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# Systematical assessment of serum indices does not impair efficiency of clinical chemistry testing: A multicenter study

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ABSTRACT

**Objectives:** Despite manufacturers' claim that systematical assessment of serum indices does not impact on testing efficiency, there is widespread perception that this practice may increase the turnaround time (TAT). A multicenter investigation was planned to verify TAT and performance of serum indices on five different clinical chemistry analyzers.

**Design and methods:** Twenty study samples prepared from pooled sera of outpatients, emergency department, intensive care unit and dialyzed patients were divided in aliquots and shipped to 5 different laboratories. According to local instrumentation (Beckman Coulter AU5800, Roche Cobas 6000, Siemens Dimension Vista 1500, Abbott Architect c 16000 and Ortho Vitros 5.1/FS) and reagents, 13 clinical chemistry parameters were assayed on all study samples, with or without contextual assessment of serum indices.

**Results:** The TAT with assessment of serum indices modestly or even negligibly increased, and varied from −0.2 to +5.0% (i.e., from −3 to +85 s). When using the lowest thresholds for sample acceptability, the agreement of hemolysis index (HI) among different instruments was comprised between 0.62 and 1.00 (all $p < 0.01$), but was higher than 0.80 in only 4/10 cases. The agreement of icteric and lipaemic indices could not be estimated due to the low number of samples exceeding acceptability criteria.

**Conclusions:** The results of this study confirm that systematical measurement of serum indices does not impair instrument efficiency. The comparison of HI also suggests that major harmonization may be advisable for this measure among different manufacturers and instrumentations.



## Introduction

The various preanalytical activities represent the most vulnerable steps throughout the total testing process. Broad experience has now been gathered to support the evidence that mishandled procedures during collection, handing and storage of blood may impair the quality of diagnostic samples, thus potentially jeopardizing clinical decision making and patient safety [1]. Along with misidentification, collection of inappropriate sample volume or blood drawing into inappropriate containers, the most frequent cause of unsuitable specimens received in clinical laboratories for routine and stat testing is represented by the presence of interference, most frequently cell-free hemoglobin (i.e., spurious hemolysis), hyperbilirubinemia and hypertriglyceridemia [2]. Each of these interfering substances is a potential source of biological and analytical biases, which ultimately compromises the reliability of testing and makes the systematical identification of unsuitable specimens virtually unavoidable for preventing that unreliable or misleading test results are released to the clinicians [3].

Since there is now convincing evidence that visual inspection of samples is an unreliable approach for identifying poor quality specimens, the use of the so-called "serum indices" is growingly seen as an appealing and suitable perspective in most clinical laboratories [4], and their systematical assessment has recently been suggested by the Clinical and Laboratory Standards Institute (CLSI) [5], as well as by some national scientific societies [6]. Basically, these features entail multi-wavelength scanning of samples as part of a preanalytical check, which thus allows semi-quantitative or even quantitative measurement of potentially interfering substances such as cell-free hemoglobin (i.e., "hemolysis index", HI), bilirubin (i.e., "icteric index", II) and turbidity principally due to hyperlipidemia (i.e., "lipaemic index", LI) [7]. The routine assessment of serum indices seems almost unavoidable when the preanalytical modules are connected with no solution of continuity to the analytical platforms [8], since this organizational framework virtually hides serum or plasma from visual scrutiny

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**Table 1**
Centers and instrumentations.

| Laboratory | Company | Instrumentation | Serum index assessment |
|---|---|---|---|
| Academic Hospital of Parma, Parma, Italy | Beckman Coulter, Brea CA, USA | AU5800 (double chemistry modules configuration) | Bichromatic readings at 410/480 + 600/800 (HI), 480/570 + 600/800 (II) and 660/800 (LI) nm |
| University Hospital of Verona, Verona, Italy | Roche Diagnostics, Basel, Switzerland | Cobas 6000 (double c501 chemistry modules configuration) | Bichromatic readings at 570/600 + 660/700 (HI), 480/505 + 570/600 (II) and 660/700 (LI) nm |
| General Hospital of Vicenza, Vicenza, Italy | Siemens Healthcare Diagnostics, Tarrytown, NY, USA | Dimension Vista 1500 | Bichromatic readings at 405/700 (HI), 452/700 (II) and scan at 700 (LI) nm |
| General Hospital of Bassano del Grappa, Bassano del Grappa (VI), Italy | Abbott Diagnostics, Lake Forest, IL, USA | Architect c 16000 | Bichromatic readings at 500/524, 572/604, 628/660 and 524/804 nm and mathematical transformation |
| University Hospital of Modena, Modena, Italy | Ortho-Clinical Diagnostics, Rochester, NY, USA | Vitros 5.1/FS | Bichromatic readings at 522/750 (HI), 502/776 (II) and scan at 700 (LI) nm |

HI, hemolysis index; II, icteric index; LI, lipaemic index.

[9]. However, due to the widespread perception that systematical measurement of serum indices on all samples may substantially decrease throughput and contextually increase turnaround time (TAT) especially for stat testing, the implementation of this practice remains a matter of debate in some laboratories, especially those where preanalytical sample management is physically separated from analytical platforms [10]. Since definitive information on the impact of serum index assessment on instrument and laboratory efficiency is lacking in the current scientific literature [11], nor precise manufacturers' data are available for all the different clinical chemistry analyzers, we planned a multicenter study with two leading goals, i.e., for establishing the impact of systematical assessment of serum indices on instrument throughput under routine laboratory conditions and using five clinical chemistry platforms from five different manufacturers, as well as for comparing values of serum indices obtained on 20 serum pools analyzed with five different analytical platforms.

## Materials and methods

### *Study design*

This multicenter study was planned to include five of the most frequently used clinical chemistry analyzers worldwide (Table 1). The preparation of study samples was centralized in the clinical chemistry and hematology laboratory of the Academic Hospital of Parma (Italy). The 20 study samples included 5 serum pools from outpatients (OUT, numbered from 1 to 5), 5 serum pools from emergency unit (ED, numbered from 1 to 5) patients, 5 serum pools from intensive care unit (ICU, numbered from 1 to 5) patients, and 5 serum pools from dialysis unit (DU, numbered from 1 to 5) patients. Each of the five serum pools for each selected group was finally composed of six different and unique patient samples, as follows:

- OUT pools: A total of 30 fresh serum OUT samples were randomly selected after routine laboratory testing had been completed. 2 mL of 6 different samples was mixed in each pool (from OUT-1 to OUT-5).
- DU pools: A total of 30 fresh serum DU samples were randomly selected after routine laboratory testing had been completed. 2 mL of 6 different samples was mixed in each pool (from DU-1 to DU-5).
- ED pools: A total of 30 fresh serum ED samples were randomly selected after routine laboratory testing had been completed. 2 mL of 6 different samples was mixed in each pool (from ED-1 to ED-5). One, two and three visually hemolyzed sera were included in pools ED-1, ED-2 and ED-3, respectively.
- ICU pools: A total of 30 fresh serum ED samples were randomly selected after routine laboratory testing had been completed. 2 mL of 6 different samples was mixed in each pool (from ICU-1 to ICU-5). One and two visually hemolyzed sera were included in pools ICU-1 and ICU-2, respectively.

Each serum pool was produced from fresh blood (within 4 h after drawing) collected in primary blood tubes containing no additives (Becton Dickinson, Franklin Lakes, NJ, USA), and centrifuged at 1300 $\times g$ for 10 min at room temperature. After preparation, the pools were gently mixed, divided in 5 aliquots of 2 mL each (one for each center participating to the study), and stored at −70 °C until shipment. The samples were then transported to the participating centers by using certified transport boxes, under controlled conditions of temperature and humidity, as described elsewhere [12]. The mean transportation time was 92 ± 7 min. Upon arrival to the different laboratories, the samples were kept stored until all centers had received the shipment, thus allowing all participants to start testing almost simultaneously. Before analysis, the samples were left to thaw at room temperature and mixed manually by 6-time inversion. According to local instrumentation and reagents, the following analyses were assessed on each of the 20 serum pools: potassium,

**Table 2**
Range of values of the 13 clinical chemistry parameters obtained in the center where sample collection was centralized.

| Analyte | Median | Range |
|---|---|---|
| Potassium (mmol/L) | 4.4 | 3.9–5.6 |
| Chloride (mmol/L) | 103 | 98–107 |
| Sodium (mmol/L) | 139 | 135–142 |
| Calcium (mmol/L) | 2.3 | 2.1–2.5 |
| Creatinine (μmol/L) | 88 | 53–946 |
| Urea (mmol/L) | 55 | 30–177 |
| Glucose (mmol/L) | 6.2 | 4.5–8.9 |
| Total bilirubin (μmol/L) | 9.0 | 6.3–23.1 |
| Albumin (g/L) | 3.8 | 2.7–4.4 |
| ALT (U/L) | 26 | 13–177 |
| LDH (U/L) | 394 | 307–897 |
| CK (U/L) | 87 | 43–315 |
| Lipase (U/L) | 35 | 24–93 |

**Table 3**
Evaluation of turnaround time (TAT) with or without systematic assessment of serum indices.

| Instrumentation | TAT | | |
|---|---|---|---|
| | Without serum indices | With serum indices | Difference |
| Beckman Coulter AU5800 | 19 min 30 s | 19 min 46 s | +16 s (+1.4%) |
| Roche Cobas 6000 | 28 min 26 s | 29 min 51 s | +85 s (+5.0%) |
| Siemens Dimension Vista 1500 | 21 min 12 s | 21 min 10 s | −2 s (−0.2%) |
| Abbott Architect c 16000 | 28 min 18 s | 28 min 44 s | +26 s (+1.5%) |
| Ortho Vitros 5.1/FS | 29 min 24 s | 29 min 21 s | −3 s (−0.2%) |