Discrepant interpretation of HIT screening results on the same sample – data from a National External Quality Assessment Scheme for Blood Coagulation (UK NEQAS BC) exercise.

UK NEQAS Blood Coagulation

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INTRODUCTION

Heparin Induced Thrombocytopenia (HIT) is an immune complication of treatment with heparin, in some cases resulting in life-threatening thrombosis. An accurate diagnosis is required to ensure appropriate clinical decisions are made. UK NEQAS (Blood Coagulation) carried out an external quality assessment (EQA) exercise in 2018 in which 79% of centres reported a negative HIT screen, and 19% reported a positive screen, for a sample from a donor previously identified as positive by an ELISA method.

AIM

We describe here a further EQA exercise in which laboratories employing different HIT assays were asked to test and interpret results for a sample from a different donor diagnosed with HIT based on clinical and laboratory findings.

METHOD

Plasma was obtained with informed consent from a patient identified as having HIT antibodies by the Werfen Acustar assay (S19:09). Plasma was buffered and lyophilised in aliquots and sent to 71 participants in the UK NEQAS for Blood Coagulation (UK NEQAS BC) HIT programme. A further sample, expected to give a negative HIT screen was also sent (S19:08). Participants were asked to perform their usual tests for investigation of possible HIT. Median, coefficient of variation (CV) and range of results were determined for each method and reagent group. Participants were also asked to make an interpretation (positive, equivocal or negative) for the two samples in the exercise.

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RESULTS

Table 1 shows the breakdown of interpretations from 66 participants who returned results for the exercise, , including those provided by centres using more than one assay method – in total, 72 sets of test results were returned.

Sample S19:08, expected to give a negative screen, was described as positive by 3 out of 71 centres.

Sample S19:09 was a sample previously identified as having raised HIT antibody levels by the Werfen Accustar assay. 25 out of 72 centres (35%) reported a negative HIT screen. Tables 2 and 3 show quantitative and qualititative assay results respectively for sample S19:09.

8 centres using the Biorad Diamed (ID-PaGIA heparin/PF4 antibody) test, 11 centres using the Stago STic Expert kit, 5 using the Werfen/IL HIT-ab (PFH-4) assay, and 1 using the AESKULISA HIT II ELISA reported a negative screen on sample S19:09 .

There was inconsistency between centres reporting their assays as detecting IgG only or IgG, IgA and IgM antibodies, when using the same assay and kit method.

1 centre reported a positive functional HIPA screen on sample S19:09, and two centres reported heparin neutralisation or inhibition of their assay on this sample.

Table 1. Interpretations

Sample	N	Participant Interpretations		
		Positive n (%)	Equivocal/ borderline n (%)	Negative n (%)
S19:08	71	3 (4)	3 (4)	65 (92)*
S19:09	72	44 (62)**	2 (3)	25 (35)*

Table 2. Quantitative assay results, sample S19:09

Method	n	Median	Range	Positive	Equivocal	Negative
ELISA methods: AESKULISA IgG	1	<12u/ml	-	0	0	1
Lifecodes/Immucor/GTI IgG	12	0.721 OD	0.421-1.887	12	0	0
Stago Asserochrom HPiA IgG	2	0.355 OD	0.234 -0.475	2	0	0
Stago Asserochrom IgG/A/M	2	23.95%	23.9-24.0	2	0	0
All ELISA methods	17	-	-	16	0	1
Werfen HIT-ab PF4-H assay	12	1.0 OD	0.4-1.3	5	2	5
Werfen Acustar assay	13	4.09 OD	3.03-4.82	13	0	0

Table 3. Qualitative assay results, sample S19:09

Method	n	Positive	Equivocal	Negative
BioRad/Diamed ID-PGIA Heparin/PF4 antibody test	14	6	0	8
Stago Stic Expert Assay	15	4	0	11

CONCLUSIONS

This exercise demonstrated further variability in interpretations for a sample with HIT antibodies. Discrepant interpretations were seen for centres using the same methodology, as observed in the previous exercise. Reasons for the discrepant results observed will be further investigated. There is a need for laboratories and clinicians to understand the clinical implications of reported HIT assay results.

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