Investigation of a prolonged APTT : Data from a UK NEQAS (Blood Coagulation) exercise

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Introduction:

The APTT is a useful screening test in the investigation of haemostatic abnormalities. A prolonged APTT may be indicative of specific or multiple factor deficiencies, the presence of a factor-specific inhibitor, or a non-specific inhibitor or lupus anticoagulant. In the laboratory investigation of an abnormal APTT there are many algorithms, which may in some examples be guided by the clinical history of the patient.
Proficiency testing programmes commonly assess one specific analyte in an EQA challenge. Such exercises rarely challenge a laboratory to determine their own course of investigation. We describe here a study in which participants were asked to investigate a prolonged APTT and suggest a clinical diagnosis based on their investigation.

Study:

A sample from a patient with severe haemophilia A was distributed with no clinical details and participants were requested to investigate the cause of the abnormal APTT. Results were collated and median values were determined for each parameter measured, but no performance analysis was applied to the data reported. A total of 103 centres provided an interpretation of their results.

Interpretations

Interpretation	n	%
Haemophilia A/ FVIII deficiency*	94	91
FVIII deficiency + Lupus a/c	5	5
FVIII & FXII deficiency	2	2
FVIII & FIX deficiency	1	1
FVIII inhibitor	1	1

* Of which 1 centre reported mild deficiency

Tests employed to investigate a prolonged APTT with no clinical details

Test	n	Test	n
APTT	94	FVIII:C assay	110
2nd APTT reagent	13	Chromogenic FVIII assay	5
PT / INR	37	FIX:C assay	92
Thrombin Time	47	FXI:C assay	83
Protamine correction	4	FXII:C assay	76
Reptilase Time	5	VWF:Ag	58
Fibrinogen	27	VWF:Rco	43
APTT 1:1 immediate mix	58	VWF:CB	6
APTT 1:4/4:1 mix	7	FII,FV,FVII,FX, FVIIIag,HMWK,PK	16
APTT incubated mix/inhibitor screen	47	Heparin Assay	3
Heparin Assay	3	FVIII inhibitor assay	60
Lupus Anticoagulant screen	61	VWF inhibitor screen/assay	3

Over 99 combinations of different tests were employed by laboratories in this exercise; the number of tests performed ranged from 3 to 13.

Screening test and factor assay results

Screening test	n	Median (ratio)	Range (ratio)
APTT	96	3.96	1.93-4.65
Thrombin time	47	1.06	0.76-1.88
Factor Assay	**n**	**Median u/dL**	**Range u/dL**
VIII:C	67	0.9	0.0-9.0
IX:C	90	75.5	29.0-94.0
XI:C	80	75.0	56.0-93.2
XII:C	75	61.0	44.0-81.0
VWF:Ag	57	80.8	59.0-121.1
VWF:RCo	41	79.1	54.9-118.0
VWF:CB	2	78.4	72.7-84.0
X:C	5	81.0	70.0-126.0

FII:C, FV:C, FVII:C, Prekallikrein and HMWK assays were performed by fewer than 4 centres each

Discussion:

All participants in this exercise correctly identified a reduction in FVIII:C activity in this sample, and over 90% were in agreement that this was the only defect present. Widely varying approaches were taken to the investigation of an abnormal APTT, and in some cases “blanket testing” of a large number of parameters was evident, suggesting an unscientific and uneconomical approach. However, the absence of clinical information may have contributed to this. One important aspect of this type of investigation, only mentioned by a few participants, is the need for repeat sampling and testing to confirm any diagnosis.

Distribution of intrinsic pathway factor assay results:

Figs 1 to 4 show the spread of results reported by centres testing the same sample.

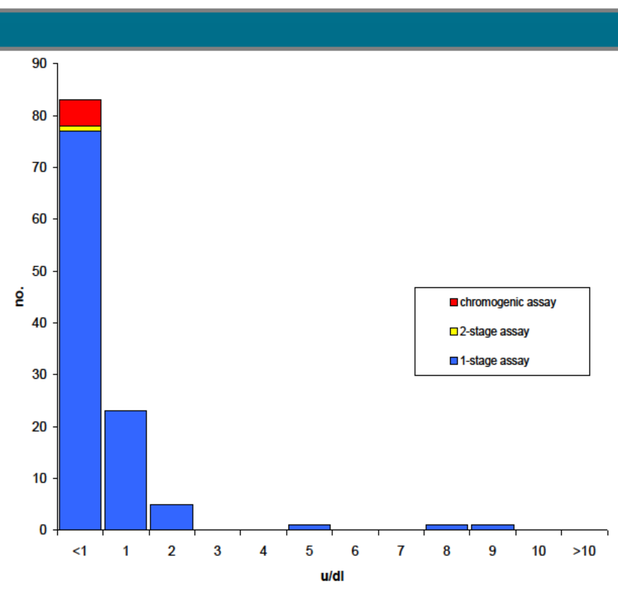

Fig 1. FVIII:C assay

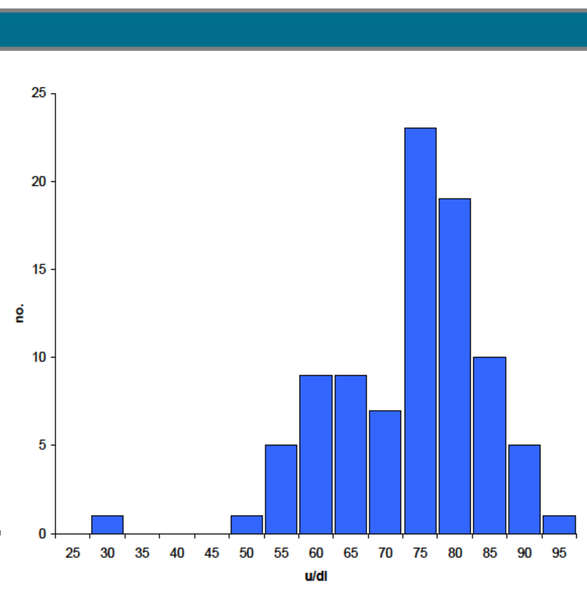

Fig 2. FIX:C assay

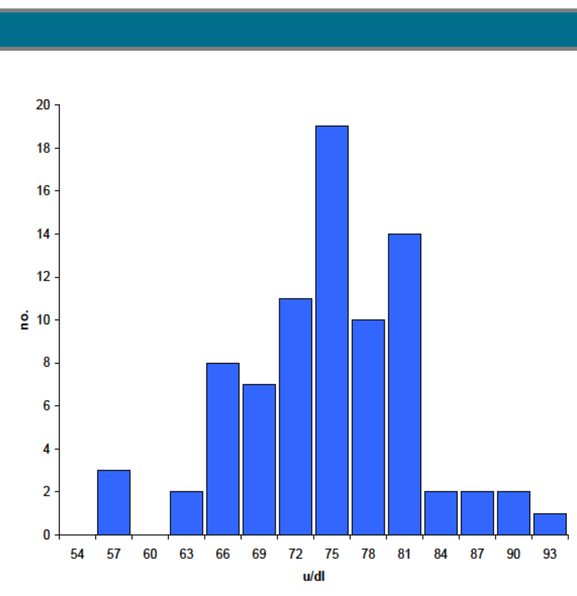

Fig 3. FXI:C assay

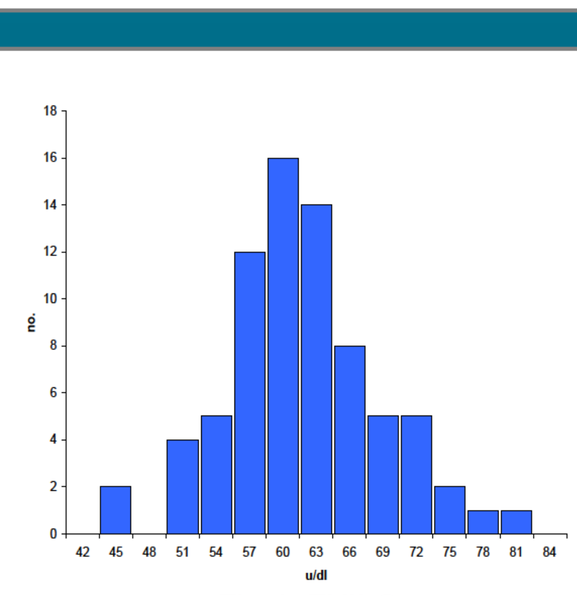

Fig 4. FXII:C assay

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