Contact Factors
Pilot Study
2024

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GENERAL INFORMATION

In 2024 a global pilot study was performed on testing for the Contact Factors Prekallikrein (PK) and High Molecular Weight Kininogen (HK). This pilot study was a collaboration between the ECAT Foundation (The Netherlands), UKNEQAS for Blood Coagulation (United Kingdom) and RCPAQAP (Australia)
The pilot study was carried out on behalf of the EQATH group following a questionnaire to EQA providers about tests performed by small numbers of centres in each individual EQA programme. This study therefore investigated the feasibility of an external quality assessment survey for Contact Factors.
This report shows the results of this pilot study. Because of the scope of this pilot study only a general report is provided and no individual laboratory reports were prepared.

PARTICIPATION

Number of participants: 32 (ECAT: 13; UKNEQAS: 12; RCPAQAP: 7)
Number of responders: 19 (ECAT: 8; UKNEQAS: 8; RCPAQAP: 3)

SAMPLES

The following samples were used in this pilot study (see table below):

Sample	Description
24.CF1	Sample with decreased Prekallikrein level (50 – 60 U/dL)
24.CF2	Sample with decreased High Molecular Weight Kininogen level (25 – 35 U/dL)
24.CF3	Normal Pooled Plasma (SSC secondary standard lot 5)
24.CF4	Sample with decreased High Molecular Weight Kininogen level (60 – 70 U/dL)
24.CF5	Sample with decreased Prekallikrein level (10 – 20 U/dL)

Samples with decreased levels for either Prekallikrein or High Molecular Weight Kininogen were prepared from mixing congenital deficient plasma with normal pooled plasma. The samples were buffered (Hepes) and lyophilised before distribution to the participants.

METHODS

Participants had the ability to report results for a screening test (APTT) and/or a functional quantitative test (APTT-based calibrated assay). The table below shows the different methods used.

Monitor	**No.**
Screening test only	4
Screening test and functional quantitative test	5
Functional quantitative test only	10

Note: None of the participants performed immunological testing.

RESULTS SCREENING TESTS

The table below shows a summary of the results and the interpretation of the obtained results.

Sample	APTT (sec)			Interpretation		
	n = 9			N = 9		
	Median	Range	CV (%)	Normal	Equivocal	Prolonged
24.CF1	35.6	33.9 – 42.3	8.2	6	1	2
24.CF2	35.4	33.5 – 44.0	10.5	6	0	3
24.CF3	32.6	31.9 – 36.5	5.2	8	1	0
24.CF4	31.8	29.8 – 37.0	7.8	7	1	1
24.CF5	44.2	39.7 – 65.0	19.1	0	1	8

Because of the limited number of responders for the screening tests, the quantitative results were not evaluated at the level of APTT reagent.
For the interpretation of the obtained APTT clotting times we looked for each of the included samples at the relationship between the provided interpretation (normal, equivocal and prolonged) and the APTT reagent used. See tables below.

	Sample 24.CF1			**Sample 24.CF2**		
	Decreased Prekallikrein level (50 – 60 U/dL)			decreased High Molecular Weight Kininogen level (25 – 35 U/dL)		
APTT reagent	Normal	Equivocal	Prolonged	Normal	Equivocal	Prolonged
Siemens Pathromtin SL	0	0	2	0	0	2
Stago PTT automate / STA APTT	1	0	0	1	0	0
Triniclot APTT S	1	0	0	1	0	0
Werfen HemosIL SynthASil	4	1	0	4	0	1

	Sample 24.CF3		
	Normal Pooled Plasma		
APTT reagent	Normal	Equivocal	Prolonged
Siemens Pathromtin SL	2	0	0
Stago PTT automate / STA APTT	1	0	0
Triniclot APTT S	1	0	0
Werfen HemosIL SynthASil	4	1	0

	Sample 24.CF4			**Sample 24.CF5**		
	Decreased High Molecular Weight Kininogen level (60 – 70 U/dL)			Decreased Prekallikrein level (10 – 20 U/dL)		
APTT reagent	Normal	Equivocal	Prolonged	Normal	Equivocal	Prolonged
Siemens Pathromtin SL	1	0	1	0	0	2
Stago PTT automate / STA APTT	1	0	0	0	0	1
Triniclot APTT S	1	0	0	0	0	1
Werfen HemosIL SynthASil	4	1	0	0	1	4

Comment:

Out of the 9 participants who performed a screening test, 6 participants performed a standard APTT test, while 3 participants indicated to have used a modified APTT test. The modification consists of a prolongation of the incubation time to 10 minutes. No differences in the reported clotting times between the two groups has been observed.
For most of the samples with a decreased Prekallikrein or High Molecular Weight Kininogen a heterogeneous pattern in the classification is observed. Only for the sample with the very low Prekallikrein level (sample 24.CF5) almost all participants found a prolonged APTT result.
This indicates that an APTT screening test can only be used to detect samples with a very low of a Contact Factor.

RESULTS QUANTITATIVE FUNCTIONAL TESTING

All participants used a calibrated APTT-based assay. In total 8 different APTT reagents were used, which implies a low number of participants per reagent (max. 3). For this reason the results were only evaluated as total group.

The table below shows a summary of the results.

Sample	Prekallikrein (U/dL)				High Molecular Weight Kininogen (U/dL)			
	N	**Median**	Range	CV (%)	N	**Median**	Range	CV (%)
24.CF1	13	**50.5 ****	46.0 – 85.0	22.5	14	**82.9**	48.0 – 147.0	32.4
24.CF2	14	**50.9**	18.0 – 67.0	31.4	13	**17.0 *****	10.0 – 54.0	65.1
24.CF3	14	**98.2**	62.9 – 132.0	20.0	14	**97.5**	59.0 – 158.0	23.3
24.CF4	14	**69.4**	39.0 – 99.8	21.8	14	**57.1**	36.0 – 78.0	22.2
24.CF5	11	**19.0 * / ****	13.0 – 91.0	84.2	13	**76.0**	17.3 – 132.0	44.0

* Two results were reported as below the lower limit of quantification (< 1 and < 25 U/dL).
** One result was excluded as an outlier from the statistical analysis.
*** One result was reported as below the lower limit of quantification (< 25 U/dL).

Comment:

A considerable between-laboratory variation has been observed for both Prekallikrein and High Molecular Weight Kininogen testing.

The table below shows the classification for both Prekallikrein and High Molecular Weight Kininogen interpretations. Because no evaluation on the level of reagent has been performed (see above), it is unknown whether there are differences in test results between reagents.

Sample	**Prekallikrein**			**High Molecular Weight Kininogen**		
	Normal	Equivocal	Decreased	Normal	Equivocal	Decreased
24.CF1	4	3	7	11	1	2
24.CF2	2	4	8	0	0	14
24.CF3	14	0	0	14	0	0
24.CF4	11	0	3	5	2	7
24.CF5	3	0	11	9	1	4

Comment:

For some of the samples a heterogeneous pattern in the classification has been observed. This is probably caused by the considerable variation in results between laboratories. This could result in the

fact that some laboratories consider a sample as normal while other laboratories consider the sample having a decreased level for Prekallikrein and/or High Molecular Weight Kininogen.
The normal sample (24.CF3) has been classified as normal for both parameters by all participants.

GENERAL REMARKS

- This pilot study has demonstrated that it is feasible to organise collaborative surveys for Contact Factors.
- The results should be interpreted with caution because of the limited number of results.
- Considerable between-laboratory variation has been observed for both Prekallikrein and High Molecular Weight Kininogen, which may result in a heterogeneous pattern in classification.

In 2026 we plan to start joint regular surveys across the EQA programmes for Prekallikrein and High Molecular Weight Kininogen (2 surveys per year).