SD, Harris NS. Coagulation Testing in the Core Laboratory. Lab Med. 2017 Nov 8;48(4):295-313. DOI: 10.1093/labmed/lmx050
2. Elbaz C, Sholzberg M. An illustrated review of bleeding assessment tools and common coagulation tests. Res Pract Thromb Haemost. 2020 Jul 6;4(5):761-773. DOI: 10.1002/rth2.12339
3. Fraser CG. Reference change values: the way forward in monitoring. Ann Clin Biochem. 2009 May;46(Pt 3):264-5. DOI: 10.1258/acb.2009.009006
4. Paal M, Habler K, Vogeser M. Estimation of inter-laboratory reference change values from external quality assessment data. Biochem Med (Zagreb). 2021 Oct 15;31(3):030902. DOI: 10.11613/BM.2021.030902
5. Harris EK, Yasaka T. On the calculation of a "reference change" for comparing two consecutive measurements. Clin Chem. 1983 Jan;29(1):25-30. DOI: 10.1093/clinchem/29.1.25
6. Plebani M, Laposata M, Lippi G. A manifesto for the future of laboratory medicine professionals. Clin Chim Acta. 2019 Feb;489:49-52. DOI: 10.1016/j.cca.2018.11.021
7. Huang Y, Zhang Y, He D, Xie Y, Xu X, Zhou C, et al. Interlaboratory reference change values for thyroid function indicators across analytical systems: a comparative analysis. International Journal of Clinical Practice. 2025;6664598:9 pages. DOI: 10.1155/ijcp/6664598
8. Westgard JO, Groth T. Design and evaluation of statistical control procedures: applications of a computer "quality control simulator" program. Clin Chem. 1981 Sep;27(9):1536-45. DOI: 10.1093/clinchem/27.9.1536
9. Fokkema MR, Herrmann Z, Muskiet FA, Moecks J. Reference change values for brain natriuretic peptides revisited. Clin Chem. 2006 Aug;52(8):1602-3. DOI: 10.1373/clinchem.2006.069369
10. Aarsand AK, Fernandez-Calle P, Webster C, Coskun A, Gonzales-Lao E, Diaz-Garzon J, et al. The EFLM Biological Variation Database. Available at: https://biologicalvariation.eu/ . Accessed July 5th 2025.
11. Fraser CG. Inherent biological variation and reference values. Clin Chem Lab Med. 2004;42(7):758-64. DOI: 10.1515/CCLM.2004.128
12. Fraser CG, Harris EK. Generation and application of data on biological variation in clinical chemistry. Crit Rev Clin Lab Sci. 1989;27(5):409-37. DOI: 10.3109/10408368909106595
13. Odabasi MS, Yalcinkaya Kara ZM. Are tube fill volumes below 90% a rejection criterion for all coagulation tests? Lab Med. 2024 Jul 3;55(4):442-446. DOI: 10.1093/labmed/lmad108
14. Lima-Oliveira G, Salvagno GL, Lippi G, Danese E, Gelati M, Montagnana M, et al. Could light meal jeopardize laboratory coagulation tests? Biochem Med (Zagreb). 2014 Oct 15;24(3):343-9. DOI: 10.11613/BM.2014.036
15. Limpornpugdee O, Tanticharoenkarn S, Thepnarin T, Yeekaday M, Riyagoon P, Laiklang W, et al. Development and assessment of autoverification system for routine coagulation assays in inpatient and outpatient settings of tertiary care hospital: algorithm performance and impact on laboratory efficiency. Diagnosis (Berl). 2025 Mar 3;12(3):452-463. DOI: 10.1515/dx-2025-0004
16. Mlinaric A, Milos M, Coen Herak D, Fucek M, Rimac V, Zadro R, et al. Autovalidation and automation of the postanalytical phase of routine hematology and coagulation analyses in a university hospital laboratory. Clin Chem Lab Med. 2018 Feb 23;56(3):454-462. DOI: 10.1515/cclm-2017-0402
17. Falay M, Senes M, Korkmaz S, Turhan T, Okay M, Öztürk BA, et al. Biological variation estimates of prothrombin time, activated partial thromboplastin time, and fibrinogen in 28 healthy individuals. Int J Lab Hematol. 2018 Dec;40(6):721-725. DOI: 10.1111/ijlh.12910
18. Chen Q, Shou W, Wu W, Guo Y, Zhang Y, Huang C, et al. Biological and analytical variations of 16 parameters related to coagulation screening tests and the activity of coagulation factors. Semin Thromb Hemost. 2015 Apr;41(3):336-41. DOI: 10.1055/s-0034-1543994
19. Zengi O, Uçar KT. Within- and between-subject biological variation of hemostasis parameters in a study of 26 healthy individuals. TJ Biochem. 2023;48(5):499-506. DOI: 10.1515/tjb-2023-0155
20. Kristoffersen AH, Petersen PH, Bjørge L, Røraas T, Sandberg S. Within-subject biological variation of activated partial thromboplastin time, prothrombin time, fibrinogen, factor VIII and von Willebrand factor in pregnant women. Clin Chem Lab Med. 2018 Jul. 26;56(8):1297-1308. DOI: 10.1515/cclm-2017-1220
21. Lou Y, Shan Z, Chen Q, Kang F. Intra-Laboratory and Inter-Laboratory Variations Analysis for HbA1c Assays in China: Using Internal Quality Control and External Quality Assessment Data. J Clin Lab Anal. 2025 Apr;39(8):e70036. DOI: 10.1002/jcla.70036