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POSTER ABSTRACTS

92 - Multicenter evaluation of nine SARS-CoV-2 serology assays

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Objectives To evaluate the performance of seven anti-SARS-CoV-2 assays across nine institutions.

Methods Seven hospital and two community laboratories contributed data from nine independent cohorts for a total of 2,275 samples from 1,791 patients. Samples were measured on nine qualitative anti-SARS-CoV-2 assays including those detecting anti-nucleocapsid antibodies, Abbott and Roche, and anti-spike protein antibodies, Beckman, Diasorin, Euroimmun, Ortho, and Siemens. Not all samples were tested on all assays. Data was collated and antibody response over time was examined. Sensitivity and specificity were calculated for each platform per site and overall. Assay concordance across all assays for samples collected >14 days post-PCR, as well as ROC were assessed.

Results All assays, except two, were able to distinguish PCR positive from COVID-19 naïve and/or PCR negative patients. Anti-SARS-CoV-2 response peaked between 3–4 weeks post-positive PCR, where the assay sensitivities ranged from 89.1-100%. The assay specificities ranged from 86.1-100%, with the Euroimmun IgA assay having the lowest specificity. Concordance (Cohen's kappa >70%) was observed between all assays except the Euroimmun IgA assay. ROC analysis showed optimal sensitivity and specificity may differ from manufacturer cutoffs.

Conclusion Antibodies peaked 3 – 4 weeks post PCR, supporting that serological testing should not be measured prior to 14 days post-positive PCR. Sensitivity and specificity of different anti-SARS-CoV-2 assays vary widely and are dependent on time since PCR positivity. ROC analysis may help identify optimal cutoffs.

91 - Capability of a business intelligence platform to support the IFCC model of quality indicators in a tertiary care academic hospital

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Objectives: The IFCC model of quality indicators (MQI) includes 34 mandatory metrics for their impact on patient safety. Automated systems to capture and report non-conformances are essential for timely, standardized review of performance. We sought to identify capability within current hospital data sources to enable efficient business intelligence (BI) monitoring of key laboratory processes.

Methods: The quality audit processes at Sunnybrook Health Sciences Centre (Toronto, ON) were reviewed. The current laboratory indicators were compared to the IFCC mandatory MQIs for compliance. Furthermore, the laboratory's capability to enumerate the IFCC MQIs was assessed against clinical and laboratory data sources that were classified according to existing linkage to BI reports, potential for database extraction, or manual reporting processes.

Results: While almost all indictors were recorded into an existing database, considerable variability exists among the systems for robustness and data structure. 6/34 (18%) of QIs were linked to BI reports where all metrics exist within the LIS and have uniform coding (e.g. TAT data). 27/34 (79%) of QIs may be accessible from the LIS through coded comments but may not be uniformly captured, where a subset of 9 QIs required secondary review of the safety reporting system (RL6). The remaining QIs were among 10 QIs that were available from middleware (n=4), other external databases (n=3), or monitoring was not applicable (n=2).

Conclusions: Most IFCC MQIs potentially may be linked to the BI platform from existing sources. However, consistency of data capture was likely hampered by operator limitations to document events or apply uniform coding.

90 - Effect of temperature and time on the stability of hemoglobin in fecal immunochemical test specimens

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Objectives:A previous pilot study from our institution demonstrated that the stability of fecal immunochemical test (FIT) samples may be less than our current seven-day window. Our objective was to further evaluate the stability of FIT specimens after refrigeration or room temperature (RT) storage.

Design and Methods:Experiments were performed with the OC-Sensor DIANA iFOB Test system (Eiken Chemical), using a positive clinical cut-off of 75 ng/L hemoglobin (Hb). Samples were analyzed at baseline, days 3, 5, 7, 14, 15, and 21 and categorized based on initial Hb concentration: Group A (n=40): 70-80 ng/ml, Group B (n=20): 90-110 ng/mL, and Group C (n=19): 190-210 ng/mL, with half stored at RT and half refrigerated. To further investigate stability of samples just above the cut-off, eight samples (Group D: 75-85 ng/mL) were measured at baseline and days 3, 4, and 7 after RT storage.

Results:Group A and B RT specimens showed significantly reduced Hb on day three and fourteen, respectively, and day five and 15, respectively, for refrigerated samples ($p<0.05$). Group C showed a significant decrease in Hb on day three, five, and 14, which then persisted until day 21; there was no persistent reduction in refrigerated samples. Combining data with pilot study for RT samples marginally above the cut-off (75-100 ng/mL) showed 100% positivity at date of collection (n=33), 63% on day 3 (n=19), 46% on days 4/5 (n=26), and 38% on days 6/7 (n=26).

Conclusions:FIT samples showed reduced concentrations of Hb compared to baseline when stored at RT; refrigeration may improve stability. Specimens near the clinical cut-off may be particularly susceptible to false negatives due to reduced stability.

89 - Towards provincial harmonization: strong correlation between lipase assays across vendors and analyzer types will enable assay harmonization across Alberta

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Introduction:

Alberta is transitioning to a shared information system and provincial harmonization is a priority. Analytes such as lipase are offered on seven different analyzers from three different vendors and lack standardization; this leads to considerable result variation between different lipase assays. Harmonization can improve patient care by providing comparable laboratory results across the province. This study compared results between lipase assays used in Alberta with the aim to harmonize lipase results across the province.

Methods:

Seven analyzers (Roche cobas c701, Roche cobas Pro, Ortho Vitros 350, Ortho Vitros 4600, Ortho Vitros XT3400, Siemens Atellica, Siemens Dimension EXL) from three different vendors were used to measure lipase in duplicate from 40 leftover patient plasma samples; these samples spanned the analytical measuring range of the Roche cobas analyzers (19.9 – 307 U/L). To assess the effect of diluting samples, an additional 25 plasma samples with high lipase concentrations were collected (295 – 4483 U/L) and measured on the Roche cobas, Ortho Vitros, Siemens Atellica, and Siemens Dimension EXL platforms. To harmonize lipase results, three correction factors were developed using weighted Deming regression analysis.

Results:

Although we observed biases between analyzers, the overall comparison was considered acceptable due to the strong linear correlations between all analyzers ($r \geq 0.99$). Lipase results on the Ortho Vitros 350, Vitros 4600, and Vitros XT3400 were considered equivalent, which allowed Ortho Vitros analyzers to be grouped into a single correction factor. Likewise, results from the Roche cobas c701 and cobas Pro were considered equivalent. Consequently, only three correction factors were required to correlate all seven analyzers to the Roche Cobas platform.

Conclusion:

Overall, correlations between instruments were considered acceptable and will allow the harmonization of plasma lipase results across Alberta. This will positively impact patient care as lipase results measured across the province will now be directly comparable.

86 - Method evaluation of an automated fecal calprotectin immunoassay

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Objectives: The presence of fecal calprotectin (fCal) is a sensitive marker of gastrointestinal inflammation that is useful for diagnosis and monitoring of inflammatory bowel diseases. The objective of this study was to evaluate the analytical performance of the automated fCal chemiluminescent immunoassay on the Diasorin Liaison® XL.

Design and Methods: Analytical evaluation included linearity, imprecision, limit of quantitation (LoQ), and method comparison to the Bühlmann fCal ELISA in clinical use at our institution. Additionally, stool extract precision and stability were assessed, with precision assessed using normal, borderline elevated, and elevated samples extracted in triplicate.

Results: The Liaison fCal assay was linear within the analytical measuring range (R^2>0.99, slope: 0.99, intercept: 8.8). The total between-day imprecision was 3%. CV's near the LOQ were 1-2%. The extract precision was 2%, 7%, and 12% for low, moderate, and high samples respectively. Extracts were stable for up to 8 hours at room temperature or 3 days at 4 °C. The method comparison against the Bühlmann fCal (n=73) had a Pearson's r of 0.89 (slope: 0.61, intercept: -29.63) and an average bias of -41.6% for Liaison fCal. The qualitative agreement was 72% overall, with 89%, 50%, and 78% concordance for normal, borderline elevated, and elevated samples respectively when compared to the Bühlmann fCal.

Conclusions: The Liaison fCal immunoassay demonstrated acceptable analytical performance. Consistent with published studies, a significant negative bias relative to Bühlmann fCal was found, and thus it is important to consult with clinicians to ensure appropriate interpretation before clinical implementation.

84 - A Case of Monoclonal Cryoglobulinemia with Positive Antiphospholipid Syndrome Serology

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Objectives

Monoclonal paraproteins with antiphospholipid activity have been increasingly reported in patients with monoclonal gammopathy and positive antiphospholipid syndrome (APS) serology. Verifying a paraprotein's specific binding to phospholipids requires its separation from other immunoglobulins which is technically challenging. In fact, the purification techniques used in several published case reports are insufficient to definitively accomplish this task. We investigated a possible association of APS with a cryoglobulin in a 63 year-old male with recurrent thrombosis, a positive anti beta-2 glycoprotein-1 (anti-b2GP1) IgM, and an IgM kappa monoclonal gammopathy, who also had significant cryoglobulinemia.

Design and Methods

With informed consent, serum was obtained and processed under temperature control. Immunofixation and SDS-PAGE were utilized to determine the cryoglobulins' constituent proteins. Precipitated cryoglobulins were resolubilized in an equal volume of APS-negative serum at 37°C. Anti-b2GP1 levels were quantified in neat serum, resolubilized cryoprecipitate, and cryoglobulin-depleted supernatant (cryo-supernatant) by ELISA (Euroimmun) performed at 37°C.

Results

Immunofixation and SDS-PAGE confirmed that the cryoglobulin's predominant component was the known monoclonal IgM-kappa. Anti-b2GP1 IgM levels were 302, 255 and 43 RU/mL, in serum, cryo-supernatant, and resolubilized cryoprecipitate, respectively. Vendor provided positivity cut-off was 20 RU/mL (at 18 to 25°C).

Conclusions

Exploiting the temperature-dependent reversible precipitation of cryoglobulins, we were able to purify and decipher the relationship between the patient's paraprotein and APS serology. ELISA results suggest that the patient's paraprotein is unlikely to have any antiphospholipid activity or cause a nonspecific false positive in the APS serologies. This supports the presence of a separate autoantibody of the same isotype.

83 - Negative bias of HbA1c results with increasing triglyceride concentration on the Roche cobas© c513 platform

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Hemoglobin A1c (HbA1c) is a marker of glycemic control used for diagnosis and monitoring of patients with diabetes mellitus. Lipemia may be prevalent in this patient population because dyslipidemia is associated with diabetes mellitus and fasting is not required for HbA1c testing. This study aims to (1) characterize lipemic interference with the HbA1c immunoassay on the Roche cobas© c513 platform and (2) identify the proportion of patients affected using provincial data. Intralipid (Sigma Aldrich),Triglyceride-rich lipoproteins (TRL) from the ASSURANCE™ Interference Test Kit (SunDiagnostics), and high endogenous triglycerides were used to spike three whole blood pools. Bias in HbA1c results compared to baseline was defined as exceeding half the total allowable error (0.25 HbA1c units (%) or 3% change). HbA1c exhibited a negative bias with increasing triglyceride concentrations of all three formulations which was more pronounced at high HbA1c concentrations. Endogenous triglycerides yielded the lowest bias but induced a significant negative bias at >13.0 mmol/L when HbA1c exceeded 9.0%. Analysis of paired HbA1c and triglycerides results (N=3.1 M) in Alberta (2019-2021) suggests at least 0.04% (±0.002%) specimens may be impacted, equating to nearly 1000 HbA1c tests annually (~2.4M HbA1c tests per year). Falsely decreased HbA1c when run on the Roche cobas c513 immunoassay may result in missed diagnoses and/or inadequate therapy in patients with elevated HbA1c and triglycerides. Recognizing that whole blood specimens do not permit easy lipemia identification, mitigation strategies can include reflexive comments when triglyceride and HbA1c are elevated on paired samples and education through communication (e.g., via test directory).

82 - Evaluation of the i-STAT Alinity point-of-care analyzer in a pediatric patient population

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Background: The i-STAT® POC Program at SickKids hospital has a significant impact in critical and emergency situations. SickKids was in the process of switching from the i-STAT® 1 device to the i-STAT® Alinity. The aim of the current study was to evaluate the performance of the CG4+/8+, Crea, and ACT kaolin cartridges on the i-STAT Alinity in pediatric patient populations. Our second aim was to evaluate the agreement between ACT celite and ACT kaolin cartridges. **Methods:** Residual heparinized whole blood samples were used for imprecision, linearity, and method comparison studies. To evaluate the agreement between ACT celite and ACT kaolin, residual samples from 14 hemodialysis patients were used. Hemodialysis patients received either regular, tight, or heparin free dosing protocols. ACT was measured at the start of treatment, 1 hour, 2 hours, and the last 30 minutes of treatment. **Results:** Total imprecision ranged from 0.1 to 3.6% on the i-STAT Alinity. Linearity was verified for the CG4+/8+, Crea, and ACT kaolin cartridges. The three i-STAT Alinity devices showed good agreement to the central laboratory analyzers ($r \geq 0.97$). A negative bias of 5.2% of 7.9 seconds was observed for ACT kaolin on the i-STAT Alinity relative to the Medtronic ACT Plus. Activated clotting time was consistently shorter for ACT kaolin. The percent difference between ACT celite and ACT kaolin ranged from 1 to 30%. A negative bias of 11.6% or 19 seconds was observed for ACT kaolin on the i-STAT Alinity relative to ACT celite on the i-STAT 1. **Conclusion:** The i-STAT Alinity has acceptable precision and linearity. Method comparison between the i-STAT Alinity and central laboratory analyzers showed good correlation. ACT thresholds established for regular, tight, and heparin free dosing protocols using ACT celite should be adjusted for ACT kaolin.

81 - Performance evaluation of pancreatic amylase and lipase assays on a Roche c702 analyzer in the clinical setting

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Objectives: Sinai Health System offers total amylase as the only blood test to aid in diagnosis and management of pancreatitis. We evaluated analytical performance of pancreatic lipase, and pancreatic amylase as alternative and more specific pancreatitis markers, on the Roche c702 system. Utilization of a more specific marker would align with directives from Choosing Wisely.

Methods: Imprecision, relative accuracy, and linearity were assessed against total allowable error goals set by Accreditation Canada Diagnostics (ACD). Additionally, 190 plasma samples from 159 patients were used to assess diagnostic agreement between total amylase, pancreatic amylase, and lipase methods. Patient chart review was performed to assess how amylase and lipase measurements may be used to support patient care.

Results: Total imprecision (%CV) was 0.5% for amylase and 1.2% for lipase. Lipase showed good correlation compared to the Sekisui Diagnostics assay performed on the Abbott Alinity instrument with R = 0.93 and mean relative bias of 13.0%. Pancreatic amylase showed good correlation with a peer Roche c702 laboratory with R = 1.0 and mean relative bias of 1.7%. Lipase was verified to be linear between 10-8500 U/L. A total of 23.9%, 21.8% and 17.0% of individuals had values above the expected range for total amylase (32-120 U/L), pancreatic lipase (13-60 U/L) and pancreatic amylase (13-53 U/L). Acute/chronic pancreatic disease was confirmed in 15.8% of people with elevated total amylase, 21.8% of people with elevated pancreatic lipase, and 18.5% of people with elevated pancreatic amylase.

Conclusions: These studies justified further validation and implementing the Roche pancreatic lipase assay given the strong clinical utility of pancreatic lipase in the diagnosis of acute pancreatitis.

80 - Spirited away: Can ethanol testing in add-on orders produce meaningful results?

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Objective: Ethanol is a volatile substance, and unopened tubes are required for testing. However, add-on requests in previously opened tubes are commonly received, yet ethanol stability in this setting is unclear. We compared analyte stability in opened versus unopened tubes with respect to time elapsed, specimen volume, and automation.

Methods: Ethanol-negative serum specimens were pooled and spiked at four different ethanol concentrations in 100 or 500µL specimen volumes. Subsequently, unopened and opened tubes of ethanol-spiked serum were stored for up to 4 hours at room temperature. Additionally, spiked specimens near the critical value threshold (~54 mmol/L) were stored for up to 4 hours exposed to air. Finally, to mimic a real-life add-on scenario, ethanol-spiked samples were subjected to automation, tested for acetaminophen, stored for 2 hours, and then assayed for ethanol. All measurements were made using the Abbott Architect platform.

Results: The mean 4-hour recovery across all concentrations in opened 500µL specimens was 87.4% (95% CI: 81.8-94.0%). With a 100µL specimen, the mean recovery dropped to 52.9% (95% CI: 50.2-55.7%). Also, a mean recovery of 85.4% (95% CI: 84.2-86.1%) was observed for specimens spiked near the critical value threshold, and only 1 specimen was misclassified. Finally, the add-on mimic experiment showed a mean recovery of 101.5% (95% CI: 97.7-105.4%) across the entire analytical measurement range.

Conclusion: Add-on ethanol orders may be accepted for specimen volumes of ≥500µL and a storage time of 4 hours. Results within a ±25% total allowable error (TAE) are feasible when add-on ethanol testing is performed using routine automation.

79 - Analytical validation and stability study of pleural fluid pH on the Radiometer ABL90 FLEX PLUS blood gas analyzer

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Objectives: Pleural fluid pH is helpful in differentiating uncomplicated from complicated pleural effusions. The Radiometer ABL90 FLEX PLUS is commonly used to test for pleural fluid pH, but it is not validated for this purpose by the manufacturer. We report the results of an in-house analytical validation, together with those of a stability study.

Methods: The study used remnant, deidentified pleural fluid samples. Precision, method comparison, and stability studies were conducted following CLSI guidelines. The Abbott i-STAT1 with CG4+ cartridges were used as the comparator in the method comparison. pH values spanning the analytical measuring range were obtained by spiking individual or pooled samples with 2% acetic acid. Sample stability was tested at room temperature and 4°C using sample aliquots in aliquot tubes or in safePICO syringes.

Results: Within-run coefficients of variation were < 1% at pH values of 6.5, 7.1, and 7.7. Passing-Bablock fit of Radiometer versus Abbott i-STAT1 results across a pH range of 6.502 to 7.810 yielded a slope of 1.006 (95% CI: 0.9483 to 1.116) and y-intercept of -0.07071 (95% CI: -0.8735 to 0.3514). Preliminary studies with aliquot tubes indicated that samples with minimal air exposure are stable at 4 °C for up to 24 hours, and at room temperature for less than 4 hours.

Conclusions: The Radiometer ABL90 FLEX PLUS demonstrates acceptable analytical performance for pleural fluid pH testing. Sample stability at 4 °C suggests that it may be feasible to consolidate testing to a single referral centre within a larger geographic region

78 - New solutions to old problems: A practical approach to identify sample with intravenous contamination in the clinical laboratory

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Background: Contamination with intravenous (IV) fluids is a common cause of specimen rejection in hospital labs. Identification of contaminated samples can be difficult. Expertise from lab staff is required because measures such as failed delta checks may not be sensitive enough. There are limited studies demonstrating algorithms with acceptable sensitivity and specificity for identifying IV fluid contamination. This study aimed to determine criteria to identify fluid contamination from commonly ordered tests (e.g. sodium, potassium, glucose), and validate the use of the proposed criteria.

Methods: Samples defined as confirmed contaminated (n=44) and non-contaminated (n=99) were used to identify patterns to develop an algorithm to detect IV contamination. This algorithm was applied to 1-month of retrospective chemistry results in 2022 (n=61776) from 3 hospital and 1 community labs to determine flagging rates. This algorithm was implemented at one hospital site to assess performance prospectively.

Results: The proposed algorithm (Sodium/Potassium ratio, critical potassium or glucose, delta potassium or glucose) had a sensitivity of 89% and specificity of 97% when two or more criteria are met during the development phase. If previous sample or delta value is not available within 48 hours, then sensitivity is 43% with specificity of 100%. The flagging rates were 0.03% to 0.07% for hospital and 0.003% for community laboratories. Findings from prospective study is ongoing.

Conclusions: The proposed algorithm identified true contamination with low false flagging rates. Preliminary data suggests the algorithm is suitable for implementation in clinical laboratories to flag samples with possible IV contamination for further investigation.

77 - Pediatric reference limits for 10 commonly measured autoimmune disease markers

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Background: The objective of this study was to establish pediatric reference limits for autoimmune disease markers in the CALIPER cohort of healthy children and adolescents to support their interpretation. The Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER) is a national study of healthy children aiming to close gaps in pediatric laboratory medicine by establishing a robust database of pediatric reference intervals for pediatric disease biomarkers (caliperdatabase.org).

Methods: Healthy children and adolescents (n=123), aged 1-19 were recruited as part of the CALIPER study with informed consent. Serum autoantibody testing was conducted using chemiluminescent immunoassays on the BIO-FLASH automated analyzer (Biokit, Barcelona, Spain) including anti-dsDNA IgG, anti-Sm IgG, anti-RNP IgG, anti-SSB/La IgG, anti-Ro60 IgG, anti-Ro52 IgG, anti-cardiolipin IgG, anti-MPO IgG, anti-PR3 IgG, and anti-tTG IgA. Pediatric reference limits representing the 95th, 97.5th, and 99th percentiles were calculated using the non-parametric rank method according to Clinical Laboratory Standards Institute C28-A3 guidelines.

Results: The proportion of samples with results above the lower limit of the analytical measuring range were: anti-dsDNA (26/119; 22%), anti-Sm (16/121; 13%), anti-RNP (1,120; 0.8%), anti-SSB/La (0/120; 0%), anti-Ro60 (0/122, 0%), anti-Ro52 (0/121, 0%), anti-cardiolipin IgG (105/117, 90%), anti-MPO (29/118, 25%), anti-PR3 (11/119, 9%), and anti-tTG IgA (34/120, 28%). Pediatric reference limits and associated 90% confidence intervals were established for all 10 markers and found to be below the manufacturer’s assay cut-offs.

Conclusions: Robust pediatric reference limits for 10 commonly clinically utilized autoimmune markers established herein will allow for improved laboratory assessment of pediatric patients using this assay platform worldwide.

76 - Deriving clinically significant thyroid reference intervals from big data

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Objectives: We sought to harmonize reference intervals (RI) for thyroid function tests and optimize the TSH reflex algorithm across Alberta laboratories using a big data approach.

Methods: One year of thyroid hormone results tested on Roche Diagnostic cobas and Siemens Atellica were extracted from the laboratory information system. Tests ordered from specialists, on inpatients, or repeat testing as well as thyroid disease, autoimmune disease, and pregnancy biomarkers were excluded. RIs were derived using a combination of statistical Bhattacharya analysis, adoption from CALIPER database, and consultation with endocrinology

Results: In total, 1,135,182, 183,236, and 99,931 TSH, fT4, and fT3 tests were included in analysis, respectively. The biggest change to RIs was observed with TSH; new RI for ≥ 14 years was defined as 0.20-6.50 mIU/L (current RI: 0.20-4.00 mIU/L). 13% of TSH tests were > 4.00 and ≤ 6.5 mIU/L suggesting the lower limit of 4.00 mIU/L is flagging too many patients as abnormal. Of the TSH test > 4.00 and ≤ 6.5 mIU/L, 99.1% had a normal matched fT4 (10.0-25.0 pmol/L). 99% of TSH tests between 6.50-10.00 mIU/L had normal fT4 and 20% of TSH < 0.20 mIU/L had a low fT4. As such, automated reflexing of fT4 testing for elevated TSH tests was removed from the provincial algorithm. Using the new thyroid RIs, we estimate that the laboratory will save $10,000-60,000/year.

Conclusion: Current TSH RIs used in Alberta flag too many patients as abnormal despite falling within the central 95% of population, however big data can help optimize RIs.

75 - Falsely elevated urine total protein (UTP) leads to the diagnosis of a rare metabolic disorder

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Objectives: To resolve underlying spectrophotometric interference in urine total protein (UTP) measurement and determine its clinical significance.

Methods: Our laboratory measures UTP on the Roche Diagnostics Cobas® c701. The method includes two key reagents: NaOH to alkalinize specimens and benzethonium chloride to produce turbidity. Change in specimen turbidity is assessed by measuring absorbance before and after the addition of benzethonium chloride. If absorbance exceeds the linear range of the instrument, results are flagged, and the specimen is automatically diluted 10x. Prior to reporting, dilutions are reviewed by technologists.

Results: A UTP specimen of 3.1 g/L was flagged for high absorbance. The automatic dilution gave a result of 0.0 g/L. Repeat testing and manual dilution agreed with initial result. The urine was clear-pale yellow and agitation of the urine did not induce bubbles. The reaction tracing was suggestive of falsely elevated protein: NaOH (without benzethonium chloride) increased absorbance by 10-fold. To investigate, NaOH was manually added to the specimen resulting in a red-brown color change. The urine was sent off-site for testing by a method does that nor require alkalinisation (pyrogallol red). UTP was reported as 0.13 g/L. A review of the reagent package insert and literature suggested homogentisic acid (metabolite found in Alkaptonuria) as a possible interferant. The ordering physician was contacted regarding the interference, urine organic acids were ordered, and the urine was found to be positive for homogentisic acid.

Conclusion: Homogentisic acid is a rare metabolite that can cause false elevated urine protein in methods that alkalinise specimens.

74 - Evaluating the analytical performance of new Strong Six Sigma clinical chemistry assays on the ARCHITECT system

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Objectives: We evaluated the analytical performance of 6 next generation clinical chemistry assays on the Abbott ARCHITECT c8000 system. Precision, linearity, method comparison, accuracy, and sigma metrics were assessed.

Methods: Imprecision was assessed by measuring 2 levels of quality control (QC) material (Biorad Chemistry UA) and 3 pooled patient samples run in replicates of 5, twice per day, for five days. Linearity testing consisted of 5-6 levels of commercially available linearity materials, with 3-4 replicates per level. Acceptable imprecision and bias were determined based on the ACD and CLIA recommendations. To determine accuracy, we measured 10 replicates of NIST 470, 456, 912B, and 927f reference materials for albumin, amylase, urea nitrogen and total protein, respectively, and used the calibrator for cholesterol. Method comparison between the new methods and the current Architect methods were evaluated using 120 serum/plasma specimens, measured in duplicate. The imprecision and bias from the target value were determined from samples with equivalent target values which were used to calculate the sigma value. Total allowable error (TEa) limits were obtained from the ACD and CLIA guidelines. Statistical analysis was performed using EP Evaluator and GraphPad Prism 9.

Results: The observed results for precision, accuracy, linearity, and method comparison for representative clinical chemistry (Serum/Plasma) assays are shown in Table 1. These 6 next generation ARCHITECT assays demonstrated ≥ 6 Sigma performance.

Conclusion: Representative next generation clinical chemistry assays utilizing photometric technology on the ARCHITECT system demonstrated acceptable performance for precision, accuracy, linearity, and agreement with on-market ARCHITECT clinical chemistry assays.

73 - Impact of sample pH on analytical recovery and stability of urinary 5HIAA, HVA and VMA

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Objectives: Conditions to ensure sample stability of urinary 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid (HVA), and vanillylmandelic acid (VMA) has been the subject of discussion for years. Urine collection requirements are variable across medical laboratories, with some preferring no preservative to be added and others requesting acidification. This study evaluated the impact of sample pH on analytical recovery and stability of 5HIAA, HVA and VMA in urine.

Design and Methods: Eight urine samples were included in the study. Four aliquots were made for each sample, and pH of each aliquot was adjusted with 6N HCL or 5N NaOH to pH of 0-1, 1-3, 3-5, and 5-7, respectively. 5HIAA, HVA and VMA were measured by LC-MS/MS on day 0, 1, 2, 5 and 7. The samples were stored at 4 °C during the study. Sample stability data was analyzed using the EP evaluator software.

Results: The average analytical recovery of 5HIAA, HVA and VMA on Day 0 was between 92-104% across the pH range studied. No clinically significant difference was observed between the four pH conditions for all three analytes. 5HIAA was stable for 4 days at pH 0-1 and for 6 days at all other pH values. The stability of HVA and VMA was not affected by sample pH values and all samples were stable for at least 7 days.

Conclusions: Sample pH had no effect on analytical recovery of urinary 5HIAA, HVA and VMA, and sample stability was only compromised in extremely acidic condition (pH 0-1).

72 - Using ensemble machine learning to optimize delta checks for the detection of multiple pre-analytical errors

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Objectives: Delta checks involve the comparison of serial patient results, and assessing the difference against an analyte-specific limit prior to reporting. While originally developed to detect sample mix-ups, delta checks may also flag specimen integrity issues. This study sought to optimize delta checks, including time between tests, by using machine learning algorithms to evaluate their efficacy in identifying common pre-analytical errors.

Methods: Optimized delta check limits were generated using the distribution of a posteriori in-patient delta values from three tertiary centres, as described in CLSI guidelines (EP33, 2016). Results from samples previously identified as contaminated within sets of routine in-patient chemistry were used to test delta check rules. Evaluation of error detection was performed by using random forests with validation by out-of-bag error computation.

Results: Intravenous normal saline contamination was effectively identified by individual or combined delta checks for potassium and chloride, with a delta time <96 hours. Optimal parameters for detection of K_2EDTA contamination used alkaline phosphatase and potassium with a delta time <72 hours. Evaluation of sample flagging rates suggested a significant reduction for albumin (-48.2%, $p<0.0001$), but not sodium (-4.79%, $p=0.2191$), and a modest increase for potassium (+1.42%). However, it was noted that 21.5% of specimens flagged by the optimized rules would likely identify significant changes in more than one analyte.

Conclusions: Using machine learning along with empirically-derived delta checks may offer concrete, population-specific measures by which multiple pre-analytical errors can be detected prior to releasing patient results, with minimal effects on overall sample flagging rates.

71 - Analytical verification of fecal calprotectin using the Buhlmann and Liaison assays on the Siemens Atellica and Liaison XL Platforms

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Objectives: Fecal Calprotectin (FC) is a noninvasive, surrogate marker of intestinal inflammation, used for triaging patients with symptoms of inflammatory bowel disease (IBD) and management of IBD patients. The study objective was to evaluate the analytical performance of the Liaison Calprotectin and the Buhlmann fCal turbo assays.

Design & Methods: Patient samples with clinical suspicion of IBD were used in the study. FC was extracted from stool samples using extraction devices provided by the manufacturers and measured following manufacturers' instructions. Precision was assessed using quality control material. Patient sample admixtures were used for linearity assessment. A three-way method comparison with our current laboratory method was also performed (Liaison, Buhlmann, and ImmunoDiagnostik (IDK) ELISA Calpro assays).

Results: The units of reporting calprotectin results differ between manufacturers and even between platforms from the same manufacturer e.g. Buhlmann on Atellica (ug/ml), Buhlmann on Roche (ug/g), Liaison (ug/g) and IDK (mg/kg).The total imprecision for the Buhlmann assay was 1.3 – 5.0% and for the Liaison assay was 7.0 – 7.5%. The assays were linear between 16.5 – 10,000 µg/ml (Buhlmann) and 20.1 to 6,750 ug/g for the Liaison XL assay. Using the difference between the results and the TAE, the two methods were not equivalent with the Buhlmann method showing a positive bias. Both assays (Buhlmann & Liaison) showed minimal agreement with our reference lab method (IDK; 21.8% and 32% agreement, respectively). Assays from the same manufacturer showed better agreement although not analytically equivalent.

Conclusions: The two FC assays showed acceptable precision and linearity but were not equivalent with minimal agreement, as the Buhlmann assay showed a significant positive bias. Calprotectin methods do not agree and thus, we recommend that the same FC method and assay-specific cut-offs be used to monitor patients during treatment and advocate for standardization of FC assays.

70 - Simultaneous Analysis of Nicotinic Acid and Nicotinamide in Human Serum by LC-MS/MS

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Objective: To develop a rapid and robust LC-MS/MS method for nicotinic acid (NA) and nicotinamide (NAM) applicable to human serum analysis

Methods: Multilevel saline calibrators and plasma controls were made in the laboratory by spiking standards. A 50 µl serum with internal standards was extracted by deproteinization with 250 µl methanol, and then 3 µl of the supernatant was analyzed on a Shimadzu HPLC and AB SCIEX 6500+ QTRAP mass spectrometer with electrospray ionization in positive polarity. The transitions used for the detection of NA vs NA $^{13}C6$ and NAM vs NAM $^{13}C6$ were 124>80>53 vs 130>83 and 123>80>78 vs 129>85, respectively. The analytes were separated using gradient elution at 40 °C with a 0.4ml/min flow rate. This method was validated and applied to clinical research projects for the determination of NA and NAM levels after administration.

Results: Total run time was 3 min. Total imprecision in two levels of quality control was less than 5% and the limit of quantification was 2.0 ng/ml for NA and NAM. The linearity was within the range 2.0-2000 ng/ml for both analytes. Ion suppression effects were observed for both analytes. No carryover and no interference by hemolysis, lipemia, icterus, and commonly used therapeutic drugs were observed. LC-MS/MS results correlated well with the expected results from mixtures of patient's sample with standards.

Conclusion: This rapid and reliable LC-MS/MS method is suitable for determination of concentrations of NA and NAM in serum or plasma sample for use in clinical research.

69 - Comparison of CSF and plasma p-tau181 concentrations in predicting clinical diagnosis of Alzheimer's disease

Pankaj Kumar[1]

[1]BC Neuroimmunology lab

Comparison of CSF and plasma p-tau181 concentrations in predicting clinical diagnosis of Alzheimer's disease

Pankaj Kumar, Mary Encarnacion, Fok Alice, Ali Mousavi, Ging-Yuek R Hsiung, Hans Frykman

Background

The feasibility of detecting tau phosphorylated at threonine-181(p-tau181) in CSF makes it a valuable biomarker for diagnosis of Alzheimer's Disease (AD). Recently, the novel technologies accurately measuring biomarkers directly in blood offer a unique advantage for use in clinical testing and trials. This study describes the correlation of a novel plasma p-tau181 assay with CSF ptau-181 in predicting clinical diagnosis of AD.

Methods

Data were obtained after analysis of EDTA plasma and CSF samples from cases with clinical AD who had been referred to the UBC Hospital Clinic and were assessed for dementia and AD between 2008 – 2018.

The plasma samples were assayed by using an ADx developed p-tau181 specific Simoa assay and the CSF samples analysed by INNOTEST FUJIREBIO immunoassay.

Results

54 cases including AD (n= 35), Non – AD (n = 19) evaluated.

The average of plasma p-tau181 was threefold in AD cases while the average of CSF p-tau181 was about twice higher in AD patients.

There was a positive correlation between elevation of plasma p-tau181 and CSF p-tau 181, but the area under curve (AUC) for plasma p-tau181 was higher than CSF (0.89 vs. 0.74).

Moreover, the mean of plasma and CSF p-tau181concentrations were significantly different between AD and Non-AD cases.

Conclusion

The CSF and plasma p-tau181 concentration in AD cases were significantly higher than non – AD cases. The specific analytic results of plasma p-tau181 shows good promise and superiority in offering a non-biased measurement and help in the clinical assessment of AD patients and clinical trials.

68 - The diagnostics usefulness of cell-based assays (CBA) to detect the autoantibodies in “double seronegative myasthenia gravis” (dSN-MG) cases

Pankaj Kumar[1]

[1]BC Neuroimmunology lab

The diagnostics usefulness of cell-based assays (CBA) to detect the autoantibodies in “double seronegative” (dSN-MG) cases

Pankaj Kumar, Anna Cruz, Ali Mousavi, Tariq Aziz, Joel Oger, Hans Frykman

Background

10 to 15% of adult type of MG are seronegative by current gold standard assays. This may relate to imperfect sensitivity in detecting low affinity Acetylcholine receptor antibodies (AChR Ab) or other autoantibodies such as Low-density lipoprotein receptor-related protein 4 (LRP4). Recent development of CBA facilitates improved detection of autoantibodies in MG patients. In this clinical study we established the important role of CBA in detecting AChR and LRP4 antibodies in dSN-MG patients.

Methods

Between June 2019 and January 2022, at BC Neuroimmunology Laboratory two different clinical validation studies were performed. In the first study we evaluated clinical charts of 177 patients that were earlier tested negative for AChR and MuSK Ab. Among the 177 cases, a total of 19 had clinical MG. We then reanalyzed a small number of sera (n=17) for AChR Ab by in-house live CBA. In a parallel study we screened another set of 150 AChR and MuSK negative sera to detect LRP4 antibodies by in-house fixed CBA.

Results

Of 170 dSN-MG cases, 19 had clinical MG (8 generalized MG and 11 ocular MG) and 4/17 were positive for AChR Ab (23.5%). Furthermore, 3 cases out of 150 dSN-MG were found positive for LPR4 antibodies (2%).

Conclusions

With improved AChR CBA, a proportion of dSN-MG patients with probable clinical MG were confirmed for the presence of AChR Ab. In addition, the fixed CBA detected a small number of LPR4 positive cases. The findings need to be further verified in a comprehensive prospective study.

67 - Performance evaluation of BiliCare™ transcutaneous bilirubin device

Yu Chen[1], Susan Lake[1], Kate Scott[1]

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Objectives: The aim of this study was to evaluate the analytical performance of a new transcutaneous bilirubin (TcB) device – BiliCare™ (Natus, Pleasanton, CA).

Design and Methods: The neonatal TcB measurements were compared between BiliCare™ and the existing BiliChek™ systems (n=30). TcB measured by BiliCare™ were also compared with total serum bilirubin (TsB) using Roche Cobas702 chemistry analyzer (n=22) and whole blood bilirubin using Radiometer ALB 835 (n=11). Reproducibility was assessed by repeating TcB measurements with a BiliCare™ on a normal neonate and one with jaundice 20 and 16 times respectively within 25 minutes.

Results: Compared with BiliChek™, BiliCare™ has demonstrated am average bias of -17.5% (BiliCare™ = 0.7166BiliChek™ +18.194, R=0.8819). BiliCare™ has a better agreement with Cobas702 (BiliCare™ = 0.776Cobas702 +48.768, R=0.8843, average bias 10.3%). Similarly, BiliCare™ has a -7.2% average bias compared with ABL835 (BiliCare™ = 0.6166ABL835 +54.464, R=0.8287). At TcB 94.5 and 269 μmol/l levels, BiliCare™ has demonstrated imprecision as 8.9% and 6.9% respectively.

Conclusions: The new BiliCare™ correlates with total serum bilirubin on Chemistry analyzer and is acceptable for neonatal transcutaneous bilirubin testing.

Key words: transcutaneous bilirubin, BiliCare™, method evaluation, comparison study

66 - Sample suitability and stability in different blood collection tubes for volatile alcohols and glycols analysis

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Objectives: Blood collection tube suitability and sample stability for volatile alcohols, ethylene glycol (EG), and propylene glycol (PG) are not standardized. This study sought to systematically examine the sample suitability and stability in different tubes.

Design and Methods: Two pools of whole blood were created and spiked with two levels of Methanol, Ethanol, Isopropanol, Acetone, EG, and PG. Spiked whole blood was added to 4 replicates of each blood collection tube (Grey/Red/Lavender top tube, SST™, PST™, and Barricor™ tube) for different storage conditions ((up to 2 days at room temperature (RT), 14 days at 4°C, and 28 days at -20°C)). An aliquot was prepared from baseline replicates. Volatile alcohols and glycols were analyzed by an Agilent 8890 gas chromatography system.

Results: All blood collection tubes have demonstrated similar performance over different storage conditions, i.e. to be statistically insignificant ($p>0.05$) with the only exception of PG at the high concentration of day 7 at 4°C condition ($p<0.05$ but clinical significance

Conclusions: Grey/Red/Lavender top tube, SST™, PST™, and Barricor™ tube are all suitable for volatile alcohol and EG/PG analysis. Samples are stable for 2 days RT, 14 days at 4°C, and 28 days at -20°C.

Key words: Sample stability, aliquot stability, blood collection tubes, volatile alcohol, glycol

65 - Multisite evaluation of high-sensitivity cardiac Troponin T with patient pools on different Roche analyzers: Interim report on observed components of variance.

Kazem Nouri[1], Andrew Lyon[2], Michael Chen[3], Angela Fung[4], Janet Simons[4], Andre Mattman[4], Albert Tsui[5], Joshua Raizman[5], Laurel Thorlacius[6], Mark Cheung[7], Ronald Booth[8], Chris McCudden[8], Vipin Bhayana[9], Barry Hoffman[7], Jennifer Taher[7], Joel Lavoie[10], Shaun Eintracht[11], Jennifer Shea[12], Amy Lou[13], Lorna Clark[1], Peter Kavsak[1]

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Objectives: The impact and prevalence of non-reproducible cardiac troponin results have been highlighted in recent publications and analyzers as it pertains to high-sensitivity cardiac troponin T (hs-cTnT) (Clin Chem Lab Med 2021;59:1972-1980). Here we offer an interim assessment of the components of variation of hs-cTnT results using patient materials across eight provinces in Canada.

Design and Methods: Plasma pools (low-level and high-level) and one serum pool (mid-level) were constructed, frozen (≤ -70^{0}C), transported (dry ice), with instructions on handling the aliquots (e.g., centrifugation for 10 minutes at 3000 *g*) prior to testing. The materials were tested on 36 different Roche instruments comprising 4 different analyzer models and 2 assay modes (9 min n=27, and 18 min n=9 assay time). Fixed and random effect multilevel models were used to assess the influence of analyzer model and hs-cTnT pool with different assay modes using categorical variables.

Results: Multivariate analyses among sites using the 18 min assay time revealed that the intra-class correlation coefficient for analyzer model was 0.197 and fixed effects indicated a statistically significant interaction ($p<0.043$) between the pool and analyzer models. There were no statistically significant fixed or random effects observed among the 9 min assay mode data.

Conclusion: These interim findings suggest that for the 18 min assay (i) analyzer model contributes ~20% of the observed variance among sites using and (ii) statistically significant changes in hs-cTnT results were observed between analyzer models for a specific sample pool. Additional rounds of testing are needed to confirm these initial findings.

64 - Screening, identification and pre-clinical validation of novel phagocytosis modulators using Parkinson's disease patients' macrophages and LRRK2 G2019S immune cells.

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Background: Parkinson's disease (PD) is the second most common age-related neurodegenerative disorder worldwide and presents as a progressive movement disorder in affected individuals. Phagocytosis a key host-defense mechanism of the innate immune system have been implicated in enhancing neuronal damage and neurodegeneration in Parkinson's disease (PD) and other neurodegenerative diseases. Methods: We developed a highly sensitive assay to screen for phagocytic modulators in the National Institute of Neurological Disorder and Stroke (NINDS) custom collection 2 library. 75% of these compounds have been approved by the US FDA. Of the 1040 compounds screened, 42 drugs can modulate phagocytosis in bone marrow-derived macrophages (BMDM) ; of these, 12 were non-toxic to cells and able to cross the blood brain barrier (BBB). Three (3) candidates were finally selected and were further tested for phagocytosis modulation using macrophages (M1 and M2) derived from peripheral blood mononuclear cells (PBMCs) isolated from PD patients' blood samples. Results: Our result show increased basal phagocytic activity in PD patients' M1 and M2 macrophages (n=15) as well as LRRK2 G2019S immune cells (microglia and BMDM) primed with lipopolysaccharide (LPS). Exposing these cells to our drug candidates led to significantly reduced phagocytosis more than Cytochalasin D (a potent phagocytosis inhibitor). Conclusion: Our drug candidates were able to modulate increased phagocytosis reported in PD using macrophages and immune cells from PD patients and animal models. By screening drugs which are already FDA approved and known to enter the brain, our candidates can be evaluated in clinical trials almost directly in an off lab-label capacity.

62 - Implementation of Ortho Clinical Diagnostic's high-sensitivity cardiac troponin-I assay at a children's health centre: elevated values under 1-year old

Nancy Barrett[1], Lori A. Beach[2]

[1]IWK Health, [2]IWK Health Centre

Objectives: Evaluation of the Ortho Clinical Diagnostic (OCD) high-sensitivity troponin-I (hsTnI) assay has been characterized by adult centres, however reports on implementation at pediatric centres are not available. Troponin is part of the order-set used by our clinicians upon suspicion of multisystem inflammatory syndrome in children (MIS-C; COVID-19 infections). Caliper data on other troponin assays has demonstrated physiological elevations in troponin under 1-year of age. We sought to verify this observation in the OCD hsTnI assay. Design/Methods: Ninety specimens leftover from outpatient collections of apparently-healthy children (upon chart review) were tested on the OCD hsTnI assay as part of our larger method verification study. Results were compared to published and internally verified adult 99th percentile data and other platforms' Caliper data. Results: In children under age 18, male:female distribution was 43:47. Previous age stratification at our centre (OCD TnI-ES) adjusted upper limits at 1-year, 5-years, and 10-years. Half of results for children under 1-year exceeded the 99th-percentile (Table 1). 98% of results for children over 1-year were under the adult-derived 99th percentiles. Detectable levels over limit-of-detection ranges were verified at 50% in this cohort with and without inclusion of under 1-year. Conclusions: OCD hsTnI values exceeding 99th percentiles are observed in under 1-year-old children, as on other platforms.

61 - COVID-19 serological survey of Nova Scotia using antenatal serum samples

Tara Dent[1], Danielle Silver[1], Nancy Barrett[1], Lori A. Beach[2]

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Objectives: Among strategies studying distribution of SARS-CoV-2 infection in Canada, assaying the presence of anti-Spike and/or anti-Nucleocapsid antibodies offers a potentially unbiased surveillance sampling. As part of a Canada-wide research study funded through the COVID-19 Immunity Task Force, we performed seroprevalence studies in Nova Scotia (NS) using antenatal specimens. Design and Methods: In NS, prenatal samples collected for routine aneuploidy screening were retrospectively tested for anti-Spike total antibodies (OrthoClinicalDiagnostics). Two time-periods were coordinated with other Canadian centres, Aug24-Sept11, 2020 and Nov16-Dec4, 2020. Age and postal code data were included for comparison and verification of distribution. Results: Prior to the COVID-19 wave following summer 2020, seropositivity in pregnant women in NS was low, with 2/490 specimens reactive for anti-Spike antibodies (August-Sept cohort), although there were no reported cases in women in Atlantic Canada between ages 20-39 in these weeks1. Twelve weeks later, 6/500 specimens were anti-Spike reactive. In Atlantic Canada at this time, 24 cases were reported in women aged 20-391. Overall, age-adjusted seroprevalence in Nova Scotia rose from under 0.5% to 0.96% from Aug-Dec2020, with December rates similar to those observed in other Atlantic provinces and below those observed in the balance of Canada2. Seropositivity was greater than PCR positivity (9-province average 4.8x greater seropositivity versus PCR-positivity2). Geographic and age-specific analysis indicated province-wide coverage and positivity in every age category. Conclusions: The use of minimally-biased antenatal specimens for COVID-19 provides both a sampling of the general population as well as the seropositivity in a pregnant population. In NS seropositivity measuring total anti-Spike antibodies was greater than PCR positivity. 1.https://www150.statcan.gc.ca/n1/pub/13-26-0003/132600032020001-eng.htm 2.Atkinson et al(2022) submitted

60 - Multicenter evaluation of nine SARS-CoV-2 serology assays

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Objectives Evaluate performance of nine anti-SARS-CoV-2 serology assays across different institutions. Methods Seven hospital and two community laboratories contributed data from nine independent cohorts for a total of 2,275 samples from 1,791 patients collected during 2020 before vaccines became available. Samples were measured on nine qualitative anti-SARS-CoV-2 assays including those detecting anti-nucleocapsid antibodies (Abbott and Roche) and anti-spike protein antibodies (Beckman, Diasorin, Euroimmun, Ortho, and Siemens) depending on the cohort. Data was collated and antibody response over time was examined. Sensitivity and specificity were calculated for each platform per site. Assay concordance between all assays for samples collected >14 days post-SARS-CoV-2 PCR were assessed. Results Detectable antibody levels on all assays, except two, were able to distinguish PCR positive and COVID19 naïve and/or PCR negative patients. SARS-CoV-2 antibody response peaked between 3–4 weeks post positive PCR. Sensitivity of the assays ranged from 89.1-100 % for samples collected at least 3 – 4 weeks post positive PCR test. The specificities of the assays ranged from 86.1 to 100 %. Concordance (Cohen's kappa >70%) was observed between all assays except the Euroimmun IgA assay. Conclusion Antibody levels are detectable at least 14 days post-diagnosis, and peak antibody levels were detected 3 – 4 weeks post PCR. Sensitivity and specificity of different anti-SARS-CoV-2 assays vary widely and are dependent on time since PCR positivity.

59 - Monitoring and adjusting for analytical bias in chemistry tests using longitudinal quality control (LQC) samples

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Objective: To assess the long-term analytical performance of chemistry tests for the Canadian Longitudinal Study on Aging (CLSA). Design and Methods: The CLSA is a 20-year longitudinal study of 50,000 Canadians aged 45 – 85 years at baseline. Comprehensive assessments are repeated every 3-years including the measurement of core biomarkers. Variation over time is minimized by using standard procedures for blood collection, processing, storage, and one analytical test method (Cobas 800 modular, Roche). Pooled human serum or whole blood sample, termed longitudinal quality control (LQC), stored in -190oC cryofreezers, was included in each box of the respective 95 aliquots sent for testing. Baseline LQC results were compared to follow-up 1 (FU1) LQC to determine whether adjustment of FU1 participants' data was required. Results: Of 13 analytes with LQC results (albumin, ALT*, cholesterol*, creatinine*, hsCRP, ferritin, FT4*, HbA1c*, HDL*, LDL*, non-HDL, triglycerides*, and TSH) at baseline and FU1, 5 had FU1 values exceeding the mean ± 3SD of baseline values. Imprecision was similar for both periods. Reference method analysis of LQC samples for 8 analytes* for these two time periods demonstrated no change in values indicating sample stability. The mean percent change in LQC results from baseline to FU1 was -1.84, -4.40, 14.20, -2.23, and -4.07 for cholesterol, creatinine, ferritin, FT4, and HDL, respectively. A manufacturer ferritin calibration set-point change and HDL reagent reformulation explained the LQC changes seen for these tests. Conclusion: Assessment of analytical results by LQC provides an effective method to adjust for bias in longitudinally obtained chemistry test results.

58 - Celiac disease testing: Improved utilization through an automated reflex algorithm in a hospital setting

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Objective Despite availability of clinical guidelines, there is a lack of laboratory testing recommendations for celiac disease. This study aimed to identify ordering practices in a hospital setting and implement utilization strategies to reduce unnecessary testing for celiac disease.

Methods Ordering practices of anti-tissue transglutaminase (anti-TTG) IgA and IgG, anti-deaminated gliadin peptide (DGP) IgA and IgG, and total IgA between different clinical departments were examined between Jan 2019 and Oct 2021. A new test code for ordering celiac testing based on the 2013 American College of Gastroenterology Guidelines and 2018 Clinical Practice Update was introduced. Ordering practices post- vs pre-implementation were compared.

Results Overall, 77.5% of all test orders pre-implementation used the test code “CELSC”, resulting in testing for all five assays. Departments were classified into three categories: those where the percentage of orders that included all five celiac tests were ³90%; 60-89%; and 55-60% of all test orders. Implementation of a new test code resulted in first line testing of two assays: anti-TTG IgA and total IgA. LIS-implemented changes drastically reduced the number of tests/order by 59.3%, 56.1% and 51.7%, respectively.

Conclusion Overutilization of celiac testing is common. Implementation of an automated reflex approach was effective in reducing unnecessary testing for celiac disease.

57 - Comprehensive serological analysis of SARS-CoV-2 infection in a well-characterized and unvaccinated community patient cohort

Nicole M.A. White-Al Habeeb[1], Marilyn Whelan[2], Yannick Galipeau[2], Corey Arnold[2], Kiran Nakka[2], Mohamed Abouelhassan[3], Danijela Konforte[3], Marc-André Langlois[2], Martin Pelchat[2]

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Objectives To profile binding and neutralizing antibody responses over time following SARS-CoV-2 infection in a well-characterized cohort of unvaccinated, community patients.

Methods Serum samples were collected over six months in 2020, prior to vaccine availability. Age, sex, time since symptom onset, time of sample collection, and PCR cycle threshold values were recorded. SARS-CoV-2 IgG, IgM and IgA antibodies to the spike trimer (S), receptor binding domain (RBD), and nucleocapsid (N) were measured using enzyme-linked immunosorbent assays (ELISA) calibrated to a reference standard from the World Health Organization. Antibody neutralization was assessed using a surrogate neutralization ELISA.

Results 751 serum samples were collected. Patient median age was 81 years (Q1=65; Q3=89). 92% of PCR positive samples had detectable level of antibodies. Principal component analysis based on anti-N, -S and -RBD IgG showed distinct clustering with PCR positive and negative populations. Antibody concentrations were highest in samples collected within 10 days of symptom onset. Increased time interval between symptom onset and serum collection inversely correlated with levels of all IgGs analyzed. Neutralization positively correlated with antibody levels. Intervals up to 162 days between symptom onset and sample collection did not reduce neutralization capacity.

Conclusions 8% of patients did not produce detectable humoral immune response following SARS-CoV-2 infection. Reduction in binding antibodies, but not neutralization, correlates with time intervals between symptom onset and sample collection. Our analysis provides important insight into community immunity, neutralization ability, and antibody levels in a well-characterized community patient cohort of non-immunized individuals.

56 - Insights into temporal and regional trends in the unregulated drug supply in Ontario and British Columbia: A collaboration between clinical laboratories and drug checking services

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Objectives: For the clinical laboratory, finding strategies to tailor urine drug screen (UDS) menus to reasonably keep up with the unregulated drug supply trends, while also managing time and resource constraints, is an ongoing challenge. This is the first Canadian study that aims to assess whether the information from the local drug checking (DC) services and cross-provincial UDS data has utility as a surveillance tool for clinical laboratories to monitor and update their mass spectrometry-based UDS menus. Design and Methods: The study analyzed community lab mass spectrometry-based UDS data from LifeLabs Ontario (n =127 529) and British Columbia (n = 5939), and from Toronto DC services (n = 3308) collected between August 2020 and October 2021. The trends in UDS and DC data in fentanyl co-positivity with toxic contaminants, such as analytically challenging designer benzodiazepines, and fentanyl analogues were examined. Results: Benzodiazepines showed the highest co-positivity with fentanyl in both urine samples and drugs checked, increasing by nearly 20% in the latter part of 2020. The percent co-positivity of fentanyl with etizolam, flualprazolam, flubromazolam, carfentanil, and acetylfentanyl in Ontario UDS and DC also showed similar monthly patterns. Regional differences were noted between Ontario and BC UDS (fentanyl/etizolam co-positivity: ON – 50-80% vs. BC – 20-40%), with trends consistent over the entire 15-month collection period. Conclusions: Clinical laboratories should partner with their local DC services to access up-to-date trends in unregulated drug supply, which can help tailor the UDS menus accordingly. UDS and DC data can be complementary in providing community-focused healthcare services.

55 - Quality control of hemolysis, icterus and lipemia indices on the Roche Cobas p8000

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Objectives The Roche Cobas 8000 is a fairly new chemistry analyzer with limited research on hemolysis, icterus and lipemia (HIL) avaiable. The Roche Cobas 8000 assesses the indices by means of spectrophotometric readings, the light source and detector are also used for routine biochemical assays such as creatinine and glucose. In that sense, would monitoring creatinine and glucose quality control (QC) be sufficient in monitoring hemolysis, icterus and lipemic indices? These indices can cause colourimetric, photometric and turbidimetric analytical interference on routinely tested patient sample analytes. This is why it is so important to ensure the analytical quality of indices results and the impact on test reporting, such as samples being cancelled, retested, recollected, or the addition of unnecessary comments. Design and Methods A method validation was run on patient pooled samples with indexes that would cause interference to common analytes most affected by hemolysis, icterus and lipemia, along with commerically prepared material from BioRad. Results The imprecision of the HIL indices compared to the BioRad target values for BioRad QC on the first line of the Roche Cobas 8000 was 1.3% for H-index, 2.4% for I-index and 9.1% for L-index. On the second line, 1.9% for H-index, 1.9% for I-index and 9.7% for L-index. The in-house QC producing values of 1.9% for H-index, 2.2% for I-index and 8.5% for L-index. Conclusions The statistics calculated from the data collected show that the system meets the manufacturer claims for method precision. The method currently in use is also working precisely as intended.

54 - The diagnostics usefulness of cell-based assays (CBA) to detect the autoantibodies in “double seronegative” myasthenia gravis (dSN-MG) cases

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Background 10 to 15% of adult type of MG are seronegative by current gold standard assays. This may relate to imperfect sensitivity in detecting low affinity Acetylcholine receptor antibodies (AChR Ab) or other autoantibodies such as Low-density lipoprotein receptor-related protein 4 (LRP4). Recent development of CBA facilitates improved detection of autoantibodies in Myasthenia gravis (MG) patients. In this clinical study we established the important role of CBA in detecting AChR and LRP4 antibodies in dSN-MG patients. Methods Between June 2019 and January 2022, at BC Neuroimmunology Laboratory two different clinical validation studies were performed. In the first study we evaluated clinical charts of 177 patients that were earlier tested negative for AChR and MuSK Ab. Among the 177 cases, a total of 19 had clinical MG. We then reanalyzed a small number of sera (n=17) for AChR Ab by in-house live CBA. In a parallel study we screened another set of 150 AChR and MuSK negative sera to detect LRP4 antibodies by in-house fixed CBA. Results Of 170 dSN-MG cases, 19 had clinical MG (8 generalized MG and 11 ocular MG) and 4/17 were positive for AChR Ab (23.5%). Furthermore, 3 cases out of 150 dSN-MG were found positive for LPR4 antibodies (2%). Conclusions With improved AChR CBA, a proportion of dSN-MG patients with probable clinical MG were confirmed for the presence of AChR Ab. In addition, the fixed CBA detected a small number of LPR4 positive cases. The findings need to be further verified in a comprehensive prospective study.

53 - New solutions to old problems: A practical approach to identify sample with intravenous contamination in the clinical laboratory

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Background: Contamination with intravenous (IV) fluids is a common cause of specimen rejection in hospital labs. Identification of contaminated samples can be difficult. Expertise from lab staff is required because measures such as failed delta checks may not be sensitive enough. There are limited studies demonstrating algorithms with acceptable sensitivity and specificity for identifying IV fluid contamination. This study aimed to determine criteria to identify fluid contamination from commonly ordered tests (e.g. sodium, potassium, glucose), and validate the use of the proposed criteria. Methods: Samples defined as confirmed contaminated (n=44) and non-contaminated (n=99) were used to identify patterns to develop an algorithm to detect IV contamination. This algorithm was applied to 1-month of retrospective chemistry results in 2022 (n=61776) from 3 hospital and 1 community labs to determine flagging rates. This algorithm was implemented at one hospital site to assess performance prospectively. Results: The proposed algorithm (Sodium/Potassium ratio, critical potassium or glucose, delta potassium or glucose) had a sensitivity of 89% and specificity of 97% when two or more criteria are met during the development phase. If previous sample or delta value is not available within 48 hours, then sensitivity is 43% with specificity of 100%. The flagging rates were 0.03% to 0.07% for hospital and 0.003% for community laboratories. Findings from prospective study is ongoing. Conclusions: The proposed algorithm identified true contamination with low false flagging rates. Preliminary data suggests the algorithm is suitable for implementation in clinical laboratories to flag samples with possible IV contamination for further investigation.

52 - Comparison of CSF and plasma p-tau181 concentrations in predicting clinical diagnosis of Alzheimer's disease

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Background The feasibility of detecting tau phosphorylated at threonine-181(p-tau181) in CSF makes it a valuable biomarker for diagnosis of Alzheimer's Disease (AD). Recently, the novel technologies accurately measuring biomarkers directly in blood offer a unique advantage for use in clinical testing and trials. This study describes the correlation of a novel plasma p-tau181 assay with CSF ptau-181 in predicting clinical diagnosis of AD. Methods Data were obtained after analysis of EDTA plasma and CSF samples from cases with clinical AD who had been referred to the UBC Hospital Clinic and were assessed for dementia and AD between 2008 – 2018. The plasma samples were assayed by using an ADx developed p-tau181 specific Simoa assay and the CSF samples analysed by INNOTEST FUJIREBIO immunoassay. Results 54 cases including AD (n= 35), Non – AD (n = 19) evaluated. The average of plasma p-tau181 was threefold in AD cases while the average of CSF p-tau181 was about twice higher in AD patients. There was a positive correlation between elevation of plasma p-tau181 and CSF p-tau 181, but the area under curve (AUC) for plasma p-tau181 was higher than CSF (0.89 vs. 0.74). Moreover, the mean of plasma and CSF p-tau181concentrations were significantly different between AD and Non-AD cases. Conclusion The CSF and plasma p-tau181 concentration in AD cases were significantly higher than non – AD cases. The specific analytic results of plasma p-tau181 shows good promise and superiority in offering a non-biased measurement and help in the clinical assessment of AD patients and clinical trials.

51 - Deriving clinically significant thyroid reference intervals from big data

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Objectives: This study aimed to harmonize reference intervals (RI) for thyroid function tests and optimize the TSH reflex algorithm across Alberta using a big data approach. Methods: One year of thyroid hormone results (TSH, free T4 [fT4], free T3 [fT3]) tested on Roche Diagnostics cobas and Siemens Atellica were extracted from the laboratory information system. Results from specialists, inpatients, or repeat testing, as well as from positive thyroid disease, autoimmune disease, and pregnancy biomarkers were excluded. RIs were derived using a combination of statistical Bhattacharya analysis, adoption from CALIPER database, and endocrinology consultation. Results: In total, 1,135,182, 183,236, and 99,931 TSH, fT4, and fT3 tests were analyzed, respectively. The biggest change in RIs was observed with TSH, with a new RI for ?14 years defined as 0.20-6.50 mIU/L (current RI: 0.20-4.00 mIU/L). 13% of TSH results were >4.00 but ?6.5 mIU/L, suggesting the lower limit of 4.00 mIU/L flags too many patients as abnormal. Of the TSH results between 4.01 and 6.5 mIU/L, 99.1% had a normal matched fT4 (current RI: 10.0-25.0 pmol/L). 99% of TSH results between 6.50-10.00 mIU/L had normal fT4, and 20% of TSH Conclusion: Big data analysis, alongside clinical consultation, is able to improve and optimize how thyroid hormone RIs more appropriately match patients in Alberta.

50 - A retrospective audit of point-of-care fetal scalp lactate analytical performance at a tertiary referral centre for high-risk pregnancies

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Objectives: Fetal scalp lactate (FSL) is used for intrapartum assessment of fetal acidosis despite the lack of quality specifications. We sought to assess long-term FSL analytical performance at our institution against currently used clinical decision limits. Design and Methods: Manufactured quality control (QC) and laboratory comparison (LC) data generated across four Nova StatStrip meters from Jan/2019 – Dec/2021 were analyzed. LC data were derived from split sample comparisons against GEM4000 (Jan/2019 – Nov/2019) and ABL90 analyzers (Dec/2019 – Dec/2021). Results: QC performance was similar for all meters with low QC consistently demonstrating higher imprecision than high QC (Table 1). LC data against both GEM4000 (n = 119) and ABL90 (n = 89) demonstrated mean biases of -0.3 mmol/L. Interestingly, moving average of bias analysis showed cyclical fluctuations between -0.1 to -0.6 mmol/L against GEM400, whereas this has held steady around -0.3 mmol/L against ABL90. This may suggest either higher calibration variance within GEM4000 lactate and/or meter strip lot-to-lot variation that fluctuates over time. Conclusions: Our FSL meters demonstrate persistent imprecision and biases that are not adequate for use with current clinical decision limits, reaffirming the need for higher analytical and quality specifications and consideration of analytical performance in setting clinical decision limits.

49 - Falsely elevated urine total protein leads to the diagnosis of a rare metabolic disorder

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Objectives: To resolve underlying spectrophotometric interference in urine total protein (UTP) measurement and determine its clinical significance. Methods: Our laboratory measures UTP on the Roche Diagnostics Cobas® c701. The method includes two key reagents: NaOH to alkalinize specimens and benzethonium chloride to produce turbidity. Change in specimen turbidity is assessed by measuring absorbance before and after the addition of benzethonium chloride. If absorbance exceeds the linear range of the instrument, results are flagged, and the specimen is automatically diluted 10x. Prior to reporting, dilutions are reviewed by technologists. Results: A UTP specimen of 3.1 g/L was flagged for high absorbance. The automatic dilution gave a result of 0.0 g/L. Repeat testing and manual dilution agreed with initial result. The urine was clear-pale yellow and agitation of the urine did not induce bubbles. The reaction tracing was suggestive of falsely elevated protein: NaOH (without benzethonium chloride) increased absorbance by 10-fold. To investigate, NaOH was manually added to the specimen resulting in a red-brown color change. The urine was sent off-site for testing by a method does that nor require alkalinisation (pyrogallol red). UTP was reported as 0.13 g/L. A review of the reagent package insert and literature suggested homogentisic acid (metabolite found in Alkaptonuria) as a possible interferant. The ordering physician was contacted regarding the interference, urine organic acids were ordered, and the urine was found to be positive for homogentisic acid. Conclusion: Homogentisic acid is a rare metabolite that can cause false elevated urine protein in methods that alkalinise specimens.

48 - Multicenter evaluation of SARS-CoV-2 serology assays shows differential response between inpatients, outpatients, and long-term care residents

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Objectives Measurement of SARS-CoV-2 antibodies has garnered interest, but its utility remains undetermined. Further research is required to better understand the immune response against SARS-CoV-2. This study evaluates the performance of four SARS-CoV-2 serology assays across different patient populations. Methods Collaboration among the Canadian clinical chemistry community allowed for the collation of SARS-CoV-2 serology data from eleven hospital and community laboratories across Canada. A total of 1,962 samples from 1,678 individuals was collected from inpatients, outpatients and long-term care (LTC) residents. Anti-SARS-CoV-2 antibodies were measured using four qualitative assays from Abbott (IgG only), Roche, Ortho, and Siemens. Not all samples were tested on all assays. Antibody response over time and between patient populations was examined. Clinical sensitivity and specificity were assessed. Results All assays demonstrated a high specificity (96.5 % - 100 %), and the sensitivity of assays were also comparable (87.4 %– 97.3 %) when considering those tested 14 days post-diagnosis. The Abbott IgG assay had the lowest sensitivity and the Siemens assay had the greatest sensitivity. Across all assays, sustained antibodies for all patient populations were observed up to 16 weeks post-positive PCR swab. A small subset of inpatients was monitored over an extended time and had detectable antibodies up to ten months post-PCR swab, measured by all four assays. Conclusion While antibody profiles varied across different patient settings (inpatient, outpatient and LTC), all assays demonstrated similar specificities. Differences in antibody kinetics between inpatients, outpatients, and LTC residents warrant assay performance validation for specific patient populations.

47 - Performance of saliva compared with nasopharyngeal swab for diagnosis of COVID-19 by NAAT in cross-sectional studies: a systematic review and meta-analysis

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Objectives: To assess the diagnostic performance of saliva compared with nasopharyngeal swab (NPS) for COVID-19.

Design and Methods: Database searches included Ovid Medline, Embase, Cochrane, and Scopus for studies that directly compared paired NPS and saliva specimens taken at the time of diagnosis. The focus was on patients presenting for initial diagnosis or screening, allowing findings to be generalizable to clinical and public health scenarios where saliva testing would be most useful. Study characteristics, pre-analytical and analytical variables were collected. Meta-analysis was performed using an exact binomial rendition of the bivariate mixed-effects regression model. Quality Assessment of Diagnostic Accuracy Studies 2 tool was used to assess risk of bias.

Results: Of 2683 records, 23 studies with 25 cohorts were included, comprising of 11,582 paired specimens. Three studies exhibited very low sensitivity (<53%) and were investigated separately as outliers. Meta-analysis showed a pooled sensitivity of 87% (95%CI=83-90%) and specificity of 99% (95%CI=98-99%), with an AUC of 0.98 (95%CI=0.96-0.99%). High heterogeneity was observed across the studies (I2 = 94%, p<.001). Pre-specified subgroup analyses revealed that outpatient setting, testing of symptomatic participants, utilization of a transport medium for saliva samples, deep throat coughing as a collection technique, employing an adequacy control, and use of a laboratory developed assay showed higher values of sensitivity (range=88-93%). Further meta-regression did not reveal any statistically significant differences. Most studies exhibited low or unclear risks of bias.

Conclusions: The results support the use of saliva NAAT as an alternative to NPS NAAT for the diagnosis of COVID-19.

46 - Who needs lights? A retrospective study on the impact of analytical bias resulting in an increase in phototherapy initiation

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Objectives: High blood total bilirubin (TBIL) can be toxic to the neonatal brain and cause kernicterus. A retrospective study was performed to identify the percentage of newborns who received phototherapy after measuring TBIL using different platforms. Design and Methods: Laboratory results (TBIL, hemolysis, arterial pH, hematological results) and clinical data (age, gestational age, and treatment with phototherapy) were analysed in 19,068 children born at William Osler Health System. TBIL was measured by diazo methods from Jan,2018-Oct,2019 (Beckman) and Apr,2018-Sep,2019 (Siemens Vista) and by vanadate oxidase (Siemens Atellica) from Mar,2019-Dec,2019. The percentage of newborns who received phototherapy during each of these time periods was reviewed. Results: When TBIL was measured by the Beckman-diazo assay, 10% of newborns underwent phototherapy (Figure 1A). A significantly larger percentage of newborns, 19.2% and 23.4%, received phototherapy when TBIL was measured by the Vista-diazo (Figure 1B) and Atellica-vanadate oxidase (Figure 1C) assays, respectively. The increase in phototherapy occurred at every age and gestational age on the Bhutani nomogram. Conclusions: Bias between different TBIL assays resulted in an increase in phototherapy rates at our hospital which led to subsequent unnecessary blood work and longer hospital stays.

45 - Shedding light on neonatal bilirubin variance across analytical methods: implications for clinical care and the need for phototherapy

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Objectives: Bilirubin is routinely measured in newborns to assess for jaundice and need for subsequent phototherapy. We sought to determine if there were significant biases between three different bilirubin assays that are routinely used in clinical practice. Design: In a prospective study, paired whole blood capillary and microtainer samples were collected in 57 newborns (22-female and 35-male, age range: 22 – 202 hours). Among them, 29 babies received phototherapy. Capillary Total Bilirubin (TBIL) was measured spectrophotometrically by ABL90. Microtainers were measured for TBIL measured on ABL90 and then centrifuged to measure TBIL using the vanadate oxidase (Siemens;Atellica) and colorimetric diazo (Roche;Cobas702) methods on resultant plasma. Results: TBIL measured by ABL90 compared very well to the diazo-Cobas. A significant negative bias was observed when vanadate oxidase-Atellica was compared to either ABL90 or diazo-Cobas methods (Figure 1). Need for phototherapy was determined using the Bhutani nomogram in 29 babies. Re-evaluation using the TBIL results from ABL90 and Cobas demonstrated a 41.4% and 47.6% reduction in the instances to either initiate or continue phototherapy based on TBIL results, respectively. Conclusions: Significant biases exists between different neonatal TBIL assays which may have a significant impact on patient management and the need for phototherapy.

44 - Using artificial intelligence to standardize SPEP albumin fraction interpretation

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Objectives: Interpretation of serum protein electrophoresis (SPEP) patterns by capillary electrophoresis (CE) is a manual process, making it susceptible to variability in interpretation. The objective of this study was to analyze historical SPEP migration patterns using artificial intelligence (AI) and standardize interpretation in the albumin fraction specifically. Design and Methods: Approximately 150,000 historical SPEP electropherograms were shared with Synthesis Health to develop a rule-based decision tree AI algorithm. The model was developed to identify a split albumin (SPLIT-A, n=123) migration pattern, where congenital or pancreatitis-induced bis-albuminemia cannot be ruled out. Migration patterns were also shared with Sebia Canada for consultation and compared to published literature. Results: Original attempts to develop a model identified 56 cases where LifeLabs interpretation and the AI model disagreed on SPLIT-A interpretation. Disagreement was due to either AI performance, or inconsistency in historical cases. Re-training interpreters for albumin interpretation did not improve AI performance. Rather, multiple reviewers for a given case disagreed 77% of the time. Consequently, new standards of practice for albumin interpretation were defined after consultation with the manufacturer and literature review. Incorporating these new standards in the AI model led to the identification of an additional 102 cases previously missed for the possible presence of bis-albuminemia. Conclusions: Using AI to analyze SPEP albumin fraction migration patterns led to the development of standardized interpretation, and consequently improved the quality of SPEP reporting at LifeLabs. This approach will be useful in analyzing other SPEP fractions relevant to the diagnosis and support of plasma cell dyscrasias.

43 - A simple rapid and robust mass spectrometry method for plasma busulfan suitable for pediatric dose optimization

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Objectives: Busulfan is an alkylating agent given as part of a conditioning regimen prior to hematopoietic stem cell transplantation. Optimal dosage in pediatric patients is individualized based on determination of area under the plasma busulfan concentration versus time curve following the first intravenous dose. A liquid chromatography-tandem mass spectrometry method (LC-MS/MS) was developed to simplify sample preparation and shorten turnaround time as compared to the previous gas chromatography electrochemical (GC) method. Design and Methods – The method uses 50 µL plasma and 50 µL busulfan-d8 labeled internal standard working solution that is liquid extracted with 1 mL of methanol. After vortexing and centrifugation, 1.0 µL supernatant is injected onto a Sciex 4500 QTRAP® LC-MS/MS system utilizing a C8 column and multiple reaction monitoring. Calibration is achieved using in-house prepared standards. Analytical run time is 6 minutes. Precision, accuracy, limit of quantification, and carryover were assessed. Results – The method was linear from 0.25 – 20 µmol/L, limit of quantitation was 0.02 µmol/L, and within- and between-run imprecision were both better than 4.7 %CV at all levels assessed. Carryover was < 0.02%. Method comparison studies found excellent correlation with GC-determined results (y = 0.97x+0.09; R2=0.977). One year after implementation, %CVs remain at 5.1 %CV or better obtained from QC data and EQA performance demonstrates excellent accuracy against reference assignment and method peers. Conclusions – A LC-MS/MS method for plasma busulfan was developed that has a low sample volume requirement and provides a rapid and simple sample preparation with short analytical time.

42 - Analytical validation and stability study of pleural fluid pH on the Radiometer ABL90 FLEX PLUS blood gas analyzer

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Objectives: Pleural fluid pH is helpful in differentiating uncomplicated from complicated pleural effusions. The Radiometer ABL90 FLEX PLUS is commonly used to test for pleural fluid pH, but it is not validated for this purpose by the manufacturer. We report the results of an in-house analytical validation, together with those of a stability study. Methods: The study used remnant, deidentified pleural fluid samples. Precision, method comparison, and stability studies were conducted following CLSI guidelines. The Abbott i-STAT1 with CG4+ cartridges was used as the comparator in the method comparison. pH values spanning the analytical measuring range were obtained by spiking individual or pooled samples with 2% acetic acid. Sample stability was tested at room temperature and 4 °C using sample aliquots in aliquot tubes or in safePICO syringes. Results: Within-run coefficients of variation were Conclusions: The Radiometer ABL90 FLEX PLUS demonstrates acceptable analytical performance for pleural fluid pH testing. Sample stability at 4 °C suggests that it may be feasible to consolidate testing to a single referral centre within a larger geographic region. Keywords: pleural fluid, pH, Radiometer, validation, stability

41 - Capability of a business intelligence platform to support the IFCC model of quality indicators in a tertiary care academic hospital

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Objectives: The IFCC model of quality indicators (MQI) includes 34 mandatory metrics for their impact on patient safety. Automated systems to capture and report non-conformances are essential for timely, standardized review of performance. We sought to identify capability within current hospital data sources to enable efficient business intelligence (BI) monitoring of key laboratory processes. Methods: The quality audit processes at Sunnybrook Health Sciences Centre (Toronto, ON) were reviewed. The current laboratory indicators were compared to the IFCC mandatory MQIs for compliance. Furthermore, the laboratory's capability to enumerate the IFCC MQIs was assessed against clinical and laboratory data sources that were classified according to existing linkage to BI reports, potential for database extraction, or manual reporting processes. Results: While almost all indictors were recorded into an existing database, considerable variability exists among the systems for robustness and data structure. 6/34 (18%) of QIs were linked to BI reports where all metrics exist within the LIS and have uniform coding (e.g. TAT data). 18/34 (53%) of QIs may be accessible from the LIS through coded comments but may not be uniformly captured, where a subset of 8 QIs required secondary review of the safety reporting system (RL6). The remaining 10 QIs (29%) were manual but available from middleware (n=4), other external databases (n=4), or monitoring was not applicable (n=2). Conclusions: Most IFCC MQIs potentially may be linked to the BI platform from existing sources. However, consistency of data capture was likely hampered by operator limitations to document events or apply uniform coding.

40 - Do instructions for at-home dried blood spot (DBS) collection affect the quality of collection? Data from the Canadian Longitudinal Study on Aging (CLSA) COVID-19 seroprevalence study

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Objectives: To understand the at-home dried blood spot (DBS) experience for aging adults through the assessment of blood collection forms and quality of blood collection, before and after improvements were made to the blood collection instructions.

Design and Methods: A total of 17,610 DBS devices (VelvetTM, Weavr Health) were mailed to participants, 14,778 devices were returned and processed. A questionnaire was developed to collect qualitative measures about the DBS experience for the first 3347 participants. Based on this data, blood collection instructions were revised for the remaining participants. Statistical analyses were completed in SPSS.

Results: The mean age was 69 (range: 51-96) years old, with 47% female. This cohort is highly educated (69% having a post-secondary degree/diploma). Younger participants (aged 50-59) were less likely to have difficulty understanding the instructions (OR:0.20, 95%CI:0.07-0.52). Participants who had difficulty understanding the instructions were more likely to experience difficulty with completing their sample (aOR:3.65, 95%CI:2.72-4.89). After improvements were made to the instructions, the number of incomplete samples returned decreased from 17% to just 3%, while those who returned a completely filled sample increased from 74% to 90%. Hemolysis decreased by 5%, samples with only a few drops decreased by 2%, and devices not returned in their biohazard bag reduced to 0. Those with improved instructions were more likely to return a complete sample, adjusted for age (aOR:1.54; 95%CI:1.24-1.92).

Conclusions: Clear instructions are critical for obtaining a sufficient at-home collected blood sample, especially in an aging population.

Keywords: COVID-19, dried blood spot, aging

39 - A case of monoclonal cryoglobulinemia with positive antiphospholipid syndrome serology

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Objectives: Paraproteins with antiphospholipid activity have been increasingly reported in patients with monoclonal gammopathy and positive antiphospholipid syndrome (APS) serology. Verifying a paraprotein's specific binding to phospholipids requires its separation from other immunoglobulins which is technically challenging. In fact, the purification techniques used in several published case reports are insufficient to definitively accomplish this task. We investigated a possible association of APS with a cryoglobulin in a 63 year-old male with recurrent thrombosis, a positive anti beta-2 glycoprotein-1 (anti-b2GP1) IgM, and an IgM kappa monoclonal gammopathy, who also had significant cryoglobulinemia. Design and Methods: With informed consent, serum was obtained and processed under temperature control. Immunofixation and SDS-PAGE were utilized to determine the cryoglobulins' constituent proteins. Precipitated cryoglobulins were resolubilized in an equal volume of APS-negative serum at 37°C. Anti-b2GP1 levels were quantified in neat serum, resolubilized cryoprecipitate, and cryoglobulin-depleted supernatant (cryo-supernatant) by ELISA (Euroimmun) performed at 37°C. Results: Immunofixation and SDS-PAGE confirmed that the cryoglobulin's predominant component was the known monoclonal IgM-kappa. Anti-b2GP1 IgM levels were 302, 255 and 43 RU/mL, in serum, cryo-supernatant, and resolubilized cryoprecipitate, respectively. Vendor provided positivity cut-off was 20 RU/mL (at 18 to 25°C). Conclusions: Exploiting the temperature-dependent reversible precipitation of cryoglobulins, we were able to purify and decipher the relationship between the patient's paraprotein and APS serology. ELISA results suggest that the patient's paraprotein is unlikely to have any antiphospholipid activity or cause a nonspecific false positive in the APS serologies. This supports the presence of a separate autoantibody of the same isotype.

38 - Sperm DNA fragmentation is not correlated with the oxidation-reduction potential in men presenting for infertility evaluation.

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Traditional semen analysis remains the standard of clinical care to initially investigate and diagnose male infertility. However, the basic semen analysis does not provide information on the oxido-reductive potential (ORP) and nuclear integrity of semen and spermatozoa, respectively. Sperm DNA fragmentation (SDF) and oxidative stress are markers believed to be implicated in the pathogenesis of male infertility. Thus, here were prompted to evaluate the relationship between ORP and SDF in infertile men receiving antioxidants. The cohort study included 64 men undergoing infertility evaluation. Sperm DNA fragmentation index (DFI) was measured with Tunel assay and ORP in semen was assessed using the standardized MiOXSYS system. Patients were then divided into two study groups according to the use of antioxidant supplementation. There was no statistically significant difference in the mean abstinence period (3.0±0.2 vs. 2.4±0.1 days), sperm concentration (64.9x106/mL (8.1) vs. 55.4x106/mL (10.4)) and DFI (15.8% (1.8) vs. 19.0% (2.3)) between groups (p=> 0.05). However, mean ORP was significantly lower in the no antioxidant compared to the FertilPro antioxidant group (1.0mV/106sperm/mL±0.2 vs. 1.6mV/106sperm/mL±0.4). We observed no significant correlations between SDF and semen ORP in the no antioxidant group (r=-0.02; p=0.89) and the FertilPro groups (r=-0.11; p=0.58). When applying the established clinical cut-off (1.34 mV/106 sperm/ml), only 6% of patients had both an abnormal SDF and ORP in the no antioxidant group and 17% of patients in the FertilPro group. These findings suggest that monitoring these markers in men with infertility may provide us with a better understanding of the complex relationship between semen

37 - Effect of temperature and time on the stability of hemoglobin in fecal immunochemical test specimens

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Objectives: A previous pilot study from our institution demonstrated that the stability of fecal immunochemical test (FIT) samples may be less than our current seven-day window. Our objective was to further evaluate the stability of FIT specimens after refrigeration or room temperature (RT) storage. Design and Methods: Experiments were performed with the OC-Sensor DIANA iFOB Test system (Eiken Chemical), using a positive clinical cut-off of 75 ng/L hemoglobin (Hb). Samples were analyzed at baseline, days 3, 5, 7, and 14 and categorized based on initial Hb concentration: Group A (n=40): 70-80 ng/ml, Group B (n=20): 90-110 ng/mL, and Group C (n=19): 190-210 ng/mL, with half stored at RT and half refrigerated. To further investigate stability of samples just above the cut-off, eight samples (Group D: 75-85 ng/mL) were measured at baseline and days 3, 4, and 7 after RT storage. Results: Group A and B RT specimens showed significantly reduced Hb on day three and seven, respectively, and day seven for refrigerated samples ($p < 0.05$). Group C showed a significant decrease in Hb on day three; refrigerated samples did not significantly decreased throughout the study. Combining data with pilot study for RT samples marginally above the cut-off (75-100 ng/mL) showed 100% positivity at date of collection (n=33), 63% on day 3 (n=19), 46% on days 4/5 (n=26), and 38% on days 6/7 (n=26). Conclusions: FIT samples showed reduced concentrations of Hb compared to baseline when stored at RT; refrigeration may improve stability. Specimens near the clinical cut-off may be particularly susceptible

36 - Towards provincial harmonization: strong correlation between lipase assays across vendors and analyzer types will enable assay harmonization across Alberta

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Objectives: Alberta is transitioning to a shared information system and provincial harmonization is a priority. This poses a challenge for lipase, which is offered on seven different analyzers from three different vendors and lacks standardization. This study evaluated the correlations between lipase assays used in Alberta with the aim to develop a series of correction factors to harmonize test results for lipase across the province. Design and Methods: Seven analyzers from three different vendors were used to measure lipase on 40 leftover patient plasma samples. Each sample was thawed and measured in duplicate on the same day at various laboratories throughout the province on the following analyzers: Roche cobas c701, Roche cobas Pro, Ortho Vitros 350, Ortho Vitros 4600, Ortho Vitros XT3400, Siemens Atellica, and Siemens Dimension EXL. Pearson correlation coefficients and correction factors were determined by ordinary Deming regression analysis using Analyse-it software. Results: Comparisons between the seven analyzers showed strong linear correlations but with large biases observed between the three vendors. Results are summarized in Table 1. Conclusions: Strong within and between vendor correlations were observed for all lipase assays ($r > 0.99$). This will enable the implementation of provincial lipase correction factors for harmonized reported results and facilitate future reference interval harmonization.

35 - Analytical validation of the Thermo Fischer Scientific B·R·A·H·M·S KRYPTOR® soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) assays in a North American setting

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Objective: Soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) testing are used for prognosis of pre-eclampsia. Our goal was to validate the B·R·A·H·M·S KRYPTOR® sFlt-1 and PlGF assays. Design and Methods: Precision [within (n=20) and between-run (n=20) using manufacturer controls and patient pools], matrix comparison [serum vs. EDTA plasma as both listed in instructions for use (IFU)], stability (2-80C), linearity and method comparison to Roche Elecsys PlGF and sFlt-1 assays (n=142) were performed. Coefficient of variation (CV), difference plots (95% levels of agreement; LoA) and Passing-Bablok regression (95% confidence intervals; CIs) were calculated. Results: Both sFlt-1 and PlGF CVs were Conclusions: Analytical performance in agreement with IFU was observed for the KRYPTOR sFlt-1 and PlGF assays; however, concentrations are different as compared to the Roche assays. Keywords: Preeclampsia, sFlt-1, PlGF, B·R·A·H·M·S KRYPTOR, Roche Figure 1. Method Comparison Between B·R·A·H·M·S KRYPTOR® and Roche Elecsys PlGF and sFlt-1 assays in serum Word count = 200 + 50 for Figure (Max = 250)

34 - Negative bias of HbA1c results with increasing triglyceride concentration on the Roche cobas© c513 platform

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Hemoglobin A1c (HbA1c) is a marker of glycemic control used for diagnosis and monitoring of patients with diabetes mellitus. Lipemia may be prevalent in this patient population because dyslipidemia is associated with diabetes mellitus and fasting is not required for HbA1c testing. This study aims to (1) characterize lipemic interference with the HbA1c immunoassay on the Roche cobas© c513 platform and (2) identify the proportion of patients affected using provincial data. Intralipid (Sigma Aldrich),Triglyceride-rich lipoproteins (TRL) from the ASSURANCE™ Interference Test Kit (SunDiagnostics), and high endogenous triglycerides were used to spike three whole blood pools. Bias in HbA1c results compared to baseline was defined as exceeding half the total allowable error (0.25 HbA1c units (%) or 3% change). HbA1c exhibited a negative bias with increasing triglyceride concentrations of all three formulations which was more pronounced at high HbA1c concentrations. Endogenous triglycerides yielded the lowest bias but induced a significant negative bias at >13.0 mmol/L when HbA1c exceeded 9.0%. Analysis of paired HbA1c and triglycerides results (N=3.1 M) in Alberta (2019-2021) suggests at least 0.04% (±0.002%) specimens may be impacted, equating to nearly 1000 HbA1c tests annually (~2.4M HbA1c tests per year). Falsely decreased HbA1c when run on the Roche cobas c513 immunoassay may result in missed diagnoses and/or inadequate therapy in patients with elevated HbA1c and triglycerides. Recognizing that whole blood specimens do not permit easy lipemia identification, mitigation strategies can include reflexive comments when triglyceride and HbA1c are elevated on paired samples and education through communication (e.g., via test directory).

33 - Application of Lean Six Sigma tools and CLSI standards to the verification and implementation of alternate phlebotomy supplies

Dana Bailey[1], Dalia Ghobrial[1], Jagath Dissanayake[1], Dhaliwal Jasmel[1], Jay Healey[1], George Ng[1], Kwabena Boateng[1], Diane Polidori[2], Tracey Henry[2], Cherry McCormick[2], Michelle Boychuk[2], Shivanthi Raveendrabose[2], Doug Tkachuk[1], Hui Li[1], Peter Catomeris[1]

[1]Dynacare, [2]Unknown affiliation

Objectives The COVID-19 pandemic has caused critical shortages in phlebotomy supplies, including vacuum tubes. Consequently, laboratories may consider products from alternate suppliers. Herein, we outline considerations required when introducing alternate products and provide correlation data between Greiner and Becton Dickinson (BD) serum gel barrier and citrate tubes. Design and Methods Lean/Six Sigma tools were used to plan, verify, implement, and manage introduction of alternate phlebotomy products. Qualitative metrics were captured regarding product interchangeability, compatibility, and sample integrity. CLSI GP34A guidelines were followed for tube comparisons. Paired serum samples from 10 outpatient volunteers were measured in duplicate for serum indices, routine chemistry, and immunoassays. Paired citrate samples from 10 volunteers prescribed warfarin were measured in duplicate for INR, PTT, and PT. BD North American and European citrate tubes were also compared. Results A toolkit based on Lean/Six Sigma principles was developed to manage tube verifications and product implementation. Using this process, we demonstrated equivalent performance of Greiner and BD tubes for routine chemistry and coagulation testing on the Roche cobas 8000 and the Sysmex CS-5100, respectively, except for magnesium, where a positive bias of 4.5% was observed with Greiner. Greiner needles and needle holders could be successfully used with BD tubes, and vice versa. Centrifugation of BD tubes at centrifugation conditions used for Greiner tubes did not compromise sample integrity or accuracy. Conclusions During supply shortages, laboratories must rapidly evaluate and implement alternate preanalytical supplies. Our toolkit and data can be used by other laboratories to expedite this process.

32 - Risperidone blood levels on the Abbott c series analyzers – faster turn-around-time

Salvatore Salamone[1], Mary Rose Hilaire[1], Rebecca Harney[1]

[1]Saladax Biomedical Inc.

Objectives: Risperidone is a drug approved for treatment of schizophrenia and bipolar disorder, and monitoring of risperidone blood levels is useful to assess medication adherence, efficacy, toxicity, and medication interactions. Currently, risperidone is measured with expensive and time-consuming liquid-chromatography/mass spectrometry methods at specialized laboratories, with significant turnaround time. Designed for use on clinical chemistry analyzers, the MyCare Psychiatry Total Risperidone Assay Kit is the first Health Canada licensed immunoassay for the measurement of risperidone active moiety. The risperidone reagents have been validated on the Beckman Coulter AU family of analyzers (AU480, AU680, and AU5800). We developed an application of the test for the Abbott Architect c4000 clinical analyzer and performed validation testing.

Design and Methods: Precision, linearity, sensitivity, and method comparison studies were performed on the Abbott Architect c4000. Precision was evaluated with three controls. Seven risperidone and 9-OH risperidone spiked serum samples throughout the assay range were used to assess linearity. Method comparison was performed compared to AU480 using 25 annotated specimens collected from patients taking risperidone.

Results: Analysis time was 10 minutes. Within-run %CVs were < 5%. The assay was linear throughout the measuring range. The Passing-Bablok regression statistics for the method comparison were R = 0.9957, slope = 0.969, and intercept of 0.835.

Conclusion: The MyCare Psychiatry Total Risperidone Assay Kit allowing rapid, precise, sensitive, and specific automated measurement of risperidone active moiety in human serum using the using the Abbott c series analysers.

31 - Risperidone blood levels on the Roche cobas c analyzers – faster turn-around-time

Salvatore Salamone[1], Mary Rose Hilaire[1], Rebecca Harney[1]

[1]Saladax Biomedical Inc.

Objectives: Risperidone is a drug approved for treatment of schizophrenia and bipolar disorder, and monitoring of risperidone blood levels is useful to assess medication adherence, efficacy, toxicity, and medication interactions. Currently, risperidone is measured with time-consuming LC-MS/MS methods with significant turnaround time. Designed for use on clinical chemistry analyzers, the MyCare Psychiatry Total Risperidone Assay Kit is the first Health Canada licensed immunoassay for the measurement of risperidone active moiety. The risperidone reagents have been validated on the Beckman Coulter AU family of analyzers. We developed an application of the test for the Roche cobas clinical analyzers and performed validation testing.

Design and Methods: Precision, linearity, sensitivity, and method comparison studies were performed on Roche cobas c501. Precision was evaluated with three controls. Seven drug-spiked serum samples were used to assess linearity. Method comparison was performed compared to AU480 using 42 annotated specimens collected from patients taking risperidone.

Results: Analysis time was 10 minutes. Within-run %CVs were < 4%, and within-laboratory %CVs were < 8%. The assay was linear throughout the measuring range. The Passing-Bablok regression statistics for the method comparison were R = 0.9848, slope = 0.925, and intercept of 0.1.

Conclusion: The MyCare Psychiatry Total Risperidone Assay Kit allows rapid, precise, sensitive, and specific automated measurement of risperidone active moiety in human serum using the Roche cobas using the Roche cobas analyzers.

30 - Clozapine blood levels on the Abbott Architect analyzers – faster turn-around-time

Salvatore Salamone[1], Mary Rose Hilaire[1], Rebecca Harney[1]

[1]Saladax Biomedical Inc.

Objectives: Clozapine is the only drug approved for treatment-resistant schizophrenia, and monitoring clozapine blood levels during treatment is useful to assess medication adherence, efficacy, toxicity, and medication interactions. Currently, clozapine is measured with time-consuming LC-MS/MS methods at specialized laboratories, with significant turnaround time. Designed for use on clinical analyzers, the MyCare Psychiatry Clozapine Assay Kit is the first FDA and Health Canada cleared immunoassay for the measurement of clozapine. The clozapine reagents have been validated on the Beckman Coulter AU family of analyzers. We developed an application of the test for the Abbott Architect c4000 clinical analyzer and performed validation testing.

Design and Methods: Precision, linearity, sensitivity, and method comparison studies were performed on the Abbott Architect c4000. Precision was tested with two clozapine-spiked serums. Seven clozapine-spiked serum samples were used to assess linearity. Method comparison was performed compared to AU480 using 25 annotated specimens collected from patients taking clozapine.

Results: Analysis time was 10 minutes. Within-run %CVs were 5%. Assay LoQ was 68 ng/ml. The assay was linear throughout the measuring range. The regression statistics for the method comparison were R = 0.9965, slope = 0.976, and intercept of -0.6.

Conclusion: The MyCare Psychiatry Clozapine Assay Kit allows rapid, precise, sensitive, and specific automated measurement of clozapine in human serum using the Abbott Architect c series analysers.

29 - Clozapine blood levels on the Roche cobas c analyzers – faster turn-around-time

Salvatore Salamone[1], Mary Rose Hilaire[1], Rebecca Harney[1]

[1]Saladax Biomedical Inc.

Objectives: Clozapine is the only drug approved for treatment-resistant schizophrenia, and monitoring clozapine blood levels during treatment is useful to assess medication adherence, efficacy, toxicity, and medication interactions. Currently, clozapine is measured with time-consuming LC-MS/MS methods at specialized laboratories, with significant turnaround time. Designed for use on clinical analyzers, the MyCare Psychiatry Clozapine Assay Kit is the first FDA and Health Canada cleared immunoassay for the measurement of clozapine. The clozapine reagents have been validated on the Beckman Coulter AU family of analyzers. We developed an application of the test for the Roche cobas c clinical analyzers and performed validation testing.

Design and Methods: Precision, linearity, sensitivity, and method comparison studies were performed on Roche cobas c501. Precision was evaluated with controls. Seven clozapine-spiked serum samples were used to assess linearity. Method comparison was performed compared to AU480 using 43 annotated specimens collected from patients taking clozapine.

Results: Analysis time was 10 minutes. Within-run %CVs were < 7%, and within-laboratory %CVs were < 8%. The assay was linear throughout the measuring range. The Passing-Bablok regression statistics for the method comparison were R = 0.9963, slope = 1.001, and intercept of 5.0.

Conclusion: The MyCare Psychiatry Clozapine Assay Kit allows rapid, precise, sensitive, and specific automated measurement of clozapine in human serum using the Roche cobas analyzers.

28 - Evidence-Based Harmonization of Adult Reference Intervals Across Canada using Big Data Analytics: A Report of the CSCC Working Group on Reference Interval Harmonization (hRI)

Mary Kathryn Bohn[1], Albert Tsui[2], Dana Bailey[3], Cynthia Balion[4], George Cembrowski[5], Jake Cosme[6], James Dalton[7], Vincent De Guire[8], Higgins Victoria[9], Trefor Higgins[10], Benjamin P Jung[11], Joseph Macri[4], Zahraa Mohammed-Ali[6], David Seccombe[12], Julia Stemp[13], Jennifer Taher[14], Allison Venner[10], Nicole M.A. White-Al Habeeb[3], Christine Collier[15], Khosrow Adeli[16]

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Background: The Canadian Society of Clinical Chemists (CSCC) Working Group (WG) on Harmonized Reference Intervals (hRIs) aims to establish hRIs for key laboratory tests and support their implementation across Canada. Harnessing the power of big data, both direct and indirect data sources were examined, and common RIs were established and verified for 17 biochemical markers. Methods: Retrospective laboratory data was extracted for the same two-year period from four community laboratories across Canada for 23 analytes. Age-, sex-, and laboratory-specific differences for each analyte were assessed and 17 hRIs were established using the indirect truncated maximum likelihood (TML) method, and verified using serum and plasma from 60 healthy Canadian adults in nine clinical laboratories with different instrumentation (i.e., Abbott-NF, Beckman-AB, Ortho-NB, Ortho-ON, Roche-AB, Roche-BC, Roche-ON, Roche-ON, Siemens-QB). Results: Analysis revealed few statistical differences between laboratory centers/provinces using different analytical platforms, supporting the feasibility of RI harmonization. Sex-specific hRIs were established for: alanine aminotransferase, alkaline phosphatase, creatinine, and total bilirubin. Age-specific hRIs were necessary for alkaline phosphatase. hRIs were verified across nine Canadian laboratories with 12 meeting the proposed hRI 80% criterion. Select exceptions (e.g. albumin) prompted further investigation and discussion. Conclusions: The comprehensive approach to RI harmonization developed by the CSCC hRI-WG, includes: (1) analysis of big-data from community laboratories across Canada; (2) statistical evaluation of age-, sex-, and laboratory-specific differences; (3) derivation of hRIs using the TML method; and (4) hRI verification across nine laboratories with different instrumentation. Future work will focus on supporting hRI implementation in Canadian laboratories.

27 - Method evaluation of an automated fecal calprotectin immunoassay

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Objectives: The presence of fecal calprotectin (fCal) is a sensitive marker of gastrointestinal inflammation that is useful for diagnosis and monitoring of inflammatory bowel diseases. The objective of this study was to evaluate the analytical performance of the automated fCal chemiluminescent immunoassay on the Diasorin Liaison® XL. Design and Methods: Analytical evaluation included linearity, imprecision, limit of quantitation (LoQ), and method comparison to the Bühlmann fCal ELISA in clinical use at our institution. Additionally, stool extract precision and stability were assessed, with precision assessed using normal, borderline elevated, and elevated samples extracted in triplicate. Results: The Liaison fCal assay was linear within the analytical measuring range (R2>0.99, slope: 0.99, intercept: 8.8). The total between-day imprecision was 3%. CV's near the LOQ were 1-2%. The extract precision was 2%, 7%, and 12% for low, moderate, and high samples respectively. Extracts were stable for up to 8 hours at room temperature or 3 days at 4 °C. The method comparison against the Bühlmann fCal (n=73) had a Pearson's r of 0.89 (slope: 0.61, intercept: -29.63) and an average bias of -41.6% for Liaison fCal. The qualitative agreement was 72% overall, with 89%, 50%, and 78% concordance for normal, borderline elevated, and elevated samples respectively when compared to the Bühlmann fCal. Conclusions: The Liaison fCal immunoassay demonstrated acceptable analytical performance. Consistent with published studies, a significant negative bias relative to Bühlmann fCal was found, and thus it is important to consult with clinicians to ensure appropriate interpretation before clinical implementation

26 - Characterizing the SARS-CoV-2 antibody response in COVID-19 inpatients and outpatients: Longitudinal serological profiling of patients enrolled in the GENCOV study

Gregory Morgan[1], Laurent Briollais[2], Karen Colwill[2], Selina Casalino[2], Chloe Mighton[3], Sunakshi Chowdhary[2], Erika Frangione[2], Monica Chung[2], Chun Yiu Jordan Fung[2], Georgia MacDonald[2], Elisa Lapadula[2], Saranya K.Arnoldo[4], Erin Bearss[5], Alexandra Binnie[6], Yvonne Bombard[3], Bjug Borgundvaag[7], Howard Chertkow[8], Marc Clausen[9], Marc Dagher[10], Luke Devine[11], Hanna Faghfoury[12], Steven M. Friedman[7], Lee W. Goneau[13], Zeeshan Khan[14], Tony Mazzulli[1], Allison McGeer[1], Shelley L. McLeod[7], Konika Nirmalanathan[15], Trevor J. Pugh[16], David C.Richardson[17], Jared Simpson[18], Seth Stern[14], Lisa Strug[19], Ahmed Taher[14], Iris Wong[14], Natasha Zarei[14], Anne-Claude Gingras[2], Jordan Lerner-Ellis[1], Jennifer Taher[20]

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Objectives

Characteristics of the SARS-CoV-2 antibody response which are associated with COVID-19 severity remain unclear. We assessed the SARS-CoV-2 antibody response in unvaccinated COVID-19 positive adults to identify differences between individuals with variable COVID-19 severity.

Design and Methods

SARS-CoV-2 antibody levels were measured in serum or plasma collected from inpatients at baseline (n=138) and 1-month (n=34), and outpatients at 1-month (n=427) post-COVID-19 diagnosis. A laboratory-developed enzyme-linked immunosorbent assay was used to measure antibody isotypes (IgG, IgA, IgM) against SARS-CoV-2 antigens, including spike (S), nucleocapsid (N), and spike receptor-binding domain (RBD). Total anti-S and anti-N antibodies were quantitatively and qualitatively measured, respectively, using Health Canada-approved Roche Elecsys Anti-SARS-CoV-2 assays. The Mann-Whitney U test was used to compare patient groups, while quantile regression was used to identify associations with patient characteristics.

Results

Compared to outpatients, inpatients were older, had a higher body mass index (BMI) and higher rates of comorbidities, including diabetes, hypertension, and cancer. Age was associated with higher anti-S, RBD, and N antibody levels in outpatients, and lower levels in inpatients at baseline. Multivariate analyses adjusted for gender, age, and BMI identified outpatients' total anti-S antibodies were positively correlated with age and BMI, and negatively correlated with white/European ethnicity. At 1-month, inpatients had significantly higher total anti-S antibodies compared to outpatients, which correlated with anti-S and RBD isotypes. When comparing inpatients' longitudinal data, all antibodies increased after 1-month except anti-N IgA and IgM.

Conclusions

Our findings inform us of associations between the SARS-CoV-2 antibody response and patient characteristics.

25 - Public knowledge of the SARS-CoV-2 antibody response and associated serological testing: A GENCOV study cross-sectional survey

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Objectives

Throughout the COVID-19 pandemic, there has been interest among the public to understand the relationship between SARS-CoV-2 antibodies and immunity. However, these concepts can be challenging to understand which may lead to false interpretations or misconceptions. We conducted a cross-sectional survey of COVID-19 positive adults residing in Ontario, Canada to explore how well people understand the SARS-CoV-2 antibody response and serological testing.

Design and Methods

Study participants were recruited through fliers or by prospective recruitment of outpatients and hospitalized inpatients with COVID-19. An 11-item questionnaire was developed by researchers, nurses, and physicians in the GENCOV study team to assess participants': 1) knowledge of SARS-CoV-2 antibodies and immune protection, 2) knowledge of serological testing, and 3) understanding of SARS-CoV-2 variants in relation to vaccination. Participants were prompted to complete the online survey upon enrolment.

Results

Responses were obtained from 739 of 859 eligible participants (86% response rate). In general, respondents understood asymptomatic infection, scientists' current knowledge of SARS-CoV-2 antibodies, and that antibody status should not influence adherence to public safety measures. Conversely, respondents poorly understood the level of immunity conferred by antibodies, the impact of SARS-CoV-2 variants on vaccine efficacy, and how seroconversion may impact the interpretation of SARS-CoV-2 antibody results. Respondents who were either: 1) more educated, 2) aged 18-44, or 3) more affluent were more likely to respond correctly to questions.

Conclusions

The findings of this study enable us to focus education efforts on populations with poorer knowledge to guide adoption of preventative health practices.

24 - Analytical verification of fecal calprotectin using the Buhlmann and Liaison assays on the Siemens Atellica and DiaSorin Platforms

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Objectives: Fecal Calprotectin (FC) is a noninvasive, surrogate marker of intestinal inflammation, used for triaging patients with symptoms of inflammatory bowel disease (IBD) and management of IBD patients. The study objective was to evaluate the analytical performance of the Liaison Calprotectin and the Buhlmann fCal turbo assays. Design & Methods: Patient samples with clinical suspicion of IBD were used in the study. FC was extracted from stool samples and measured following manufacturers' instructions. Precision was assessed using quality control material and patient samples. Patient sample admixtures were used for linearity assessment. A three-way method comparison with our current laboratory method was also performed (Liaison, Buhlmann, and ImmunoDiagnostik ELISA Calpro assays). Results: Total imprecision for the Buhlmann assay was Conclusions: The two FC assays showed acceptable precision and linearity but minimal agreement, as the Buhlmann assay showed a significant positive bias. Calprotectin methods do not agree and thus, we recommend that the same FC method and that assay-specific cut-offs be used to monitor patients during treatment and advocate for standardization of FC assays.

23 - Multisite evaluation of high-sensitivity cardiac Troponin T with patient pools on different Roche analyzers: Interim report on observed components of variance

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Objectives: The impact and prevalence of non-reproducible cardiac troponin results have been highlighted in recent publications and analyzers as it pertains to high-sensitivity cardiac troponin T (hs-cTnT) (Clin Chem Lab Med 2021;59:1972-1980). Here we offer an interim assessment of the components of variation of hs-cTnT results using patient materials across eight provinces in Canada.

Design and Methods: Plasma pools (low-level and high-level) and one serum pool (mid-level) were constructed, frozen (≤ -70^{0}C), transported (dry ice), with instructions on handling the aliquots (e.g., centrifugation for 10 minutes at 3000 *g*) prior to testing. The materials were tested on 36 different Roche instruments comprising 4 different analyzer models and 2 assay modes (9 min n=27, and 18 min n=9 assay time). Fixed and random effect multilevel models were used to assess the influence of analyzer model and hs-cTnT pool with different assay modes using categorical variables.

Results: Multivariate analyses among sites using the 18 min assay time revealed that the intra-class correlation coefficient for analyzer model was 0.197 and fixed effects indicated a statistically significant interaction ($p<0.043$) between the pool and analyzer models. There were no statistically significant fixed or random effects observed among the 9 min assay mode data. **Conclusion:** These interim findings suggest that for the 18 min assay (i) analyzer model contributes ~20% of the observed variance among sites using and (ii) statistically significant changes in hs-cTnT results were observed between analyzer models for a specific sample pool. Additional rounds of testing are needed to confirm these initial findings.

22 - A national study to evaluate analytical performance specifications for high-sensitivity cardiac troponin assays

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Objectives: The impact and prevalence of non-reproducible cardiac troponin results have been highlighted in recent publications. Here we offer an interim assessment of different analytical performance specification (APS) targets for high-sensitivity cardiac troponin (hs-cTn) assays using patient materials across eight provinces in Canada.

Design and Methods: Plasma pools (low-level and high-level) and one serum pool (mid-level) were constructed, frozen (≤ -70^{0}C), transported (dry ice), with instructions on handling the aliquots (e.g., centrifugation) prior to testing. The materials were tested on 36 Roche instruments, 8 Beckman instruments, 8 Abbott instruments, and 6 Siemens instruments. Two different APS criteria were used: Model-2 (biological variation(BV): short-term BV estimates from Clin Chem 2021;67:256-264) and Model-3 (state-of-the-art: ±3.4 for hs-cTn <15 ng/L and ±20% for ≥15 ng./L from Clin Chem Lab Med 2021;59:e267-e270).

Results: Model-2 identified 20 discordant results at the low-level and 10 results at the mid-level, as compared to 0 discordant results with Model-3 (Table 1). At the high-level no discordant results were obtained with either APS criteria.

Conclusion: The findings from this multisite study suggest that APS targets obtained from BV estimates (Model-2) are too stringent, especially at normal concentrations (i.e., <10 ng/L) for hs-cTn assays.

Keywords: Proficiency testing, Quality control, Troponin.

21 - Multisite testing with different high-sensitivity cardiac troponin I assays in the normal range and near the 99th percentiles

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Objectives: Previously we created patient plasma pools that have been used to establish precision and assay performance for several high-sensitivity cardiac troponin I (hs-cTnI) assays (CMAJ Open 2020;8:E676-E684). Now we wish to assess these materials in a multisite study with several different hs-cTnI assays and platforms. Design and Methods: Two plasma pools (Normal-A; 99th-percentile) that were tested in 2014 and another Normal-B pool in 2017 (storage ? -700C) were utilized (Clin Chim Acta 2019;498:27-29). Normal-A and 99th-percentile materials were tested on 9-different Abbott platforms [i1000(n=2)/i2000(n=5)/Alinity(n=2)], 7-different Siemens platforms [ADVIA(n=1)/Atellica(n=4)/Vista(n=2)], with Normal-B and the 99th-percentile material tested on 9-different Beckman platforms [Access(n=2)/DxI600(n=2)/DxI800(n=5)] (as Normal-A hs-cTnI concentration was at the limit of detection for Beckman). The laboratories were instructed to thaw aliquots (sent on dry ice and kept frozen) at room temperature (15-min), mix, and centrifuge (3000g for 10-min) prior to testing. Results: The overall mean [ng/L]/SDs/CVs for Normal-A and 99th-materials obtained in 2022 for Abbott hs-cTnI was 4.8/0.8/17% and 31.5/4.1/13% as compared to 4.4/0.3/6.8% and 30.1/2.0/6.6% in 2014 (1st 9-measurements on 1 i2000-instrument). The Atellica/ADVIA estimates on these materials were 4.8/0.7/14% and 40.7/2.8/6.9% with Vista estimates of 9.0/1.1/12% and 57.7/1.1/1.9%. Normal-B measured in 2022 for Beckman hs-cTnI was 4.1/0.9/22% as compared to 3.7/0.5/14% in 2017 (1st 9-measurements on 1 Access-instrument). The 99th-percentile material yielded estimates of 22.6/2.3/10% for the Beckman assay. Conclusions: These data further demonstrate the utility of patient pools for long-term monitoring for hs-cTnI. Higher variation is evident via measurement on multiple analyzers especially in the normal range.

20 - Performance evaluation of BiliCare™ transcutaneous bilirubin device

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Objectives: The aim of this study was to evaluate the analytical performance of a new transcutaneous bilirubin (TcB) device – BiliCareTM (Natus, Pleasanton, CA). Design and Methods: The neonatal TcB measurements were compared between BiliCareTM and the existing BiliChekTM systems (n=30). TcB measured by BiliCareTM were also compared with total serum bilirubin (TsB) using Roche Cobas702 chemistry analyzer (n=22) and whole blood bilirubin using Radiometer ALB 835 (n=11). Reproducibility was assessed by repeating TcB measurements with a BiliCareTM on a normal neonate and one with jaundice 20 and 16 times respectively within 25 minutes. Results: Compared with BiliChekTM, BiliCareTM has demonstrated am average bias of -17.5% (BiliCareTM = 0.7166BiliChekTM +18.194, R=0.8819). BiliCareTM has a better agreement with Cobas702 (BiliCareTM = 0.776Cobas702 +48.768, R=0.8843, average bias 10.3%). Similarly, BiliCareTM has a -7.2% average bias compared with ABL835 (BiliCareTM = 0.6166ABL835 +54.464, R=0.8287). At TcB 94.5 and 269 μmol/l levels, BiliCareTM has demonstrated imprecision as 8.9% and 6.9% respectively. Conclusions: The new BiliCareTM correlates with total serum bilirubin on Chemistry analyzer and is acceptable for neonatal transcutaneous bilirubin testing. Key words: transcutaneous bilirubin, BiliCareTM, method evaluation, comparison study

19 - Sample suitability and stability in different blood collection tubes for volatile alcohols and glycols analysis

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Objectives: Blood collection tube suitability and sample stability for volatile alcohols, ethylene glycol (EG), and propylene glycol (PG) are not standardized. This study sought to systematically examine the sample suitability and stability in different tubes. Design and Methods: Two pools of whole blood were created and spiked with two levels of Methanol, Ethanol, Isopropanol, Acetone, EG, and PG. Spiked whole blood was added to 4 replicates of each blood collection tube (Grey/Red/Lavender top tube, SSTTM, PSTTM, and BarricorTM tube) for different storage conditions ((up to 2 days at room temperature (RT), 14 days at 4oC, and 28 days at -20oC)). An aliquot was prepared from baseline replicates. Volatile alcohols and glycols were analyzed by an Agilent 8890 gas chromatography system. Results: All blood collection tubes have demonstrated similar performance over different storage conditions, i.e. to be statistically insignificant ($p>0.05$) with the only exception of PG at the high concentration of day 7 at 4oC condition (p Conclusions: Grey/Red/Lavender top tube, SSTTM, PSTTM, and BarricorTM tube are all suitable for volatile alcohol and EG/PG analysis. Samples are stable for 2 days RT, 14 days at 4oC, and 28 days at -20oC. Key words: Sample stability, aliquot stability, blood collection tubes, volatile alcohol, glycol

18 - Performance evaluation of pancreatic amylase and lipase assays on a Roche c702 analyzer in the clinical setting

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Objectives: Currently, Sinai Health System offers total amylase as the only blood test to aid in diagnosis and management of pancreatitis. We sought to evaluate analytical performance of pancreatic lipase, and pancreatic amylase as another alternative pancreatitis marker, on the Roche c702 system. Methods: Imprecision, relative accuracy, and linearity were assessed against total allowable error goals set by Accreditation Canada Diagnostics (ACD). Additionally, 190 samples from 159 unique patients were used to assess diagnostic agreement between total amylase, pancreatic amylase, and lipase methods. Patient chart review was performed to assess how amylase and lipase measurements may be used to support patient care. Results: Total imprecision (%CV) was 0.5% for amylase and 1.2% for lipase. Lipase showed good correlation compared to the Sekisui Diagnostics assay performed on the Abbott Alinity instrument with R = 0.93 and mean relative bias of 13.0%. Pancreatic amylase showed good correlation with a peer Roche c702 laboratory with R = 1.0 and mean relative bias of 1.7%. Lipase was verified to be linear between 10-8500 U/L. A total of 23.9%, 21.8% and 17.0% of individuals had values above the expected range for total amylase (32-120 U/L), pancreatic lipase (13-60 U/L) and pancreatic amylase (13-53 U/L). Pancreatic disease was confirmed in 15.8% of people with elevated total amylase, 21.8% of people with elevated pancreatic lipase, and 18.5% of people with elevated pancreatic amylase. Conclusions: These studies justified further validation and implementing the Roche pancreatic lipase assay given the strong clinical utility of pancreatic lipase in the diagnosis of acute pancreatitis.

17 - Spirited away: Can ethanol testing in add-on orders produce meaningful results?

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Objective: Ethanol is a volatile substance, and unopened tubes are required for testing. However, add-on requests in previously opened tubes are commonly received, yet ethanol stability in this setting is unclear. We compared analyte stability in opened versus unopened tubes with respect to time elapsed, specimen volume, and automation. Methods: Ethanol-negative serum specimens were pooled and spiked at four different ethanol concentrations in 100 or 500µL specimen volumes. Subsequently, unopened and opened tubes of ethanol-spiked serum were stored for up to 4 hours at room temperature. Additionally, spiked specimens near the critical value threshold (~55 mmol/L) were stored for up to 4 hours exposed to air. Finally, to mimic a real-life add-on scenario, ethanol-spiked samples were subjected to automation, tested for acetaminophen, stored for 2 hours, and then assayed for ethanol. All measurements were made using the Abbott Architect platform. Results: The mean 4-hour recovery across all concentrations in opened 500µL specimens was 87.4% (95% CI: 81.8-94.0%). With a 100µL specimen, the mean recovery dropped to 52.9% (95% CI: 50.2-55.7%). Also, a mean recovery of 85.4% (95% CI: 84.2-86.1%) was observed for specimens spiked near the critical value threshold, and only 1 specimen was misclassified. Finally, the add-on mimic experiment showed a mean recovery of 101.5% (95% CI: 97.7-105.4%) across the entire analytical measurement range. Conclusion: Add-on ethanol orders may be accepted for specimen volumes of ?500µL and a storage time of 2 hours. Results within a ±25% total allowable error (TAE) are feasible when add-on ethanol testing is performed using routine automation.

16 - Postprandial inflammation and metabolic dysfunction in adolescents with obesity and insulin resistance

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Objectives: Postprandial dyslipidemia is an independent risk factor for cardiovascular disease (CVD). The objective of the current study was to characterize the postprandial inflammatory and metabolic profiles of adolescents with obesity and insulin resistance (IR), and to assess their role in the pathogenesis of postprandial dyslipidemia. Design and Methods: Adolescents with normal weight (NW; N=15), obesity and mild IR (N=20), and obesity and severe IR (N=10) were recruited. All participants (12- Results: Among inflammatory profiling, levels of fasting and postprandial interleukin (IL)-6 and calprotectin were significantly elevated in both obese groups compared to the NW response (P Spearman rho>0.5, P In metabolomic profiling using NMR, valine, leucine, and isoleucine (branched-chain amino acids, BCAAs) and alanine were significantly elevated in obesity, particularly those with IR (P 0.7, P Conclusions: Adolescents with obesity and IR exhibit significant fasting and postprandial dysregulation of several inflammatory and metabolic markers integral to lipid metabolism. These data may offer novel subclinical biomarkers for early metabolic and cardiovascular diseases, such as postprandial dyslipidemia, in at-risk adolescents.

15 - Continuous reference intervals using an LMS-based approach for 14 clinical parameters in the CALIPER cohort of healthy children and adolescents

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Objectives: Continuous LMS-based reference intervals have been suggested to assist pediatric test result interpretation by enabling improved visualization of complex analyte concentration patterns and calculation of percentile scores adjusted for both gender and age. The current study established LMS-based continuous reference intervals for 14 biomarkers in the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER) cohort of healthy children and adolescents. Design and Methods: Data from healthy children and adolescents aged 6 months to Results: LMS-based models and percentile curves were established for 14 common pediatric biomarkers that exhibit dynamic covariance with age (e.g., alkaline phosphatase) and/or wherein the magnitude of difference from the population mean may be clinically relevant (e.g., triglycerides). The LMS model captured age- and sex-specific distributions accurately and was not substantially influenced by outlying points. Conclusions: This is the first study to establish LMS-based continuous reference intervals for biochemistry markers in a healthy pediatric population. The current LMS-based approach serves to provide comprehensive reference interval models and mathematically interpolated percentiles to improve test result interpretation, particularly with repeated measures and during patient follow-up over time. This method may assist in facilitating a patient-centered approach to laboratory medicine and improve pediatric test result interpretation.

14 - Clinical validation and prospective monitoring of adult and pediatric SARS-CoV-2 antibody response using the SeroIndex Kantra ELISA: Potential utility and applications

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Objectives: Characterizing the pediatric serological response to SARS-CoV-2 is critically required as infection and vaccination rates rise; however, an evidence gap persists. The objective of this study was to clinically validate the COVID-SeroIndex IgG ELISA and characterize antibody titres among pediatrics and adults. Design and Methods: The COVID-19 SeroIndex is a two-phase assay: a qualitative and quantitative ELISA, which test for antibodies reactive to the recombinant receptor-binding domain of the SARS-CoV-2 Spike protein and to the full-length Spike protein, respectively. Clinical validation of the COVID-SeroIndex was completed, including precision, sensitivity (n=7 PCR-positive patients), and specificity (n=30 pre-2019 specimens). Approximately 500 asymptomatic subjects (6-78 years) were recruited from the community. Participation included informed consent, a health questionnaire, and blood donation. Serum specimen results were considered in reference to COVID-19 vaccination and infection history. Results: Clinical validation demonstrated excellent precision (CV=160 AU/mL). A decrease in antibody titres was observed after 150 days post-double vaccination; however, antibodies were still detectable at 300 days. Conclusion: This study demonstrates excellent performance of the COVID-SeroIndex for the quantitative characterization of SARS-CoV-2 IgG antibodies in pediatric and adult populations. This assay may have particular utility in rural communities or small laboratories given its low resource requirements.

13 - Serological Antibody Response to SARS-CoV-2 Vaccination in a Large Cohort of Canadian Children, Adolescents, and Adults

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Background: Quantitative anti-SARS-CoV-2 antibody immunoassays present potential utility as surrogates of breakthrough infection risk. Children have been differentially impacted by the SARS-CoV-2 pandemic, presenting with unique immune response to naïve infection relative to adults. It is essential to investigate age-specific differences in antibody response to SARS-CoV-2 vaccination.

Methods: 938 specimens (451 adult and 487 paediatric) were collected in this cross-sectional study with informed consent. Participation required completion of a health questionnaire and blood donation. A subset of participants were longitudinally monitored over a nine month period (Aug-Apr 2022). Sera were assayed by two immunoassays DiaSorin LIAISON SARS-CoV-2 TrimericS IgG and Abbott AdviseDx SARS-CoV-2 IgG II assays.

Results: Serokinetic antibody response in participants who received two doses of an mRNA vaccine demonstrated a strong negative correlation with time post-dose (n=394). A statistically significant difference was observed between pediatric (mean±SD=2037±1515 BAU/mL) and adult (1444±1277 BAU/mL) antibody titres when adjusting for time post-dose (p=0.018). A strong correlation between titres on the AdviseDx and TrimericS assays was determined, with high proportional bias.

Conclusions: This is the largest evaluation of commercially available quantitative SARS-CoV-2 antibody assays in a cohort of Canadian children, adolescents, and adults. Findings suggest children have higher antibody titres as compared to adults post-administration of an mRNA vaccine. Future work is needed to relate antibody presence to functional immune response as well as risk of breakthrough infections.

12 - Pediatric reference interval verification for special chemistry, immunoassay, and cancer markers on the Abbott Alinity ci system

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Background: The Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER) has developed an extensive database of reference intervals (RIs) for several biomarkers on various analytical systems, including special chemistry, immunoassay and cancer markers used to inform pediatric clinical decisions. In the current study, pediatric RIs were verified for 28 assays on the Abbott Alinity system based on the analysis of samples collected from healthy children and adolescents (birth-18 years) and comparison to comprehensive RIs previously established for Abbott ARCHITECT assays.

Methods: Analytical performance of Alinity assays was assessed through precision, linearity, and method comparison. 100 serum samples from healthy children recruited with informed consent were analyzed for 28 Alinity assays. The percentage of results falling within published CALIPER ARCHITECT reference and confidence limits was determined. RIs were considered verified if <90% of laboratory test results fell within previously established confidence limits.

Results: All assays demonstrated acceptable performance on the Alinity ci system. Of 28 assays assessed, 26 met the criteria for verification. Several pediatric reference values were below the limit of detection for cancer markers (i.e. CEA, CA 19-9, total PSA). Only 71% and 81% of pediatric samples fell within past CALIPER ARCHITECT RIs for anti-CCP and alpha-1-Antitrypsin, and thus a new Alinity-specific reference interval may be needed.

Conclusions: These data demonstrate marked concordance between ARCHITECT and Alinity systems for 26 assays, as well as the robustness of previously established CALIPER RIs in healthy children. Expanding the utility of the CALIPER database (www.caliperdatabase.org) to include Alinity assays for special chemistry and cancer markers will assist clinical laboratories using this new platform and contribute to improved clinical decision-making.

11 - Pediatric reference intervals for serum calprotectin in the CALIPER cohort of healthy children and adolescents: A potential biomarker for neonatal and pediatric bacterial infection

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Background: Measurement of serum calprotectin in neonates and children with suspected bacterial infection has been suggested to improve outcomes due to higher diagnostic sensitivity relative to C-reactive protein and procalcitonin. The objective of the current study was to analytically evaluate an automated serum calprotectin assay and establish accurate pediatric reference intervals RIs in the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER) cohort.

Methods: An analytical validation was completed, including precision, linearity, and method comparison. 300 healthy children and adolescents (0 to <19 years) were recruited by the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER). Health information, anthropometric measurements, and blood samples were collected in the Greater Toronto Area. Serum samples were analyzed at using the Gentian serum calprotectin assay on the Abbott Architect system. Data were analyzed in accordance with CLSI EP28-A3c guidelines.

Results: The calprotectin immunoassay demonstrated acceptable precision and was linear across the reporting range (slope:0.97, intercept:0.12, R2:0.999). Method comparison evaluation demonstrated reproducible performance on two systems (slope:0.95, intercept:0.08, R2:0.997, bias:0.18mg/L). No significant age and/or sex-specific differences were observed in CALIPER cohort (RI:0.15-2.97mg/L). Significantly higher concentrations were observed in children with obesity.

Conclusions: In the current study, an analytical validation of a serum calprotectin immunoassay was completed and pediatric RIs were established in the CALIPER cohort. Presented data contribute to our knowledge of serum calprotectin levels from birth to adolescence in healthy children relative to disease states. Future work will focus on delineating the clinical utility of calprotectin in identifying pediatric bacterial infection.

10 - Pediatric reference interval establishment for 79 hematology parameters on the Mindray BC6800 Plus System in the CALIPER cohort of healthy children and adolescents

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Background: Hematological parameters vary significantly throughout growth and development due to physiological processes such as fetal-to-adult erythropoiesis and puberty. Pediatric age- and sex-specific reference intervals (RIs) are thus needed for appropriate clinical decision-making. Critical gaps exist in pediatric hematology reference intervals for modern laboratory platforms, increasing risk of diagnostic error.

Methods: 687 children and adolescents from birth to 18 years of age were enrolled. Exclusion criteria included pregnancy, history of chronic illness, acute illness, and regular prescribed medication use. Whole blood was collected and analyzed for 79 hematology parameters, including erythrocytes, leukocytes, platelets, and research use-only parameters, on the Mindray BC6800 Plus System within 8 hours of collection. Reference intervals were established as per Clinical and Laboratory Standards Institute EP28-A3c Guidelines.

Results: Dynamic reference value distributions were observed for several hematology parameters. Age partitioning was required for 52 parameters. Sex partitioning was required for 11 erythrocyte parameters, demonstrating significant elevations in males relative to females from 14-19 years.

Conclusions: The current study established reference standards for 79 hematology parameters on the BC6800Plus system in a healthy cohort of Canadian children and adolescents. This is the first study to report health-associated pediatric concentration profiles for novel research parameters. These data emphasize the complex biological patterns of hematology parameters in childhood necessitating age- and sex-specific reference intervals for evidence-based clinical interpretation.

9 - Evaluating the analytical performance of new Strong Six Sigma clinical chemistry assays on the ARCHITECT system

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Objectives: We evaluated the analytical performance of 6 next generation clinical chemistry assays on the Abbott ARCHITECT c8000 system. Precision, linearity, method comparison, accuracy, and sigma metrics were assessed. Methods: Imprecision was assessed by measuring 2 levels of quality control (QC) material (Biorad Chemistry UA) and 3 pooled patient samples 5x twice per day, for five days. Linearity testing consisted of 3-4 replicates per 5-6 levels of commercially available linearity materials. Comparison between the new and current ARCHITECT methods was performed by measuring 120 serum/plasma specimens in duplicate. Accuracy was determined by testing 10 replicates of NIST 470 and 456 materials for albumin and amylase, respectively, or calibrators for cholesterol, total protein, and urea. Sigma value was calculated from accuracy study results. Acceptable imprecision, bias, and total allowable error were based on Accreditation Canada Diagnostics guidelines. Statistical analysis was performed using EP Evaluator. Results: Accuracy, linearity, and method comparison results for 6 clinical chemistry assays are shown in Table 1, where all assays demonstrated ? 6 Sigma performance. Conclusion: Representative clinical chemistry assays utilizing photometric technology on the ARCHITECT system demonstrated acceptable performance for precision, accuracy, linearity, and agreement with on-market ARCHITECT clinical chemistry assays.

8 - Performance of the Cascadion(TM) SM, a fully automated liquid chromatography mass spectrometry analyzer, for the measurement of total 25-hydroxy vitamin D

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Objectives: Evaluate the performance of Thermo Fisher's CascadionTM SM Clinical Analyzer for the measurement of total 25-hydroxy vitamin D (Vit.D). Design and Methods: Accuracy and precision on the Cascadion analyzer was verified by analyzing 4 replicates of quality control material (3 levels) per day, over 5 days, and long term over 3 months. Vit.D results on the Cascadion instrument were compared to 3 immunoassays (Beckman DXI800, Siemens Atellica IM, Roche Cobas Pro) and an in-house manual LC-MS assay using patient samples. CDC certified reference samples were also analyzed on the Cascadion. Results: Within-run, total CV, and mean bias were all 5% or lower. Over 3 months, total CV were less than or equal to 5.1%. The different immunoassays showed an overall good agreement with Cascadion, with mean biases of 9.4%, -7.4%, and -3.6% (DXI800, Atellica IM, and Cobas Pro, respectively), but with 95% limits of agreements (LoA) of -54% to 73% for DXI800 (n=122), -44% to 29% for Atellica IM (n=104), and -26% to 19% for Cobas Pro (n=120). A proportional bias was observed in our in-house LC-MS assay (mean 19.4%, LoA -9% to 47%, n=120). The Cascadion was well aligned with CDC's reference method (mean bias -3.8%, LoA -16% to 9%, n=113). Conclusions: The Cascadion clinical analyzer is an easy to use, automated LC-MS that produces accurate Vit.D results. Since LC-MS is largely recognized as a gold standard methodology, the advent of automated analyzers will possibly lead to wider implementation of mass spectrometry in clinical laboratories.

7 - Impact of sample pH on analytical recovery and stability of urinary 5HIAA, HVA and VMA

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Objectives: Conditions to ensure sample stability of urinary 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid (HVA), and vanillylmandelic acid (VMA) has been the subject of discussion for years. Urine collection requirements are variable across medical laboratories, with some preferring no preservative to be added and others requesting acidification. This study evaluated the impact of sample pH on analytical recovery and stability of 5HIAA, HVA and VMA in urine. Design and Methods: Eight urine samples were included in the study. Four aliquots were made for each sample, and pH of each aliquot was adjusted with 6N HCL or 5N NaOH to pH of 0-1, 1-3, 3-5, and 5-7, respectively. 5HIAA, HVA and VMA were measured by LC-MS/MS on day 0, 1, 2, 5 and 7. The samples were stored at 4 °C during the study. Sample stability data was analyzed using the EP evaluator software. Results: The average analytical recovery of 5HIAA, HVA and VMA on Day 0 was between 92-104% across the pH range studied. No clinically significant difference was observed between the four pH conditions for all three analytes. 5HIAA was stable for 4 days at pH 0-1 and for 6 days at all other pH values. The stability of HVA and VMA was not affected by sample pH values and all samples were stable for at least 7 days. Conclusions: Sample pH had no effect on analytical recovery of urinary 5HIAA, HVA and VMA, and sample stability was only compromised in extremely acidic condition (pH 0-1).

5 - Evaluation of the i-STAT Alinity point-of-care analyzer in pediatric patient populations

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Objectives: Point-of-care testing allows for improved turn-around-times, which, in turn expedites diagnosis and treatment initiation. We evaluated the performance of the CG4+/8+, Crea, and ACT kaolin cartridges on the i-STAT Alinity in pediatric patient populations. We also evaluated the agreement between ACT celite and ACT kaolin cartridges. Design and Methods: Residual heparinized whole blood samples were used for imprecision, linearity, and method comparison studies. To evaluate the agreement between ACT celite and ACT kaolin, residual samples from 14 hemodialysis patients were used. Hemodialysis patients received either regular, tight, or heparin free dosing protocols. ACT was measured at the start of treatment, 1 hour, 2 hours, and the last 30 minutes of treatment. Results: Total imprecision ranged from 0.1 to 3.6% on the i-STAT Alinity. Linearity was verified for pH, blood gases, electrolytes, lactate, glucose, and creatinine. The three i-STAT Alinity devices showed good agreement to the central laboratory analyzers (r ? 0.97). Serial ACT results were consistently shorter for kaolin. The percent difference ranged from 1 to 30%. A negative bias of 11.6% or 19 seconds was observed for ACT kaolin on the i-STAT Alinity relative to ACT celite on the i-STAT 1. Conclusions: The i-STAT Alinity has acceptable precision and linearity. Method comparison between the i-STAT Alinity and central laboratory analyzers showed good correlation. ACT thresholds established for regular, tight, and heparin free dosing protocols using ACT celite should be adjusted for ACT kaolin. Overall, the i-STAT Alinity is suitable for use in pediatric patient populations.

4 - Comparison of medical error disclosure policies among health regions of western canada

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Objectives: In any health care process, adverse events resulting from errors are inevitable. Disclosure of an adverse event is an important element in managing the consequences of a medical error. The objective of this study was to review and compare the disclosure policies implemented by individual health regions in western Canada (Manitoba, Saskatchewan, Alberta, and British Columbia). Methods: The evaluation of policies of health regions was based on the inclusion of various guidelines including avoidance of blame; support to the staff; an apology or expression of regret; avoidance of speculation; some form of patient support; and education/training to health care workers. Results: Avoidance of blame in the British Columbia disclosure policies was minimal (40%) as compared to 82%, 100%, and 75% in Saskatchewan, Alberta and Manitoba respectively. Support for health care providers was included in less than half of the disclosure policies in Saskatchewan (45%) while its inclusion in the policies of Alberta, Manitoba and British Columbia was 100%, 88%, and 60% respectively. 18% and 38% of the policies included training/education for staff in Saskatchewan and Manitoba respectively, with 0% in British Columbia. Conclusion: The complexities of medical error disclosure to patients present ideal opportunities for medical educators to probe how learners are balancing the ethical complexities in error disclosure. The designing of error disclosure policy requires integration of various aspects including bioethics, physician-patient communication, and team-based care delivery. We suggest that the disclosure policies can provide framework and guidelines for appropriate disclosure which can lead to more transparent practices.

3 - Using ensemble machine learning to optimize delta checks for the detection of multiple pre-analytical errors

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Objectives: Delta checks involve the comparison of serial patient results, and assessing the difference against an analyte-specific limit prior to reporting. While originally developed to detect sample mix-ups, delta checks may also flag specimen integrity issues. This study sought to optimize delta checks, including time between tests, by using machine learning algorithms to evaluate their efficacy in identifying common pre-analytical errors.

Methods: Optimized delta check limits were generated using the distribution of a posteriori in-patient delta values from three tertiary centres, as described in CLSI guidelines (EP33, 2016). Results from samples previously identified as contaminated within sets of routine in-patient chemistry were used to test delta check rules. Evaluation of error detection was performed by using random forests with validation by out-of-bag error computation.

Results: Intravenous normal saline contamination was effectively identified by individual or combined delta checks for potassium and chloride, with a delta time <96 hours. Optimal parameters for detection of K_2EDTA contamination used alkaline phosphatase and potassium with a delta time <72 hours. Evaluation of sample flagging rates suggested a significant reduction for albumin (-48.2%, $p<0.0001$), but not sodium (-4.79%, $p=0.2191$), and a modest increase for potassium (+1.42%). However, it was noted that 21.5% of specimens flagged by the optimized rules would likely identify significant changes in more than one analyte.

Conclusions: Using machine learning along with empirically-derived delta checks may offer concrete, population-specific measures by which multiple pre-analytical errors can be detected prior to releasing patient results, with minimal effects on overall sample flagging rates.

2 - Simultaneous Analysis of Nicotinic Acid and Nicotinamide in Human Serum by LC-MS/MS

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Objective: To develop a rapid and robust LC-MS/MS method for nicotinic acid (NA) and nicotinamide (NAM) applicable to human serum analysis Methods: Multilevel saline calibrators and plasma controls were made in the laboratory by spiking standards. A 50 ?l serum with internal standards was extracted by deproteinization with 250 ?l methanol, and then 3 ?l of the supernatant was analyzed on a Shimadzu HPLC and AB SCIEX 6500+ QTRAP mass spectrometer with electrospray ionization in positive polarity. The transitions used for the detection of NA vs NA 13C6 and NAM vs NAM 13C6 were 124>80>53 vs 130>83 and 123>80>78 vs 129>85, respectively. The analytes were separated using gradient elution at 40 °C with a 0.4ml/min flow rate. This method was validated and applied to clinical research projects for the determination of NA and NAM levels after administration. Results: Total run time was 3 min. Total imprecision in two levels of quality control was less than 5% and the limit of quantification was 2.0 ng/ml for NA and NAM. The linearity was within the range 2.0-2000 ng/ml for both analytes. Ion suppression effects were observed for both analytes. No carryover and no interference by hemolysis, lipemia, icterus, and commonly used therapeutic drugs were observed. LC-MS/MS results correlated well with the expected results from mixtures of patient's sample with standards. Conclusion: This rapid and reliable LC-MS/MS method is suitable for determination of concentrations of NA and NAM in serum or plasma sample for use in clinical research. Keywords: nicotinic; nicotinamide; liquid