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Severe acquired chylomicronaemia syndrome – a challenge to the routine laboratory

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Lipaemia is a common interfering (spectral or chemical) factor that can complicate biochemical analysis.[1,2] In patients with chylomicronaemia syndrome, gross elevations of plasma triglyceride-rich lipoproteins, particularly chylomicrons and/or very-low-density lipoproteins are found.[3,4] This causes sample turbidity that can interfere with some analytical methodologies involving spectrophotometric measurements. Hence, special attention must be paid to the removal of such interfering lipaemia prior to analysis.

Recently, a case of poorly controlled diabetes complicated by severe hypertriglyceridaemia (maximum plasma triglyceride [TG] concentration: 130 mmol/L) was encountered. Samples received for lipid profile and liver/renal function tests (L/RFT) were grossly milky.

The aim of this short study is to discover which tests in the routine L/RFT profile are affected, what mechanism is involved and what appropriate measures should be used in the clinical laboratory for adequate lipaemia clearance at various hypertriglyceridaemia levels.

Pooled plasma with a clear appearance and normal L/RFT was used (neat TG: 1.2 mmol/L). Intralipid (20% emulsion; KabiVitrum, Stockholm, Sweden) was spiked into the pooled plasma at four TG levels (23, 49, 58 and 95 mmol/L). The samples were then analysed by both wet and dry chemistry analysers (Hitachi 747-100 [Roche/Boehringher Mannheim, Germany]) and Ortho Vitros-950 (Johnson & Johnson, Ortho Clinical Diagnostics, USA) for alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), glucose, lactate dehydrogenase (LDH),) phosphate and urea. Only tests quantitated at an ultraviolet wavelength were selected.

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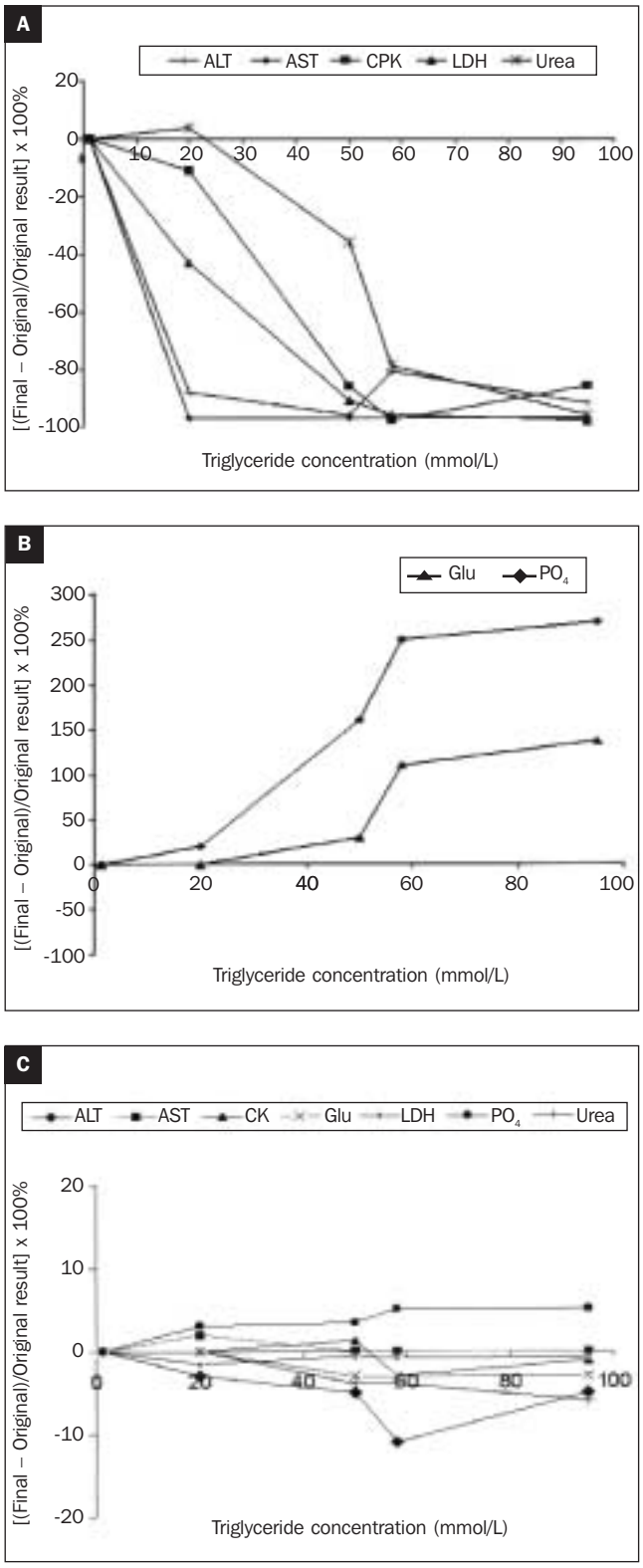

Fig. 1. Triglyceride interferographs. A and B) Hitachi 747-100; C) Vitros-950.

Subsequently, a further set of TG concentrations (26, 48, 78 and 126 mmol/L) was prepared and each of these was subjected to three lipaemia clearing procedures (high-speed

Table 1. Liver/renal function profile of patient's plasma sample.

Test	LIP	HS	UC	Vitros	Units	Reference range
Triglyceride	95	46	14	95	mmol/L	<2.0
Sodium	125	132	135	136	mmol/L	136 – 148
Potassium	4.7	4.8	5.0	4.9	mmol/L	3.6 – 5.6
Chloride	93	100	102	100	mmol/L	100 – 110
Urea	6.3	11.1	10.9	10.8	mmol/L	2.5 – 6.4
Creatinine	<10	97	101	99	mmol/L	60 – 106
Calcium	2.57	2.61	2.59	2.57	mmol/L	2.11 – 2.55
Total protein	10	84	87	85	g/L	70 – 86
Albumin	41	45	46	43	g/L	42 – 54
Alkaline phosphatase	46	56	54	55	U/L	34 – 104
Alanine aminotransferase	<1	25	27	28	U/L	5 – 31
Aspartate aminotransferase	<1	33	30	35	U/L	12 – 28

LIP: Original lipaemic sample analysed using an Hitachi 747-100.
HS: Pretreated by high-speed centrifugation and analysed using an Hitachi 747-100.
UC: Pretreated by TL-100 ultracentrifuge and analysed using an Hitachi 747-100.
Vitros: Sample analysed using a Vitros 950.

centrifugation [MSE-Micro Centaur, 10,000 x*g*], Airfuge [Beckman A-95, 134,000 x*g*] and TL-100 Ultracentrifuge [Beckman TL-100.2 Rotor, 356,000 x*g*]) for 10 min. The infranatants were collected and analysed for residual TG concentrations using an Hitachi 912.

Samples from the poorly controlled diabetic patient were subjected to two out of the three clearing procedures (MSE-Micro Centaur and Beckman TL-100), as detailed above.

All but two colorimetric tests performed on the Hitachi 747-100 at 340 nm showed significant negative interferences with the levels of hypertriglyceridaemia chosen. In contrast, glucose and phosphate showed a positive bias (Fig. 1). However, tests performed on the Vitros analyser showed no significant discrepancies.

Of the three lipaemia-clearing procedures used, ultracentrifugation proved to be the most efficient method of reducing TG concentration. Triglyceride level in the four samples spiked to 26 mmol/L, 48 mmol/L, 78 mmol/L and 126 mmol/L was reduced to 7 mmol/L, 13 mmol/L, 20 mmol/L and 28 mmol/L, respectively.

Lipaemia is a well-known spectral interference at 340 nm;[5] thus, spectrophotometric analyses for ALT, AST, CK, glucose, LDH, phosphate and urea are affected. The decrease in NADH is directly proportional to the analyte concentration in all assays except glucose and phosphate, hence lipaemic spectral interference causes the detector to indicate a high absorbance and give a false low result. With glucose and phosphate estimations, increased absorbance at 340 nm is directly proportional to the analyte concentration and lipaemia causes false high results.

Not surprisingly, irrespective of hypertriglyceridaemia level, the Vitros analyser showed no significant interference. In dry chemistry technology, large particles, particularly chylomicrons, are filtered out by the sample slide before reaching the reagent layer. However, problems associated with lipaemic samples may occur due to the partitioning and volume exclusion effect. Similar observations were found in the patient's sample (Table 1).

Although ultracentrifugation is the best method for clearing lipaemia, it is tedious and is not available in most laboratories. Nonetheless, commonly used lipaemia-clearing polymers, such as LipoClear (StatSpin, MA, USA), are less efficient in removing chylomicrons from milky samples, especially when TG exceeds 28 mmol/L.

Therefore, from comparisons of the three lipaemia-clearing procedures used here, the following TG concentration cut-points can be recommended:

- High-speed centrifugation (e.g., MSE-Micro Centaur; 10,000 x*g*) for TG <50 mmol/L.
- Airfuge (e.g., Beckman A-95 Rotor; 134,000 x*g*) for TG between 50–100 mmol/L.
- Ultracentrifugation (e.g., Beckman TL-100.2 Rotor; 356,000 x*g*) for TG >100 mmol/L.

In summary, grossly lipaemic samples should be processed with special preanalytical precautions, including adequate removal of chylomicrons prior to assay, especially for wet-chemistry colorimetric analysis. However, if available, use of a multilayered film analyser offers a suitable alternative. □

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