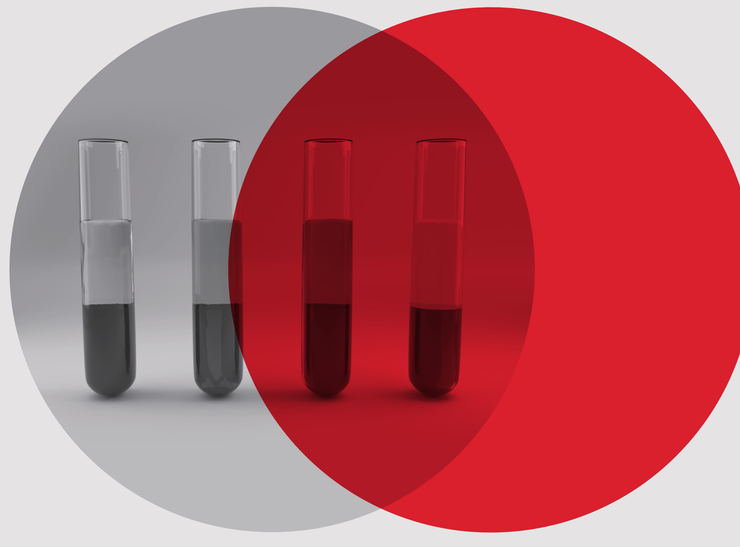
How comparable are serum indices measurements between laboratories?



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Introduction

Haemolysis (H), Icterus (I) and Lipaemia (L) are known interferants (collectively HIL) for many biochemistry assays, where excessive concentrations of any, or in combination, can lead to spurious results.

As a routine quality measure, most laboratories now quantify serum indices on patient samples and selectively withhold reporting results when interferences are identified.

Data on how different measurement systems compare was somewhat limited by the lack of an external quality assurance (EQA) program for these parameters. The RCPAQAP, in collaboration with ASE, developed a serum indices EQA program to address this. It was launched as an accredited program in July 2019 following a pilot/ feasibility study.

Methods

Serum was pooled, supplemented and lyophilised to create six linearly related samples (levels) which were distributed to the 70 laboratories who enrolled in the 2019 program. Results were returned for three measurands (Haemolysis, Icterus and Lipaemia), each with three options for reporting (Quantitative, Numerical Index and/or Qualitative). The RCPAQAP performed data analysis on returned results from 97 instruments representing five major manufacturer groups using in-house software.

Results

Out of 97 returned results, 60 reported quantitative data, 7 returned a numerical index value and 30 provided a qualitative (+ symbols) assessment. All instruments appear to be following the manufacturers' recommended (spectrophotometric) methods. From the quantitative data, Haemolysis performed consistently well with the overall (All Results) coefficient of variation (CV) averaging 6.1%, whereas Icterus and Lipaemia CV's averaged 22.7% & 14.1% respectively **(Figure 1)**.

A consistent bimodal distribution was noted for Icterus **(Figure 2)**, with each population representing specific measurement systems, suggestive of between-method bias. The medians of each population were shown to be significantly different when a t-test was performed; t(55) =14.9 & 15.9, p< 0.01.

Overall unit selection proved to be a significant source of error and confusion among labs. Up to 50% of all participants reported Lipaemia with incorrect units for the first survey, which were subsequently corrected over the course of the program **(Table 1)**.

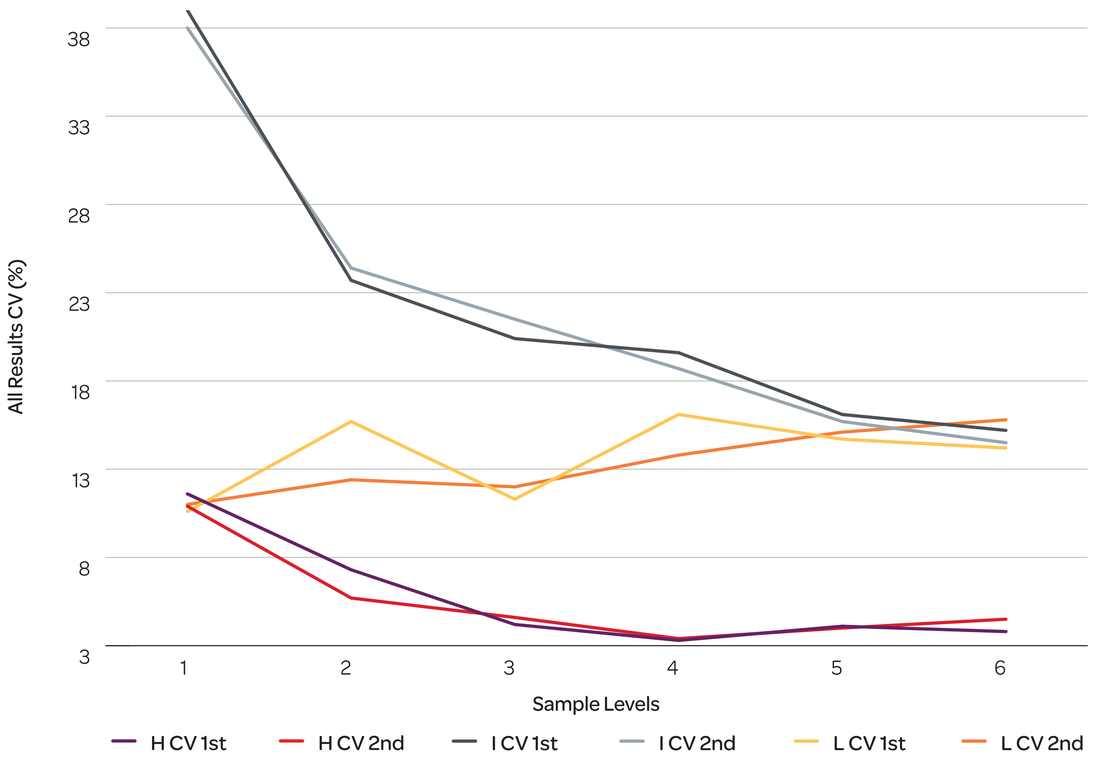

Figure 1. Line graph representing the All Results CV across the 6 sample levels analysed in the program. Each sample was run twice over the course of the program. (Note: To replicate more common patient scenarios and aid in recovery post lyophilisation, Lipaemia levels are designed to be high in Level 1 and low in Level 6, Haemolysis and Icterus are low in Level 1 and highest in Level 6)

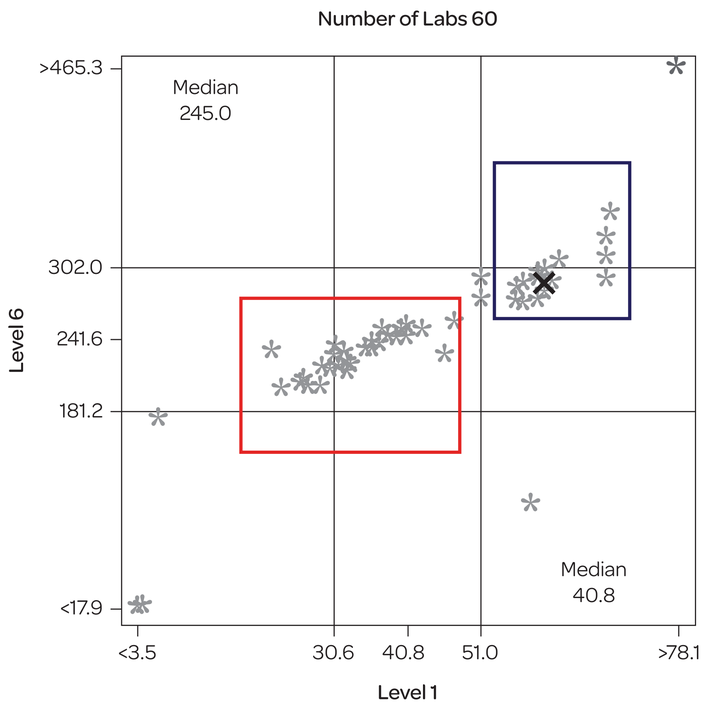

Figure 2. Icterus bimodal population. QAP Level 1 vs Level 6 Youden plot demonstrating the bi-modal population of Icterus. Red box denotes the consistent low population (M= 226.5, SD= 15.2 & M=33.8, SD= 6.1) and Blue box shows the high population (M= 292.3, SD= 17.5 & M=60.3, SD= 6.3)

Table 1. Summary of Units used in the last run of the program (Primary = Units used for statistical analysis; Secondary = Other options which were then converted to Primary)

Analyser	Haemolysis		Icterus		Lipaemia	
	Primary unit g/L	Secondary units (mg/dL, mg/L, umol/L)	Primary unit µmol/L	Secondary unit (mg/dL)	Primary unit mmol/L	Secondary units (g/L & mg/dL)
Abbott Architect	12	6	18	0	15	3
Abbott Alinity C	6	19	21	0	3	19
Beckman Coulter Unicel	2	0	1	0	0	0
Siemens Atellica/ Advia	19	2	1	0	1	0
Roche Integra	1	1	1	0	0	0
Roche Cobas c501/c502	0	14	11	5	1	15
Roche Cobas c701/c703	0	12	6	7	1	12
O.C.D Vitros 4600/5600	2	1	0	1	1	1

Discussion

The spread of results returned is of concern, particularly if labs use the manufacturers' cut points without having done their own assessments on the impact of Haemolysis, Icterus and Lipaemia on their assay results. The bimodal distribution observed for Icterus was an unexpected finding given the methodology (spectrophotometric) should be similar across most platforms.

Independent protocols developed by manufacturers is likely contributing to the variability of results and report styles; e.g. quantitative vs numerical index vs qualitative. It is possible this may have arisen due to proprietary ownership/patents, or instrument related limitations.

The variability in reporting units for Lipaemia is also an area for improvement. The 2019 results for this program demonstrated that units played a significant role in the lack of harmonisation of indices. This lack of harmonisation carries through to inconsistent reporting styles that may also be impacting how laboratories choose to accept or reject patient results.

Conclusion

This new program demonstrates the need for an ongoing peer comparison to monitor performance of serum indices that are used on a daily basis to make decisions on accepting or rejecting patient results. Further studies on the levels of interference that laboratories use to flag reviews are planned.

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