

Tuesday, July 28, 2015

Poster Session: 9:30 AM - 5:00 PM

Clinical Studies/Outcomes

**A-001****Association between laboratory test turnaround time and emergency department length of stay: a retrospective US electronic health database analysis**D. Mitra<sup>1</sup>, E. Erdal<sup>1</sup>, V. Khangulov<sup>2</sup>, R. Tuttle<sup>1</sup>. <sup>1</sup>*Becton, Dickinson and Company, Franklin Lakes, NJ*, <sup>2</sup>*Boston Strategic Partners, Inc., Boston, MA***Background:**

Rapid and accurate diagnosis is critical to providing timely and appropriate care in the emergency department (ED). Longer lengths of stay (LOS) in the ED correlate with higher inpatient service admission rates and additional inpatient LOS [1-2]. 'Treat and release' patients (i.e. patients treated in the ED and subsequently discharged rather than admitted to inpatient services) represent a large proportion of ED visits in the US. In spite of the importance of laboratory test results in guiding patient management, there is currently a lack of studies examining the association between laboratory test turnaround time (TAT) and ED LOS. The objective of the present study was to examine the relationship between laboratory test TAT and ED LOS via retrospective analysis of a 'treat and release' ED population from a large US electronic health record (EHR) database (Cerner Health Facts®).

**Methods:**

ED visits from 2012 were included in the analysis if the patient was ≥18 years old, ≥1 laboratory test was ordered during the visit, ED LOS was <7 h, and the patient was discharged to home or the care of their family/caregiver. Laboratory test TAT for each patient was defined as the overall TAT (time between first test order and last returned result) for all tests ordered within 30 min of the first test ordered. LOS was defined as the time elapsed between ED admission and discharge. The relationship between TAT and LOS was examined via linear regression modeling, with and without adjustment for confounders, including patient and hospital characteristics. For regression analyses, the strength of the relationship between the TAT and LOS was assessed based on the statistical significance of the slope coefficient (p-value of <0.05 denoted statistical significance).

**Results:**

In total, 463,712 patient visits in the database met the defined inclusion criteria. After adjustment for confounders, regression modeling revealed a positive, statistically significant relationship between laboratory test TAT and ED LOS, such that a 10 min decrease in laboratory test TAT was associated with a 6.7 min reduction in ED LOS (p<0.0001). Examination of mean and median ED LOS revealed a similar relationship, and a 30 min decrease in laboratory test TAT from 61-75 min to 31-45 min resulted in a 19 min decrease in median ED LOS (from 226 to 207 min).

**Conclusion:**

The results of this analysis reveal a statistically significant association between laboratory test TAT and ED LOS, and suggest that laboratory test TAT is a key factor to consider during any efforts to improve ED efficiency. These results highlight the importance of developing and measuring shared TAT metrics between the ED and laboratories to help reduce LOS, as well as the potential benefits of processes aimed at improving laboratory efficiency. In order to more fully understand the implications of lab TAT and LOS reductions in different hospitals, future studies investigating the impact of lab TAT on factors such as wait time and ED throughput are warranted.

1. Carrier E et al. *JAMA Intern Med* 2014; 174:1843-62. Liew D et al. *Med J Aust* 2003; 179:524-6**A-002****Simple laboratory test results and mortality following coronary catheterization in Calgary, Alberta**L. de Koning<sup>1</sup>, B. Abdalla<sup>2</sup>, M. Gerling<sup>3</sup>, M. Knudtson<sup>3</sup>. <sup>1</sup>*Calgary Laboratory Services, Calgary, AB, Canada*, <sup>2</sup>*University of Alberta, Edmonton, AB, Canada*, <sup>3</sup>*University of Calgary, Calgary, AB, Canada***Background:**

Simple laboratory tests such as the complete blood count and electrolytes are frequently measured in the acute care setting as they provide clinical information about immediate and short-term risk. They may also provide prognostic information on hospitalization and death following invasive procedures and discharge, although they are not frequently used for this purpose. Our objective was to examine the relationship between pre-procedural laboratory test results and mortality in patients undergoing coronary catheterization in Calgary, Alberta, Canada.

**Methods:**

Complete blood count, sodium, potassium, chloride and creatinine along with provincial healthcare number and test verification date were extracted from the laboratory information system of Calgary Laboratory Services (November 2009-June 2013) and merged to patient demographic (age, sex, smoking status) and outcome data from the Alberta Provincial Project for Outcome Assessment (APPROACH), a province-wide cardiac catheterization registry. We included only data for the last lab panel run prior to catheterization. Logistic regression models using backwards elimination with 60-day post-catheterization mortality as the outcome were used to generate a parsimonious model containing only significant demographic and lab data predictors. All continuous variables were coded into quintiles. In the final model, we used interaction terms to test whether time between laboratory testing and catheterization had any impact on our results.

**Results:**

The final data set included 6275 patients and 301 deaths within 60 days of catheterization. After backwards elimination, the final model (odds ratios evaluated per 1 quintile increase) contained age (OR = 1.24, p=0.02), sex (OR = 1.75 for men vs women, p=0.04), sodium (OR = 0.75, p < 0.01), white blood cell count (OR = 1.30, p=0.02), mean corpuscular hemoglobin concentration (OR = 0.63, p<0.01), and red blood cell count (OR = 0.77, p<0.01). The c-statistic, an overall measure of model classification power, for these variables was 0.79. We found no clinically relevant differences in lab data-mortality relationships according to time between measurement and catheterization.

**Conclusions:**

In addition to age and sex, laboratory tests including sodium, white blood cell count, red blood cell count, and red cell hemoglobin concentration were predictive of 60-day mortality in patients undergoing coronary catheterization. These simple variables, many of which are automatically collected in lab information systems with minimal error, should be considered in risk assessments of coronary disease patients.

**A-003****Clinical validation of the ReEBOV™ Antigen Rapid Test Kit for the point of care detection of Ebola Virus Disease**M. Boisen<sup>1</sup>, R. Cross<sup>2</sup>, L. Branco<sup>3</sup>, A. Goba<sup>4</sup>, M. Momoh<sup>4</sup>, J. Hartnett<sup>5</sup>, J. Schieffelin<sup>6</sup>, L. Moses<sup>5</sup>, M. Fullah<sup>4</sup>, F. Baimba<sup>4</sup>, M. Gbokie<sup>4</sup>, S. Safa<sup>4</sup>, M. Millett<sup>1</sup>, D. Nelson<sup>1</sup>, D. Oottamasathien<sup>1</sup>, R. Wilson<sup>7</sup>, P. Kulakowsky<sup>8</sup>, D. Simpson<sup>1</sup>, S. Kahn<sup>4</sup>, D. Grant<sup>9</sup>, J. Schaffer<sup>6</sup>, E. Saphire<sup>10</sup>, T. Giesbert<sup>2</sup>, K. Pitts<sup>1</sup>, R. Garry<sup>5</sup>. <sup>1</sup>*Corgenix Inc., Broomfield, CO*, <sup>2</sup>*UTMB, Galveston, TX*, <sup>3</sup>*Zalgen, Germantown, MD*, <sup>4</sup>*Lassa Fever Program, Kenema, Sierra Leone*, <sup>5</sup>*Tulane University, New Orleans, LA*, <sup>6</sup>*Tulane University, School of Medicine, New Orleans, LA*, <sup>7</sup>*Autoimmune Technologies LLC, New, LA*, <sup>8</sup>*Autoimmune Technologies LLC, New Orleans, LA*, <sup>9</sup>*Ministry of Health and Sanitation, Freetown, Sierra Leone*, <sup>10</sup>*TSRI, La Jolla, CA*

**Background:** Ebola virus (EBOV) causes severe and often fatal viral hemorrhagic fever (Ebola Virus Disease; EVD). The 2014-2015 outbreak of EVD in West Africa is the deadliest of its kind, and has resulted in at least 9,556 deaths prompting an international emergency response. During the course of this outbreak, FDA and WHO approved qRT-PCR as a molecular diagnostic to detect EVD clinically; however with this technique a result is not available for 24hr or more and requires significant laboratory infrastructure and power. It became evident that there was a need for an easy-to-use, point-of-care test that can be performed in any clinical facility or field laboratory to aid in the rapid triage of suspect EVD cases. To assist in this effort

the Viral Hemorrhagic Fever Consortium (VHFC.org) led by Tulane University and Corgenix Inc. accelerated the development timeline of the ReEBOV™ Antigen Rapid Test Kit. This dipstick-format lateral flow immunoassay incorporates recombinant EBOV VP40 antigen and VP40-specific polyclonal antibodies to detect EBOV antigenemia in whole blood or plasma samples. Methods: Two clinical studies were performed with Tulane IRB and Sierra Leone Ethics Committee approval. A Corgenix sponsored banked plasma study (n=176) was conducted at Kenema Government Hospital (KGH), Kenema, Sierra Leone. Reference qRT-PCR utilized EBOV Zaire GP primers and probes (Trombley et al., 2010). The WHO conducted an independent clinical trial in field laboratories at Hastings and Prince of Wales, Sierra Leone that included venous whole blood (n=152) and banked plasma (n=140). WHO reference qRT-PCR was the RealStar® Filovirus Screen RT-PCR Kit 1.0 (Altona Diagnostics GmbH). Results: Analysis of the banked plasma sample study conducted at KGH did not include the estimated cut-off for qRT-PCR cycles (Ct). As such, the RDT Negative Percent Agreement (NPA) with qRT-PCR was 96.7% (58/60; CI 88.6% - 99.1%) and Positive Percent Agreement (PPA) was 62.1% (72/116; CI 53.0 - 70.4%). The qRT-PCR cycle range within the PPA included a Ct range of 24.7 ±4.4 for true positives and Ct range of 37.0 ±3.4 for false negatives which corresponded to the estimated Ct cut-off. The combined results of the WHO clinical study generated NPA 84.6% (165/195; CI 78.8 - 89.4%) and PPA of 91.8% (89/97; CI 84.4 - 96.4%). True positive range for qRT-PCR cycles was whole blood Ct 20.2 ±3.0 and plasma Ct 20.2 ±4.8. Conclusion: These clinical validation studies have demonstrated the ReEBOV™ Antigen Rapid Test is capable of detecting Ebola VP40 with sufficient accuracy as an aid to the diagnosis of acute EVD. Based in part on these findings, the ReEBOV™ Antigen Rapid Test Kit was granted FDA Emergency Use Authorization and the WHO listed the test as eligible for procurement in February 2015. The intended use is for the presumptive detection of Zaire EBOV in individuals with signs and symptoms of EBOV infection in conjunction with epidemiological risk factors. This Point of Care RDT represents a breakthrough in the detection of EVD for this and future Ebola virus outbreaks. This work is dedicated to our friends and colleagues who lost their lives during this tragic outbreak.

#### A-004

##### Estimation of Age and Gender- Specific Reference Intervals for Turkish Children Based on Hospital Patient Data

T. Cevlik, R. Turkal, A. Yaman, P. Vatanserver, D. Coban Ramazan, O. Sirikci, G. Haklar. *Marmara University Pendik Research and Training Hospital, Biochemistry Department, Istanbul, Turkey*

Clinical interpretation of laboratory test results is heavily dependent on the availability of reference intervals. For some parameters, pediatric test reference values vary from those of adults and/or among children of different ages based on their development and growth. Therefore, it is crucial to obtain age-matched laboratory test reference values. As the acquisition of samples from healthy children has become extremely difficult in recent years, clinical reference ranges calculated from routine laboratory data of patients using a statistical method have been used. Serum alkaline phosphatase (ALP) levels show great variation in infants, children and adolescents. The aim of this study was to establish reference values of serum ALP in infants, children and adolescents up to 18 years using hospital data.

Nineteen thousand two hundred thirty-one test results belonging to infants, children and adolescents stored in laboratory information system of Marmara University Pendik E&R Hospital between June 2014 and January 2015 were included in this study. ALP measurements were done according to IFCC method (AU 5800, Beckman Coulter, USA). Data were analyzed in accordance with CLSI C28-A3 guidelines on defining, establishing, and verifying reference intervals in the clinical laboratory. Outliers were removed after visual inspection and the Dixon test. The data is partitioned according to age and gender based on the partitions identified by CALIPER. Additionally, we used the 90% confidence intervals as change by CALIPER. This subset of analyte values was used to check Gaussian distribution and establish lower and upper reference interval limits and the mean values.

These results suggest that calculating pediatric reference intervals from hospital-based data may be useful. The database will also be global benefit while establishing reference intervals. The data showed complex patterns in the concentrations of ALP during child growth and development, as well as sex differences.

ALP (U/L) Female Reference Intervals	Age	0-14 days n:182	15 days-<1year n:137	1-<10 years n:10856	10-<13 years n:3039	13-<15 years n:730	15-<17 years n:883	17-<19 years n:797
Lower Limit		73	55	89	98	59	49	44
Upper Limit		228	377	362	418	275	154	192
Mean		153	195	206	222	138	87	88
ALP (U/L) Male Reference Intervals	Age	0-14 days n:182	15 days-<1year n:137	1-<10 years n:10856	10-<13 years n:3039	13-<15 years n:867	15-<17 years n:1069	17-<19 years n:671
Lower Limit		73	55	89	98	90	64	58
Upper Limit		228	377	362	418	432	339	213
Mean		153	195	206	222	240	162	114

#### A-007

##### Serum Biomarkers and Obstructive Sleep Apnea

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**Background:** Obstructive sleep apnea (OSA) is a common disorder, characterized by repetitive episodes of complete (apnea) or partial (hypopnea) obstructions of the upper airway during sleep, with decreasing oxygen saturation and sleep fragmentation. More than 22 million American adults have OSA. Diagnosis is currently based upon overnight polysomnography, and patients are often not referred for this definitive testing. Up to 90% of individuals with OSA remain undiagnosed. OSA prevalence is increasing and may soon become the most common chronic disease in industrialized countries. Untreated OSA can lead to serious health consequences, including increased mortality. Patients with OSA have an elevated risk of coronary artery disease, cardiac arrhythmia, myocardial infarction, heart failure, stroke, diabetes, obesity, metabolic syndrome, memory decline, and work-related or driving accidents.

**Objective:** Given the significant health issues associated with untreated OSA, early diagnosis of this treatable disorder is critical. There is a large unmet need for biomarkers to identify individuals with possible OSA. Here we present data that demonstrates an association between OSA and metabolic and endocrine biomarkers.

**Methods:** A multicenter prospective trial was conducted enrolling consecutive symptomatic patients with suspected OSA. All subjects underwent a diagnostic sleep study (polysomnography). A non-symptomatic control group was also obtained from a separate Healthy Controls study. Eleven biomarkers were tested: HbA1c, CRP, IL-6, uric acid, EPO, cortisol, hGH, prolactin, testosterone, DHEA (Beckman Coulter UniCel DxC 600i Synchron® Access® Clinical Systems), and IGF-1.

**Results:** A total of 128 subjects have been enrolled in this ongoing study. Of these, 26 were diagnosed with moderate to severe OSA. OSA is more prevalent in males, and a Receiver Operating Characteristic (ROC) curve analysis of results from male subjects (n=70) was performed. Areas Under the Curve (AUCs) for diagnosis of moderate/severe OSA were >0.70 for HbA1c and CRP (p<0.001). AUCs were >0.60 for uric acid, IL-6, and EPO. AUCs were >0.60 for gender-specific markers (prolactin, testosterone, DHEA). AUCs were >0.50 for hGH, IGF-1, and cortisol. Many of the moderate/severe OSA subjects were pre-diabetic (A1c ≥ 5.7%), with high cardiovascular risk (CRP > 0.3). Individual biomarkers performed better or worse in specific clinical subgroups, e.g. A1c achieved significant group separation in obese subjects (p<0.05), as did CRP in non-obese subjects (p<0.01).

**Conclusion:** Our results identified promising biomarkers that may be useful in the diagnosis of patients with OSA.

## A-008

**Serum Neutrophil Gelatinase Associated Lipocalin (NGAL) can predict Chronic Kidney Disease stage and risk category proposed by KDIGO 2012, in a primary care population.**

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**Background:** Chronic Kidney disease (CKD) affects more than 10% of the population in many countries worldwide, and is an important cause of death and loss of disability-adjusted life-years. On the other hand, awareness of health care providers and individuals is low. CKD is defined by a reduction in glomerular filtration rate (GFR) and increased urinary albumin excretion. GFR can be accessed or calculated by various methods. NGAL is a biomarker of acute kidney injury, but there is also evidence that its levels may reflect the active renal damage that underlies chronic disease.

**Methods:** The aim of this study was to evaluate serum NGAL levels association with various markers of renal impairment and its ability to predict CKD category and risk by the proposed Kidney Disease: Improving Global Outcomes (KDIGO) classification. We conducted a cross-sectional study of 334 outpatients assisted by the Family Medicine Program of Niterói, Brasil, aged over 44 years-old, from August 2011 to August 2012. Demographic and epidemiological data were obtained, serum creatinine, serum cystatin C, and urine microalbumin were tested. NGAL serum levels were determined by sandwich ELISA (Bioporto Diagnostics) from -80°C preserved samples, until first thawed. KDIGO G category was calculated according to creatinine and cystatine C formulas. Urinary albumin-creatinine rate (ACR) was also calculated, in order to determine KDIGO risk category.

**Results:** Two hundred ninety-six (88.6%) outpatients (182 women) were identified as G1 and G2 KDIGO categories, and 38 (11.3%) at G3a and higher categories (25 women). This findings, added to ACR results, led to the following risk category distribution: 73.6% low, 17% moderate, 5.3% high, 4% very high.

We observed statistically significant univariate correlations between NGAL and age ( $p=0.02$ ), creatinine ( $p<0.000$ ), cystatine C ( $p=0.02$ ), microalbuminuria ( $p=0.002$ ), and urinary albumin-creatinine rate ( $p=0.013$ ), and GFR ( $p<0.000$ ). However, none of those correlations were stronger than of creatinine ( $R^2=0.28$ ). When GFR was calculated by serum creatinine formula, a NGAL cut-off of 205.7 ng/ml predicted KDIGO category equal or higher than G3a, with a AUC\_ROC 0.723, sensitivity of 63.2% and specificity of 74%. When GFR was calculated by cystatin C, a cut-off of 226.7 ng/ml showed a AUC-ROC 0.741, sensitivity of 63.3% and specificity of 78.5%. NGAL predicts moderate and/or higher CKD risk category with a cut-off of 226.7 ng/mL, a AUC-ROC 0.829, 70.4% sensitivity and 79.7% especificity.

**Discussion:** Serum creatinine, cystatin C and urinary albumin loss are commonly used to determine the level of impairment function and/or kidney injury. NGAL, a member of lipocalin superfamily, is highly expressed and released from renal tubular cells after various sources of renal injury. NGAL levels are associated with the severity of CKD, reflecting the phenomena of active and continuous kidney injury underlying the chronic condition. This study observed an association between serum NGAL and other markers of renal impairment, also NGAL levels were able to predict the presence of moderately decreased renal function or worse. NGAL showed good specificity to predict a poor condition prognosis, determined by KDIGO 2012 higher risk categories.

## A-009

**Detoxifying activity of serum albumin demonstrated diagnostic utility in patients with kidney transplant dysfunction and pregnant women with preeclampsia**

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**Background:** Serum albumin (SA) is an important component of the detoxifying system of the organism. In the circulatory system, SA is the main carrier protein whose detoxifying activity is the binding of hydrophobic toxins and their transport to hepatocytes. The detoxifying activity of SA can be significantly reduced when the SA molecules are overloaded with excessively high level of toxins. This significant reduction in the SA activity leads to an inadequate overall elimination of toxins from the organism. High overall toxin levels cause further deactivating of the SA transport molecules themselves. Such conditions finally result in the escalating intoxication of the patient. We investigated the clinical relevance of the novel, in vitro laboratory test

for the detoxifying activity (DTE) of serum albumin, based on Electron Paramagnetic Resonance (EPR) spectroscopy of SA labeled with 16-doxyl stearic acid. Recent clinical study of post-surgery patients has already confirmed the clinical utility of the EPR test for prediction and diagnosis of septic intoxication.

**Objective:** To evaluate the clinical relevance of the EPR test of SA for patients who have a risk for developing intoxications of a non-infective origin.

**Methods:**

We used EPR analyzer AXM-09 (Albutran) and the set of reagents "ATA-test-T" to measure detoxifying activity of albumin in blood samples.

**A)** The observation study included 92 (45 males and 47 females) kidney transplant recipients. 54 of them had the kidney transplant dysfunction such as acute resection (30), ischemia/reperfusion injury (15), nephrotoxicity of calcineurin inhibitors (4) and combination of pathologies (5). The control group included 38 patients, which were observed in early (19/38) and late (19/38) postoperative periods.

**B)** The observation study included 189 pregnant women, including 97 with uncomplicated pregnancy (15-40 weeks) and 92 who suffer from preeclampsia (17-39 weeks).

**Results:**

**A)** In the patients with kidney transplant dysfunction, there the median value of DTE was found as 55% (34%; 81%) versus 123% (77%; 157%) for the patients of the control group. The diagnostic sensitivity and specificity of the test were 73% and 78%, respectively, for diagnosis of kidney transplant recipients with transplant dysfunction. The cut-off value of DTE was 80%. The ROC-analysis showed AUC of 0.86.

**B)** In the pregnant women with severe preeclampsia, there the mean value of DTE was 57% for second and 42% for third trimesters of pregnancy, versus 82% and 56%, respectively, for women with uncomplicated pregnancy. The diagnostic sensitivity and specificity of the test for were 64% and 92% (cut-off of DTE was 52%, AUC=0.79) for diagnosis of severe preeclampsia in second trimester, and 59% and 82%, respectively, in third trimester (cut-off 42%, AUC=0.75).

**Conclusion:** The in vitro EPR test of the detoxifying activity of serum albumin is a sensitive and noninvasive method, which clearly has a demonstrated diagnostic utility, for patients with kidney transplant dysfunction as well as for pregnant women with severe preeclampsia. Our results suggest that the detoxifying activity of serum albumin would be applicable as the marker for prediction and diagnosis of escalating intoxications of various origins.

## A-010

**Validation of anti-phospholipase A2 receptor antibody testing by ELISA and immunofluorescence**

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**Background:** Recently, antibodies against phospholipase A2 receptor (PLA2R) in the kidney were determined to be a major target antigen among patients with idiopathic membranous nephropathy (iMN). In order to clinically interpret anti-PLA2R results, reference ranges need to be established in healthy individuals as well as patients with proteinuric renal diseases, including secondary causes of membranous nephropathy (those associated with systemic lupus, malignancy, infection). Importantly, it is currently unknown if patients with other proteinuric renal diseases can develop anti-PLA2R antibodies. The objective of this study was to measure anti-PLA2R antibodies in a cohort of normal individuals as well as a cohort with a diverse set of biopsy-proven renal diagnoses.

**Methods:** This study was reviewed and approved by the Mayo Clinic Institutional Review Board. Serum from Mayo Clinic, Rochester patients who had recently undergone diagnostic native kidney biopsy to diagnose renal disease was obtained within two weeks of biopsy and frozen at -80°C until tested. Patients receiving protocol kidney transplant biopsies were excluded. Serum was assayed for anti-PLA2R antibodies using IFA (positive/negative) and quantitative ELISA kits from Euroimmun US (Morris Plains, NJ) in the Renal Testing Laboratory. Additionally, sera from 120 adult and 20 pediatric patients were obtained from the Mayo Clinic Department of Laboratory Medicine and Pathology Quality Management Services Biorepository and analyzed by IFA and ELISA in order to verify reference ranges.

**Results:** A total of 202 consecutive biopsy patients with available waste serum were identified. Of these, 6 (3%) had a biopsy diagnosis of iMN. Of these, 2 (33%) had a positive IFA and 1 (7%) a positive ELISA (>20 RU/mL). IFA and ELISA were negative for the remaining patients with biopsy diagnoses of amyloidosis (n=11), acute tubular necrosis (n=15), diabetic nephropathy (n=10), focal segmental glomerular sclerosis (n=23), IgA nephropathy (n=25), interstitial nephritis (n=9), minimal change disease (n=10), monoclonal protein-related diseases (n=13), vasculitis (n=20), other immune

complex mediated diseases (n=18) and other disorders (n=41). Among adult reference donors, IFA was negative in 114 (95%) and indeterminate in 6 (95%) due to high background staining. ELISA analysis was negative in all 120 (<14 RU/mL, lower 95<sup>th</sup> reference range  $\leq 4.04$  RU/mL). Among the pediatric samples (n=20) all had negative IFA and ELISA ( $\leq 4.04$  RU/mL) results.

**Conclusion:** Both the IFA and ELISA assays were 100% specific for anti-PLA2R mediated disease in normal reference range population and among a cohort with diverse biopsy proven renal diseases. Due to a low number of iMN cases in our cohort, assay sensitivity could not be assessed, nor could the prevalence of PLA2R versus non PLA2R-mediated disease be estimated. Furthermore, many patients with iMN had already been treated and may have been in serological remission. The reference range results suggest the adult range can be used in children.

### A-011

#### An Exploratory Factor Analysis of Biomarkers in Patients with the First Anterior ST-Segment Elevation Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention

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**Background:** Despite advances in treatment, acute coronary syndromes, which consist mainly of ST-segment elevation myocardial infarction (STEMI) and unstable angina/non-STEMI, present an enormous medical, social, and economic burden worldwide. Primary percutaneous coronary intervention (pPCI) is a therapy of choice for the management of patients with acute STEMI. Despite the improvement in morbidity and mortality in these patients, groups at high risk of complications and adverse clinical events remain. Identification of patients at risk for major adverse cardiovascular events (MACE) might help selecting candidates for aggressive treatment which may improve outcome or early discharge after pPCI. The aim of this study was to explore the factor structure of a circulating biomarkers of potential predictive value, measured in patients with the first anterior ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention.

**Methods:** A total of 100 consecutive patients with the first anterior STEMI successfully treated by pPCI (< 20% of residual stenosis and TIMI flow 3) within 6 hours after the onset of the chest pain were included. Blood samples were obtained immediately before starting cardiac catheterization. Quantification of biomarkers (IL-6, IL-7, IL-8, IL-15, MCP-1, MIP-1 $\alpha$ , ICAM, L-selectin, E-selectin, TNFR1, TNFR2, and MMP-9) concentration was performed by Randox, Ltd. (Crumlin, UK), by using a biochip array analyzer (Evidence Investigator<sup>®</sup>). Factor analysis was carried out using the principle components analysis with Varimax orthogonal rotation of examined biomarkers. Multivariable logistic regression analysis was performed for prediction of 30 day MACE (cardiac death, non-fatal reinfarction, and target vessel revascularization) by using the individual factor scores as covariates in addition to significant univariate predictors of outcome. Kaplan Meier survival curves were generated for tertiles of the remaining significant factor from the multivariable analysis and the log rank test was used to compare event rate over time for the respective tertiles.

**Results:** Factor analysis yielded 4 uncorrelated factors (1 [log<sub>2</sub>TNFR1, sTNFR2, MMP-9], 2 [sICAM-1, sE-selectin is L-selectin], 3 [log IL-6, log IL-8, log MCP-1], and 4 [MIP-1 $\alpha$ , log IL7, log IL15]). These factors explained approximately 67.6% of the total variance. Multivariable analysis, including all significant univariate predictors of outcome (atrial fibrillation, left ventricular ejection fraction, smoking) revealed factor 2 and factor 3 as a potent independent predictors of 30 day MACE. Kaplan-Meier survival estimates for MACE were lower in patients with factor 2 or factor 3 score in the highest tertile compared with those in the mid and in the lower tertile (Log rank test  $\chi^2 = 9.44$ ,  $P < 0.01$ ; Log rank test  $\chi^2 = 8.37$ ,  $P = 0.01$ , respectively).

**Conclusion:** Clustering of multiple biomarkers by exploratory factor analysis is feasible and may give useful information in exploring different biomarkers in prognosis of STEMI patients. However, larger, prospectively designed trials would be required to further explore the utility of exploratory factor analysis for this application.

### A-012

#### A New Theory For Reference Intervals and Analyte Test Reporting Based on Clinical Risks Derived from Readily-Available EMR Data

A. B. SOLINGER, S. I. ROTHMAN, G. FINLAY. *FAR INSTITUTE, SARASOTA, FL*

**Background:** Reference interval cut-points for general diagnostic screening are usually determined by a methodology unrelated to medical outcomes: the central 95%

of test values for a “healthy” cohort are defined as being the “Reference Interval” and the other 5% are flagged as “Low” or “High” to guide the physician toward diagnosis. Problems with this method include difficulty of identifying a healthy cohort, assembling the number of subjects required for statistical power, and the leap of faith required to flag those outside the central area (indefensible logically: the entire cohort is defined as healthy a priori). These problems arise from an antiquated methodology, established in an era long before access to electronic medical records (EMR).

**Methods:** We extracted in-hospital tests (first test after admission) for serum potassium, sodium, and chloride (K, Na, Cl), discharge dispositions and demographics for 375,747 adult patient visits from Sarasota Memorial Hospital (Florida) EMR during the years 1998-2014. Similar extracts were performed at a major academic medical center in the northeast and a regional hospital in the southwest for 2012-2014. For each analyte, we calculated an Outcome Risk function:

$$OR(x) = (ONOWithin\Delta x) / (ONOWithout\Delta x)$$

where ONOWithin $\Delta x$  = odds of Negative Outcome for test results within  $\Delta x$ ;

ONOWithout $\Delta x$  = odds of Negative Outcome for those not within  $\Delta x$ ;

$x$  = mean value of test results within an interval  $\Delta x$ ;

Negative Outcome = all-cause in-hospital mortality.

The final OR(x) for each analyte was determined using JMP software to generate logistic regressions, adjusted for confounding variables.

**Results:** We found risk of mortality to be below average within these analyte intervals: K = 3.4 to 4.4 mEq/L; Na = 136 to 144 mEq/L; Cl = 100 to 109 mEq/L.

Further, we provide evidence-based risk estimates (mortality odds ratios) for values outside of these cut-points. Identical cut-points were found with other Negative Outcomes, e.g. 1-year post-discharge mortality; and when using data from other medical centers. Our high K cut-point is much lower than the current standards (which vary from 5.1 to 5.4), but is in excellent agreement with recent clinical studies of AMI patients.

**Conclusions** We have sought a replacement methodology for reference intervals from perspective of modern clinical chemistry, and propose a novel method to associate risk of patient outcomes with analyte test values. Gathering tests and outcomes from whole populations via hospitals' EMR's, we avoid problems of defining a “healthy” population, relying instead upon the analysis of big data to determine clinically-safe reference interval cut-points. This allows reference interval cut-points to be generated by calculation of outcome risk functions and enables readily-available EMR data to be utilized in situ, associating actual patient outcomes with analyte values by each lab. We suggest replacing the old population-distribution method with this risk-function method for more meaningful guidelines from the lab to physicians.

### A-013

#### Reduction of False-positive Bilirubin Results on the CLINITEK Novus Automated Urine Chemistry Analyzer

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**Background:** Urinary bilirubin is rarely an incidental finding. Patients with urinary bilirubin have either a transient or permanent interruption in the biliary tree and subsequent bile excretion, ultimately leading to the presence of urinary bilirubin. When detectable levels of bilirubin occur, an underlying pathology is possible and indicates the need for further clinical investigation. Unfortunately, even the most established methods can generate a high percentage of false-positive bilirubin results, often due to interfering substances and/or abnormal urine color. The CLINITEK Novus<sup>®</sup> Automated Urine Chemistry Analyzer employs a unique algorithm to decrease false-positive bilirubin results associated with these influences on the bilirubin reagent pad. Utilizing camera-based detection technology, this algorithm allows for the improved detection of true bilirubin, as confirmed by Icotest<sup>®</sup> reflex testing. We assessed false-positive CLINITEK Novus analyzer bilirubin results versus incidence on the CLINITEK Atlas<sup>®</sup> analyzer along with correlation of bilirubin results.

**Methods:** A clinical investigation was conducted to assess false-positive incidence using 1033 clinical samples ran on one CLINITEK Novus system and one CLINITEK Atlas system at three clinical sites. These 1033 samples consisted of 534 positive bilirubin results on the CLINITEK Atlas system from a total clinical population of 2773 specimens and a random assortment of 498 negative bilirubin results from the same clinical population. Reflex testing was conducted using one reagent lot of Icotest tablets to identify false-positive results. Results were compiled in frequency tables. Positive agreement, negative agreement, exact agreement were calculated.

**Results:** All 499 of the negative specimens obtained from the CLINITEK Atlas system remained negative by the reference Icotest assay. 496 of these samples were

also negative by the CLINITEK Novus analyzer for a concordance of 99.4% (95% CI: 98.3-100%).

When the 534 positive samples from the CLINITEK Atlas system were tested with Icotest, 417 of these samples were confirmed as positive and 117 were reported as negative. This is a false-positive rate of 21.9% on the CLINITEK Atlas analyzer, with a 95% CI for this false-positive rate between 18.5 and 25.7%. Of the 117 CLINITEK Atlas system-positive/Icotest-negative samples, 94 of them (80.3%; 95% CI: 72.0-87.1) were also negative by the CLINITEK Novus system. Of the 417 CLINITEK Atlas system and Icotest-positive samples, 407 of these were also positive by the CLINITEK Novus analyzer, corresponding to a concordance of 97.1% (95% CI: 95.0-98.5%).

In terms of clinical sensitivity and specificity, the CLINITEK Atlas system demonstrated 100% sensitivity and 67% specificity. The CLINITEK Novus analyzer demonstrated 97% sensitivity and 95% specificity with the same population of clinical samples.

**Conclusions:** The CLINITEK Novus analyzer showed improved accuracy of bilirubin results compared to reference Icotest assay. Greater accuracy (fewer false positives, balanced sensitivity and specificity) in routine bilirubin urinalysis with the CLINITEK Novus analyzer served to decrease the time and costs associated with potentially unnecessary follow-up bilirubin testing.

**A-014**

**Improving the diagnostic yield among catheter and non-catheter associated UTI's**

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**Background**

Urinary tract infections (UTIs) are one of the most common types of healthcare associated infections. Catheter-associated urinary tract infections (CAUTIs) account up to 75% of all UTIs. Long term complications of CAUTI include longer hospital stays, patient discomfort and increased mortality/morbidity secondary to disseminated infections both locally and systemically.

**Methods**

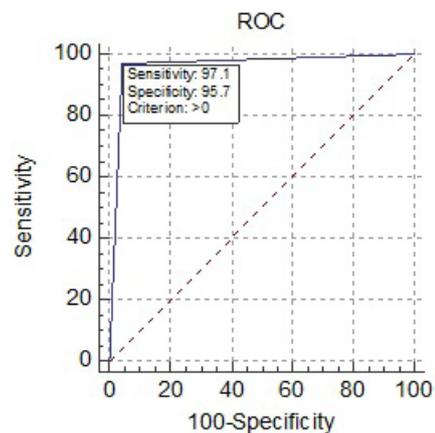
Using a Sysmex UF-1000i™ urine particle analyzer, we examined a case series of CAUTI and SUTI (symptomatic or non-catheter associated) patients to model the likelihood of a positive screen prior to the diagnosis of a UTI by culture. In the initial study, a retrospective analysis of reviewed urine samples was collected over three months. Data was reviewed from traditional urine culture and urinalysis using the Sysmex UF-1000i™. Logistic regression was used to define what parameters were predictive of a positive culture: 1). Trace bacteria, 2). Trace yeast and 3). WBC greater than 15 k/μL. Using data mining, we identified 81 patients with either CAUTI (26) or SUTI (55) based on traditional urine culture. We then compared the likelihood that a patient in either group would have a positive screen.

**Results**

In the initial study, 4088 results were obtained. Screen performance revealed: a sensitivity of 98% (CI 97.4-98.4%), a specificity of 93.7% (CI 92.1-94.9%) and a positive predictive value (PPV) of 97.0% (CI 96.4%-97.6%). An ROC curve was obtained (see Figure 1). The positive LR is 15.5 (CI 12.57-19.12). Among the CAUTI patients, 100% had a positive screen on the UF-1000i™ and 90.9% of the SUTI patients had a positive screen.

**Conclusions**

The UF-1000i™ particle analyzer shows a high PPV and a high LR. Using a retrospective case series analysis, we confirm these values with a 93% positive screen among culture positive patients. This will allow clinicians to feel confident in accurately interpreting a screen result and treat patients before waiting 24-48 hours for culture results.



**A-015**

**Diagnosis of Gestational Diabetes Mellitus by American Diabetes Association's and World Health Organization's Criteria and outcome in Pregnant Nigerian Women**

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**Background:** Prevention of adverse pregnancy outcomes is an important goal in good obstetric practice. Gestational Diabetes Mellitus (GDM) is associated with adverse pregnancy outcomes. Several diagnostic criteria for GDM have been proposed and adopted in different countries. Recently, the American Diabetes Association (ADA) adopted the "International Association of Diabetes in Pregnancy Study Groups" (IADPSG) recommended diagnostic criteria for GDM. In Nigeria, there are no universally accepted diagnostic criteria for GDM. The ADA and World Health Organization's (WHO) diagnostic criteria are among the commonly used criteria. Clinical outcome data of diagnostic performance of these diagnostic criteria is lacking. The objective of this study was to compare the ADA diagnostic criteria for GDM with the WHO diagnostic criteria on the basis of predicting pregnancy outcome.

**Method:** This was a longitudinal study involving 130 pregnant women between 24-32 weeks of gestation. During a 75g-Oral Glucose Tolerance Test (OGTT), after at least 8hrs of overnight fast, venous blood samples were collected at 0hr (fasting), 1hr and 2hr for measurement of fasting, 1-hour and 2-hour glucose as well as fasting and 2-hour Insulin. Participants were classified as GDM and non GDM women based on the ADA and WHO diagnostic criteria. Five pregnancy outcomes were observed: pre-eclampsia, shoulder dystocia or birth injury, birth weight ≥ 4.0kg, clinical neonatal hypoglycaemia and birth asphyxia.

**Results:** Twenty-eight participants (21.5%) had GDM by ADA criteria (GDM<sub>ADA</sub>) and 21 (16.2%) of women had GDM by WHO criteria (GDM<sub>WHO</sub>). Only 15 (11.5%) met criteria for GDM by both criteria. Ten percent of Participants had GDM by ADA but not by WHO criteria whereas 4.6% had GDM by WHO but not by ADA criteria. The association of GDM with macrosomia was stronger in GDM<sub>WHO</sub> women [OR=13.1, 95%CI(3.4-50.6)] compared to the GDM<sub>ADA</sub> women [OR=5.3, 95%CI(1.5-18.9)]. GDM<sub>WHO</sub> women were more likely to be associated with "one or more adverse pregnancy outcomes" compared to GDM<sub>ADA</sub> women; OR=4.9, 95%CI (1.8-13.3) vs OR=3.5, 95%CI (1.4-8.8). Macrosomia or at least one adverse outcome, were more likely in patients with GDM who met the diagnostic criteria by both ADA and WHO criteria (P< 0.01). Conversely, women who met diagnostic criteria of GDM by one criterion but not the other criterion were not associated with macrosomia or at least one adverse pregnancy outcomes (P> 0.05).

**Conclusion:** Although ADA diagnostic criteria was more sensitive, diagnosis of GDM by WHO criteria was associated with higher adverse pregnancy outcomes in Nigerian women. A diagnosis of GDM that meets both WHO and ADA criteria provides stronger prediction for macrosomia or at least one adverse pregnancy outcome than a diagnosis that meets only WHO or ADA criteria. Therefore, a GDM diagnostic guideline that incorporates the strengths of both diagnostic criteria may be more useful in preventing adverse pregnancy outcome.

## A-016

**Intracranial gadolinium deposition quantified by ICP-MS following multiple contrast-enhanced MRI exams**

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**Background:** Intravenous gadolinium-based contrast agents (GBCAs) are widely used in MR imaging, yet their safety and chemical stability remain topics of active investigation. In the current study, we sought to determine if repeated intravenous exposures to GBCAs are associated with neuronal tissue deposition.

**Methods:** In this single center study, we compared T1-weighted signal intensities from MRI exams and post-mortem neuronal tissue samples on 13 patients who underwent 4 or more gadolinium-enhanced brain MRIs between 2000-2014 (contrast exposed group) to 10 gadolinium-naïve patients (control group). All contrast-exposed patients had relatively normal renal function at the time of examination. Neuronal tissues from the dentate nuclei, pons, globus pallidus, and thalamus of these 23 deceased patients were harvested from our institutional biospecimen archive and subsequently analyzed by inductively coupled plasma mass-spectrometry (ICP-MS), transmission electron microscopy (TEM) and light microscopy to quantify, localize, and assess the effects of gadolinium deposition. Results were correlated with Pearson's test.

**Results:** Compared to neuronal tissues of control patients, all of whom demonstrated undetectable levels of gadolinium, neuronal tissues of GBCA-exposed patients contained between 0.2-58.8 µg gadolinium/g tissue, in a significant dose-dependent relationship that strongly correlated with signal intensity changes on precontrast T1 weighted MR images ( $p=0.38-0.95$  for various tissues). Gadolinium deposition in the capillary endothelium and neuronal interstitium was only observed in the contrast-exposed group.

**Conclusion:** Intravenous gadolinium contrast material exposure is associated with neuronal tissue deposition in the setting of relatively normal renal function. Additional studies are needed to investigate the clinical significance of these findings.

## A-019

**Evaluation of early changes of cartilage biomarkers following arthroscopic meniscectomy in young Egyptian adults**

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**Abstract Background:** The metabolic imbalance in the articular cartilage following meniscectomy includes an increase in cartilage degradation with an insufficient reparative or anabolic response resulting in structural, biochemical and mechanical changes that can progress from pre-clinical, to pre-radiographic, to radiographic damage of the joint.

**Purpose:** To evaluate combinations of imaging and biochemical biomarkers for cartilage breakdown, synthesis and quantity in the early period of post-arthroscopic meniscectomy.

**Subjects and methods:** Twenty young adults (three of them were females) who underwent unilateral arthroscopic partial meniscectomy were evaluated. The patients had a mean age of 32.5 years (range, 24-39), mean BMI of 28.5 kg/m<sup>2</sup> (range, 24-34). Preoperative and six months postoperative US and MRI-based markers (cartilage thickness and volume, respectively) were quantified for medial and lateral tibio-femoral compartments for both knees. Preoperative, three and six months postoperative biochemical markers serum assays were measured; COMP and Col II (cartilage matrix breakdown) and PIICP (cartilage synthesis). These three markers were measured in an age, sex and BMI matched twenty healthy subjects for comparison.

**Results:** The meniscectomized knees had significantly lower total knee cartilage volume,  $P < 0.05$  but non-significant mean thickness than the intact contralateral knees. Among the individual biochemical markers, PIICP had the highest significant diagnostic accuracy quantified as the area

under the receiver-operator characteristics curve (AUC) of 0.75 (95% confidence interval: 0.509- 0.912) higher than all others,  $P < 0.05$  to distinguish subjects with progressive cartilage loss from non-progressors. Diagnostically, ratio of COMP and Col II to PIICP scored AUC of 0.90 (0.69- 0.98, higher than PIICP:  $P = 0.0001$ ). For prediction of cartilage loss, none of the individual markers could be used.

**Conclusion:** Cartilage volume loss by MRI combined with changes in cartilage matrix turnover detected by molecular biomarkers may reflect the initial changes associated with cartilage degeneration that account for early OA.

## A-020

**Prevalence of Metabolic Syndrome among Ethnic Groups in China**

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**Background:** To explore the prevalence of Metabolic Syndrome (MetS) among ethnic groups living in China.

**Methods:** A cross-sectional study was performed among 13263 subjects aged 35-98 years from five provinces in the North and South of China, including Han ethnic and six minorities: Mongolians, Korean, Miao, Li, Tibetan and Tujia. The modified National Cholesterol Education Program Adult Treatment Panel III criteria were adopted to diagnose MetS.

**Results:** The crude prevalence of MetS ranged from 10.3% to 30.3%. Koreans had the highest prevalence and the Miao had the lowest prevalence. After standardization of age using the data of the fifth national census conducted in 2000, the order of prevalence of MetS was Korean (24.1%), Mongolians (21.2%), Li (15.5%), Han (13.6%), Tibetan (12.7%), Miao (12.4%) and Tujia (10.1%). The prevalence of high blood pressure, hypertriglyceridemia and impaired fasting plasma glucose in Koreans was higher than in the other ethnic groups. Mongolians had the highest prevalence of central obesity; and the Tujia had lower high-density lipoprotein (HDL) cholesterol. Consistent with previous research, logistic regression analyses showed that uric acid was significantly and positively correlated with MetS in the different ethnics.

**Conclusions:** The prevalence of MetS in Korean and Mongolians is higher than the other ethnics. Measures should be focused on these groups with high prevalence to promote disease prevention and control.

**Keywords:** Metabolic Syndrome, nationalities ethnic group, China

## A-021

**Investigation of role of food allergies in functional constipation etiology in childhood**

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**Introduction and Aim**

Approximately 97% of cases with chronic constipation in childhood are associated with functional reasons. Some causes such as the delayed defecation, inadequate fluid and fiber intakes are important risk factors for functional constipation. In recent studies are shown that food allergy is also a risk factor for developing of functional constipation. However, the prospective studies in this subject are limited. Aim of this study is to determinate prevalence and effect of food allergies for functional constipation in children.

**Methods**

Functional constipation's diagnosis was performed according to Roma III criteria. Total 119 children with functional constipation were included in this study [61 female (51.3%), 58 male (48.7%)]. The mean age of these cases was  $4.1 \pm 2.6$  (1-14) years. In each case, for the definitive and differential diagnosis, the results of hemogram, total IgE, specific IgE for the suspicious food allergens (cow's milk, egg-white, fish, wheat, peanut, soya bean, etc) and respiratory allergens (inhalant pollens, mites, animal hairs, etc), thyroid hormones, serum tissue transglutaminase-IgA, sweat test, and stool microbiological/parasitological tests were recorded. Also, the results of abdominal ultrasound and X-ray radiography were evaluated. The cases caused

by organic diseases such as anatomic disorders, chronic illness, genetic syndromes, hypothyroidism, celiac disease and cystic fibrosis were excluded from the study. For the diagnosis of food allergy were used the elevated total IgE and specific IgE values and/or food elimination tests, and endoscopic methods.

**Results**

The significant IgE values (>100 IU/ml) were defined in 29 cases (24.4%). Food allergies were determined in 23 cases (19.3%), inhalant allergies were in 6 cases (5.0%). All cases diagnosed allergy had suffered from perianal disease (anal fissure and/or dermatitis). The most frequent food allergens were cow's milk and egg's white.

**Conclusion**

Food allergy has a high prevalence for functional constipation of childhood. Therefore, food allergy should be investigated in the cases with functional constipation.

**A-022**

**Diagnosis of Infection Utilizing Accellix CD64**

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**Background:**

Differentiating patients who are infected or not in the ICU can be very difficult. Present diagnostic tests remain inadequate. CD64 is constitutively expressed on the cell surface of PMNs and monocytes, but at low levels during the absence of infection. Upon invasion of a pathogen into the circulation, at a very early step of the immune host response, the expression level of CD64 on neutrophils increases dramatically. CD64 has a high specificity as its expression is not significantly elevated in malignancy of myeloid cells, any drug therapy (other than cytokines), clinical conditions with localized tissue damage, pregnancy and auto-immune disorders. The purpose of this study was to evaluate the Accellix CD64 instrument which provides results in 20 minutes in ICU patients with and without infections.

**Methods:**

The Accellix CD64 cartridge has all pre-analytical & analytical processing performed in the cartridge without further user intervention. This has been enabled by the development of a onetime use cartridge which includes onboard reagents and control material as well as an integrated flow cell. Infected (ICUi) and non-infected ICU patients (ICU Control-ICUC) and normal volunteers (C) had CD64 levels measured by the Accellix CD64

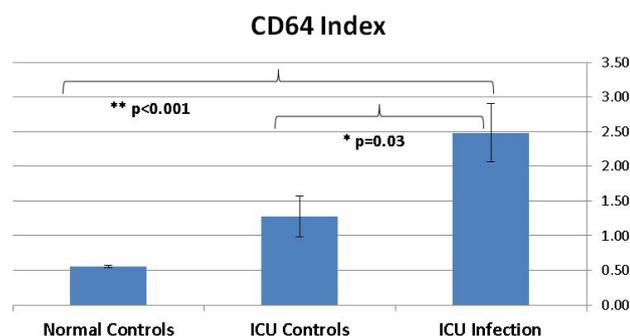
instrument. Measurements were calculated as 'CD64 index', i.e. the ratio

between the fluorescence of the PMN population and the fluorescence of control beads. ICU infection, ICU control and normal control patients' results can be seen in Figure 1.

**Results:**

Sixty patients were studied (ICUi-17, ICUC-13 and C-30). CD64 Index levels were higher (mean ± SEM) in ICU infection patients than ICU control and normal control patients (2.49 ± 0.42 vs. 1.28 ± 0.30 vs. 0.56 ± 0.02, p = 0.03 for ICU populations).

**Conclusion:** CD64 Index levels are higher in infected than non-infected ICU patients. Accellix CD64 is a promising instrument to differentiate infected from non-infected ICU patients in a timely manner.



**A-023**

**Diagnosis and Prognosis of Sepsis in the Emergency Department - Usefulness of the Point-of Care Test PATHFAST Presepsin**

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**Background:** Presepsin (sCD14-ST) serves as a mediator of the response to lipopolysaccharid from infectious agents. First evidence suggested that presepsin may be utilized as sepsis marker.

**Objective:** To examine the suitability of presepsin for diagnosis, prognosis and disease monitoring in patients suspicious of sepsis admitted to the emergency department (ED).

**Methods:** Presepsin was determined at presentation (baseline), after 8, 24 and 72 hours in 123 individuals admitted to the ED with signs of SIRS

(systemic inflammatory response syndrome) and/or infection. APACHE II score was established 24 and 72 hours after admission. 123 healthy individuals served as control group. Primary endpoint was death within 30 days. Presepsin was determined using the POC assay PATHFAST

**Presepsin.**

**Results:** Mean presepsin concentrations of the patient group at presentation and of the control group were 1945 ng/L and 130 ng/L, respectively (p<0.0001). Median presepsin levels at first presentation were 304, 544, 1944 and 2796 ng/L in differed highly significant in patients with SIRS (n=9), sepsis (n=74), severe sepsis (n=34) and septic shock (n=6), respectively. between comparable to the APACHE II score which has been established 24 hours after admission.

24 patients died during 30 days. The 30-day mortality was 19.5% ranging from 10 % to 32% between the 1<sup>st</sup> and the 4<sup>th</sup> quartile of presepsin concentration. ROC analysis revealed an AUC of 0.705. Non-survivors showed high presepsin values with increasing tendency during follow-up while surviving patients exhibited significant lower values with decreasing tendency.

**Conclusion:** Presepsin demonstrated a strong relationship with disease severity and outcome. Presepsin provided reliable discrimination between SIRS and sepsis as well as prognosis and early prediction of 30-day mortality already at admission. Moreover, presepsin values showed close association to the course of the disease.

Presepsin Median (IQR), ng/L	Course of presepsin during follow-up			
	Baseline	8 hours	24 hours	78 hours
Survivors, n=114	590 (345-1396)	622 (367-1912)	574 (336-1610)	533 (324-1246)
Non-survivors, n=24	1763 (705-6616)	1859 (1001-5744)	1731 (809-4586)	2056 (811-5540)
p-value	0.0046	0.0005	0.0033	0.0013

**A-025**

**Effect of a hypnotic drugs on glycemic control in type 2 diabetes mellitus :Prediction of clinical improvement**

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**Objective:**

Sleep disorder and/or increased stress are known to be worsening factors for glycemic control in patients with type 2 diabetes mellitus (DM). Some reports stated that better sleep improves insulin resistance, and that the combination of conventional antidiabetic and hypnotic drugs is sometimes administered to DM patients with a sleep disorder. This study was performed to evaluate whether the combination therapy with a hypnotic drugs improves HbA1c, and to establish a method of using clinical laboratory data to predict patients whose HbA1c will be improved.

**Method:**

We extracted 20,630 patients with type 2 DM who have been taking antidiabetic drugs and a hypnotic drug such as Zopiclone, Estazolam, Triazolam, Brotizolam, Zolpidem, and Diazepam, from a data warehouse of Kochi Medical School Hospital (from October 1981 to December 2014).

The starting day of this study was determined as period of 120 days without hypnotic drugs. HbA1c level at the starting day was determined as the pretreatment data. HbA1c level 30 to 120 days after the starting day was determined as the post-treatment data, and the difference of the HbA1c levels were compared. Cutoffs to identify HbA1c improvement were obtained by logistic regression and decision tree analyses by defining improvement and nonimprovement of HbA1c as the criterion variables, and the biochemical data and complete blood count data before the hypnotic therapy as explanatory variables.

#### Result:

The group receiving diazepam (n = 4,313) showed the greatest rate of HbA1c improvement (54.9%), followed by the group receiving zopiclone (n = 2,324; improvement rate, 48.4%). The other hypnotic groups also showed a similar rate. According to the logistic regression analysis (stepwise method), HbA1c, glucose (GLU), high-density lipoprotein cholesterol (HDLc), total cholesterol (T-CHO), and total protein (TP) were the important variables, with an area under the curve (AUC) of 0.68. The median of the selected group according to the prediction formula was -0.3 NGSP (%), whereas the median of the nonselected group was 0 NGSP (%). The Mann-Whitney U-test showed  $P < 0.001$ , suggesting a significant difference. According to the major cutoffs obtained by using the decision tree, patients showing HbA1c 6.3, T-CHO 156 and HDLC 29 or those showing HbA1c > 8.8; or those showing HbA1c > 7.0 and TP 6.1 tended to have improved HbA1c due to the hypnotic therapy.

#### Conclusion:

In type 2 DM patients receiving the combination therapy with a hypnotic drugs, HbA1c, T-CHO, HDLC and TP, identified those patients whose HbA1c will improve with the treatment. Moreover, diazepam had the greatest effect on glycemic control compared with other hypnotic drugs.

### A-026

#### Novel Markers of Gestational Diabetes mellitus (GDM)

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**Introduction:** Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance that occurs with pregnancy or is first discovered during pregnancy. The detection of GDM is important because of its associated maternal and fetal complications. At present, the standard protocol includes glucose challenge test (GCT) screening followed by a diagnostic 3-h oral glucose tolerance test (OGTT) at 24-28wks of gestation. These glucose-load methods have associated practical difficulties, poor patient compliance (prolonged fasting) and additional blood draws. Although glycosylated hemoglobin (HbA1c) has been a standard measure for monitoring diabetes, studies recommend limited utility of routine measurement of HbA1c for assessing glycemic control in pregnancy. Previous studies have proposed clinical utility of nontraditional shorter term glycemic biomarkers in gestational diabetes. Thus, the main objective of our study was to evaluate the efficacy of glycemia markers such as fructosamine (FRA), glycated albumin (GA), and 1, 5-anhydroglucitol (1, 5-AG) over the conventional 3-h OGTT in diagnosing GDM. Further, we wanted to establish diagnostic cut-off values for these markers.

**Study Design:** The current study was conducted at the Texas Children's Hospital laboratory using archived samples and was approved by Baylor IRB. A total of 124 samples were included in the study group categorized as group 1 (controls-normal screen; normal OGTT; n=34), group 2 (impaired GT-abnormal screen; normal OGTT; n=50) and group 3 (diagnosed GDM-abnormal screen; abnormal OGTT; n=40 according to the ADA criteria). Patient health information (PHI) was procured using the electronic medical records (EMR). All the three groups were analyzed for FRA, GA and 1,5-AG using the quantitative Enzyme linked immuno-sorbent assays (ELISA) using manufacturer instructions. The coefficient of variation (%CV) of these assays was <20%. Nonparametric statistical analysis was performed.

**Results:** Among the three proteins analyzed, fructosamine levels were not significantly different between the 3 groups by ANOVA ( $p > 0.05$ ) whereas glycated albumin levels were significantly different ( $p < 0.1$ ) in groups 1 (controls) versus 2 (IGT) but not for groups 1 and 3 (GDM) respectively. 1, 5-AG levels were significantly different amongst all the groups [Controls - Median, Inter-Quartile Range 1.47U/L (1.21, 2.01); IGT- 1.01U/L (0.88, 1.15); GDM -1.16U/L (1.02, 1.26)] ( $p < 0.05$ ). Further, the cut-off values for each of these biomarkers were established using the receiver operator curves (ROC). Using 1.27U/L as the cut-off, 1, 5-AG represented 75% sensitivity and 65% specificity for diagnosing gestational diabetes.

**Conclusion:** Novel markers of GDM are urgently needed. These studies if confirmed with a larger sample size will provide an effective alternative to the diagnosis of GDM.

**Keywords:** Gestational diabetes mellitus, fructosamine, glycated albumin, 1, 5-anhydroglucitol, impaired glucose tolerance, biomarkers

### A-027

#### Performance of Sofia Influenza A+B test compared to Luminex x-TAG respiratory viral panel assay in the context of institutional respiratory outbreak.

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**Introduction:** Influenza is an acute respiratory illness caused by Influenza A or B viruses that occur in outbreaks, mainly during the winter season. Rapid laboratory diagnosis of Influenza can help guide the clinical management of suspected patients effectively. Clinical sensitivities and specificities of the rapid influenza diagnostic tests varied considerably in the literature. Most of these studies are evaluated using previously frozen or stored specimens that had been previously tested positive. This study compares the performance of rapid Sofia Influenza A + B test to nucleic acid multiplex test x-TAG respiratory viral panel (RVP) assay in freshly collected nasal aspirates and measured simultaneously by both assays.

**Methods:** Retrospective data from 707 nasal aspirates (September 2014 to January 2015) collected from both adults and children tested simultaneously by both rapid Sofia Influenza A+B FIA immunofluorescence (Quidel, San Diego, CA) and qualitative nucleic acid multiplex RVP assay X-TAG Luminex technology (Luminex, Austin, TX) were analyzed.

**Results:** Concordance, analytical sensitivity and specificity were evaluated for both Influenza A, Sub types H1 and H3 and Influenza B. Prevalence for Influenza A by RVP is 16.3% and for Sub type H3 was 13.7%. Both non specific Influenza A and subtype H3 were both positive in 13.8% of above population. None of the aspirates are positive for Influenza A Subtype H1. Only one out of 707 specimens was positive for Influenza B.

	Influenza A (Sofia- A vs. RVP-A)		Influenza A (Subtype H3) (Sofia-A vs. RVP-H3)	
	%	95% CI	%	95% CI
<b>Sensitivity</b>	56.7	46.1-64.9	65.0	54.6-74.4
<b>Specificity</b>	99.5	98.5-99.9	99.3	98.3-99.8
<b>Positive Predictive Value</b>	95.5	87.5-99.0	94.0	85.4-98.3
<b>Negative Predictive Value</b>	92.0	89.6-94.0	94.7	92.6-96.3
<b>Agreement</b>	92.4%		94.6%	

**Conclusion:** Sofia Influenza rapid test demonstrated good specificity and low sensitivity compared with a nucleic acid test for both Influenza A and Subtype H3. Sofia Influenza A + B test performed well in providing a rapid diagnosis, however confirmatory molecular testing is recommended for negative test results. Reevaluation of test performance should be periodically performed during outbreaks with the emergence and circulation of new influenza strains.

### A-028

#### Cost-effectiveness Analysis in Prognosis of ST-Segment Elevation Myocardial Infarction: Choice of Optimal Laboratory Marker

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**Background:** The aim of this study was to explore discriminative abilities of several biomarkers of inflammation and hemodynamic stress as predictors for major adverse cardiovascular events (MACE) in patients with ST-segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (pPCI). Also, to assess their cost-effectiveness compared with the RISK-PCI score for the prediction of MACE during a 30-day follow-up after pPCI.

**Methods:** Using a decision model, we evaluated the costs, accuracy, and cost-effectiveness of each model. The RISK-PCI score was used as the baseline model. Other models were formed with the consecutive addition of selected markers: myeloperoxidase (MPO), high sensitive C-reactive protein, adiponectin, B-type natriuretic peptide (BNP), N-terminal-proBNP to the baseline model. A best-case model was formed from a combination of biomarkers to yield the best patient stratification algorithm. All models were assessed by their predictive probabilities using receiver operating characteristic curves. To accomplish our goals, we recruited 150 STEMI patients treated by pPCI. Composite 30-day major adverse cardiovascular events (MACE) was defined as cardiac death, non-fatal reinfarction, and target vessel revascularization. The analysis was performed from a third-party payer perspective.

**Results:** Only two strategies had outstanding discriminative abilities: the best-case model (RISK-PCI score+BNP+MPO) and RISK-PCI score plus BNP with area under

the curve (AUC) values of 0.869 and 0.851, respectively. The cost-effectiveness ratio varied between 5199 € per AUC for the baseline model to RSD 9011€ per AUC for RISK-PCI score+NT-proBNP. After elimination of dominant strategies, the incremental cost-effectiveness ratio (ICER) for the remaining three strategies (baseline, RISK-PCI score plus BNP, and the best-case model) were calculated. For the RISK-PCI score plus BNP, the ICER (compared with the baseline model) was 18106 € per additional accuracy calculated for 100 analyses. The ICER for the best-case model (compared with the baseline model) was 84961€ per additional accuracy calculated for 100 analyses. Strategy involving hemodynamic stress biomarker BNP was more cost-effective than strategies involving inflammatory markers. Sensitivity analysis indicated that results were robust.

Conclusion: Our results support the feasibility of a multimarker approach for MACE prediction in STEMI patients treated by pPCI. The introduction of BNP in the clinical laboratory would be convenient and cost-effective.

### A-029

#### Investigation of Red Blood Cells Alloantibodies after Transfusions in Southern Taiwan

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##### Background:

Development of red blood cell alloantibodies may lead to severe complications in patients receiving multiple blood transfusions and compromise the therapy.

Previous studies indicated that the rate of alloimmunization in chronically transfused patients was as high as 60 percent and specificity of alloantibodies varied for different regions, ethnics, and diseases.

##### Methods:

The study investigated the prevalence and type of unexpected red cell antibodies in a medical center with more than 1,200 beds. A total of 19,821 pre-transfusion records in 2012 were retrospectively reviewed for antibody screening tests at the facility in southern Taiwan where Han Chinese dominantly inhabited. Descriptive statistics were applied to determine the figures, based on the time interval between transfusion therapy and antibody detections.

##### Results:

The antibody screening test showed positive in 163 of the 19,821 patients, indicating the overall alloimmunization rate of 0.82%. Further analysis revealed that 42.3 % (69/163) of cases with antibodies were found before arriving at the facility. The most common alloantibody identified was anti-Mi<sup>a</sup> (47.9%), followed by anti-E (17.8%), anti-E+c (6.7%), anti-P1 (6.1%), anti-Le<sup>a</sup> (5.5%), anti-M (4.9%), anti-Mi<sup>a</sup>+E (2.5%), anti-Jk<sup>a</sup> (1.8%), anti-S (1.2%) and the others (5.6%).

Additionally, 50.9 % (83/163) cases with alloantibodies were first identified after transfusion in this facility. Major antibodies detected after 7 days of transfusion included anti-Mi<sup>a</sup>, anti-E, anti-P1 and anti-Jk<sup>b</sup>.

Within one week, antibodies were found in 5 patients (6.0%), between 8-14 days in 11 patients (13.3%), between 15-30 days in 10 patients (12.0%), between 31-60 days in 6 patients (7.2%), between 1-12 months in 18 patients (21.8%) between 13-24 months in 10 patients (12.0%), and more than 2 years in 23 patients (27.7%). One specific case showed anti-S in 18 months and anti-E in 21 months.

Furthermore, 45 cases (54.2 %, 45/83) of alloantibodies were developed after 2 units packed RBC administered and 33 cases (39.8 %, 33/83) were detected alloantibodies after more than 3 units packed RBC administered. Four cases (4.8%, 4/83) also developed alloantibodies after 12 units platelet concentrations administered, and 1 case (1.2%, 1/83) did them after 1 unit of Apheresis platelet was administered.

##### Conclusion:

In conclusion, the alloantibodies develop on the fifth day at the earliest posttransfusions. Platelet products containing small volume of red blood cells can stimulate formation of alloantibodies. Therefore, this study recommended that pre-transfusion testing be performed on blood samples collected within three days.

### A-030

#### Potential role of biomarkers and cardiac imaging in scleroderma patients with subclinical myocardopathy

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##### BACKGROUND

Scleroderma (Systemic sclerosis) (SSc), is a chronic autoimmune connective tissue disease which extensive fibrosis, vascular alterations and autoantibodies against various cellular antigens area among the principal features. SSc can cause pulmonary arterial hypertension (PAH) that is a major risk factor for death.

##### AIM

To evaluate in patients with SSc the relationship between different biomarkers and the clinical, immunological and biological profiles (inflammatory and profibrogenic) and parameters of the cardiac magnetic resonance imaging (MRI) and echocardiography.

##### METHODS

Twenty patients diagnosed with SSc were prospectively enrolled and compared to nine healthy controls. All underwent screening for cardiac complications evaluated by MRI and echocardiography. Systolic eccentricity index (Elsys) >1) and pulmonary-artery mean velocity (APVEL) <11.7 cm/s were defined as pathological. We measured different serum biomarkers by multiplex technology for inflammation (IL-13, IL-6, TNF $\alpha$ ), vasculopathy (VEGF), and fibrosis (endoglin, GDF-15, PDGFR and TGF $\beta$ ) and cardiac biomarkers (NT-proBNP - Siemens Vista and hs-cTnT - Roche) by chemoluminescence assays.

##### RESULTS

Mean age was 54 years and 80% were women. Two patients develop PAH. In multivariate analysis, TNF- $\alpha$  and GDF-15 were significantly higher in patients. We found a significant positive correlation between hs-cTnT in patients with arterial hypertension. Patients with SCL-70, anticentromere antibody and diffuse disease showed higher concentrations of PDGFR. One patient with PAH showed higher concentration for inflammatory and vascular biomarkers. We couldn't establish any correlation between biomarkers and right ventricular thickness. A positive correlation was found between hs-cTnT, endoglin and TGF $\beta$ 2 and Elsys. Similar results were observed for NT-proBNP and APVEL.

##### CONCLUSIONS

PDGFR (biomarker for fibrosis) is increased in patients with autoantibodies.

Cardiac biomarkers (hs-cTnT and NT-proBNP) may be useful screening tools to identify subclinical cardiac disease in SSc patients which can develop PAH leading to right ventricular dysfunction, heart failure and death.

We couldn't establish a relation between concentrations fibrotic biomarkers and ventricular thickness.

### A-031

#### Evaluation of Soluble Urokinase Plasminogen Activator Receptor and Presepsin in Patients Presenting with Sepsis in the Emergency Department

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**Background:** Urokinase plasminogen activator receptor is expressed on the cell membrane of various cell types. Its soluble form (suPAR) is increased in critical ill patients especially with infectious diseases and sepsis. First evidence suggested that suPAR may serve as a prognostic marker. As presepsin has already shown convincing results in prognostication we compared suPAR and presepsin (PSEP) with procalcitonin (PCT) and the APACHE II score in patients presenting with sepsis in the emergency department (ED).

**Methods:** suPAR, PSEP, PCT were determined using commercial available assays (suPARnostic virogates, PATHFAST, BRAHMS Kryptor) in 69 patients with sepsis at admission to the ED. Primary endpoint was death within 30 days. The combined endpoint "major adverse event" (MAE) consisted of at least either the primary or at least one of the secondary endpoints intensive care, mechanical ventilation or dialysis.

**Results:** PSEP, PCT and APACHE II score differed significantly between patients with sepsis, severe sepsis and septic shock (p-values: 0.0028, 0.01 and <0.0001,

respectively) whereas the difference of suPAR was only slightly significant (p=0.0752). The 30-day mortality was 27.5%, ranging from 7.3% in sepsis to 44% in severe sepsis and 80% in septic shock. ROC analysis for discrimination between survivors and non-survivors revealed AUC values of 0.883, 0.727, 0.568 and 0.835 for PSEP, suPAR, PCT and APACHE II score, respectively. PSEP demonstrated a stronger relationship with 30-day MAE compared with suPAR and PCT: AUC-values: 0.753, 0.615, 0.610, respectively.

**Conclusion:** The prognostic accuracy of suPAR was superior to PCT but not to PSEP. Although suPAR provided reliable prognosis and prediction of 30-day mortality, the prognostic power of PSEP was superior to PCT and suPAR as well as to the APACHE score for outcome prediction (mortality and MAEs). PSEP was also superior in discrimination between sepsis, severe sepsis and septic shock.

Biomarker values in patients with or without MAEs and in survivors and non-survivors				
Medians (95% CI)	suPAR	Presepsin	PCT	APACHE II
No MAE, n=43	8.6(6.9-10.4)	782(556-988)	1.35(0.69-2.73)	14(12-19)
MAE, n=26	11.0(8.2-17.7)	1777(1081-3135)	2.17(1.08-15.9)	29(24-35)
p-value	0.1096	0.0003	0.1083	0.0001
Survivors, n=50	8.6(7.0-10.4)	804(615-992)	1.56(1.13-3.39)	18(13-23)
Non-survivors, n=19	13.2(8.5-18.9)	2124(1376-3563)	2.78(0.38-20.9)	29(24-36)
p-value	0.0643	0.0001	0.6917	0.0003
AUC	0.727	0.833	0.568	0.835

**A-032**

**Molecular cytogenetic study of deletion on derivative chromosome 9 in a CML patient with BCR/ABL rearrangement**

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**Background:** The BCR/ABL gene rearrangement is the causing factor in chronic myeloid leukemia (CML). In most cases, it is cytogenetically identified a translocation between chromosomes 9 and 22, resulting in the presence of the Philadelphia chromosome (Ph). Deletions around the breakpoints on the derivative chromosome 9 including ABL and BCR sequences in Ph+ CML patients are thought to have prognostic value. The present study reports a case of translocation involving chromosomes 9 and 22, with a possible deletion on derivative 9 identified by conventional cytogenetic and confirmed by fluorescence in situ hybridization (FISH).

**Methods and results:** In september 2014, sample of a 41 year old patient with leucocytosis, severe anemia and thrombocytosis was referred to our institution to perform cytogenetic and molecular testing. Cytogenetic analysis showed the presence of the translocation between chromosomes 9 and 22 as well as a possible deletion of the derivative chromosome 9 in sixteen among the twenty examined metaphases. The karyotype was: 46,XX,t(9;22)(q34;q11.2)?del(9)(q22q13)[16]/46,XX[4]. FISH using the LSI BCR/ABL Dual-Color, Dual Fusion (D-FISH) probe showed one fusion, one green and one red signal (1F1G1R) confirming the presence of the BCR/ABL1 translocation and deletion on derivative chromosome 9. Multiplex qualitative reverse transcriptase-polymerase chain reaction detected the transcript BCR/ABL, isoform p210 (b3a2). Real-time quantitative polymerase chain reaction (RQ-PCR) was performed after the beginning of Gleevec therapy to quantify BCR/ABL1 transcript and evaluate the treatment response. The level of BCR/ABL1 expression was 0.54% (IS), indicating a good molecular response.

**Conclusion:** FISH can be used as an adjunct to the karyotyping to detect the deletion on derivative chromosome 9. Patients evaluated in this study were good molecular response to treatment, although some authors suggest inferior survival as well as poor response to therapy in CML patients carrying derivative 9 deletions.

**A-033**

**The Economic Burden of Confirmatory Testing for Cardiac Troponin and Human Chorionic Gonadotropin: A Multi-Site Laboratory Database Analysis.**

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**Background:** Erratic false positive human chorionic gonadotropin (hCG) and cardiac troponin (cTn) results have been reported on multiple analytical platforms. Many laboratories minimize the reporting of such results through confirmatory testing i.e. re-centrifugation and reanalysis of select patient samples. However, this practice delays clinical decision making and also increases healthcare costs. We analyzed retrospective data from Edmonton, Alberta to quantify the economic burden of such confirmatory testing to the laboratory.

**Methods:** hCG confirmatory testing practices are uniform across the city; any sample with 5 U/L < hCG < 100 U/L is re-centrifuged and reanalyzed. Four months of hCG data were extracted from three laboratories. In contrast, cTn confirmatory testing varies across the city. One laboratory re-centrifuges and reanalyzes all first-time results >0.15 microgram/L; a second laboratory does so if cTn >0.10 microgram/L; a third laboratory does not regularly confirm results. Four months of cTn data were extracted only from the two laboratories that perform confirmatory testing. We analyzed the data for the total number of tests, number of first-time positive results, and number of false positive results. This information was combined with costing for test supplies and technician time to calculate the overall cost of confirmatory testing.

**Results:** The table summarizes the results of our analysis. The overall financial burden of hCG and cTn testing ranged from 8,154 USD per annum (small community hospital) to 11,816 USD per annum (large academic center).

**Conclusions:** To limit the risk of using a potentially false-positive hCG or cTn result to inform clinical decision-making, many laboratories have confirmatory testing policies in place. Our results indicate that such retesting is of considerable economic burden to any laboratory. Improvements in analytical precision of these assays as well as improvements to preanalytical sample quality could reduce or eliminate this burden.

	Patients Seen Annually	Total # Tests (doesn't include repeats)	First-Time Positives	Repeated First-Time Positives	False Positives	False Positive Rate (%)	Cost to Lab Per Annum (USD)
<b>HCG</b>							
Academic Center	700,000	2,342	108	99	44	44	2,417
Large Community Hospital	450,000	9,076	188	173	35	20	4,223
Small Community Hospital	11,900	826	71	63	0	0	1,538
<b>cTn</b>							
Academic Center	700,000	13,465	1180	385	26	7	9,399
Small Community Hospital	11,900	5,289	344	271	17	6	6,616

**A-034**

**Plasma cytokines augment Procalcitonin levels in septic patients admitted to Oncological Intensive Care Unit**

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**Background:** Sepsis biomarkers may be useful to rule out infection, serve as markers of disease severity including need for ICU admission, and in evaluating the patient's clinical course.

**Objective:**

Our objective was to evaluate the diagnostic and prognostic value of procalcitonin (PCT) and 5 select cytokines (TNF-α, IL-1β, IL-6, IL-8, interferon-gamma (IFN-γ)) in cancer patients admitted to the ICU with suspected severe sepsis and septic shock.

**Methods:** We conducted an observational quality improvement study that evaluated 25 patients who were admitted to the ICU with suspected severe sepsis or septic shock over a 6-month period. One patient was

excluded due to specimen availability limitation.

**Design:** Prospective, observational study.

**Setting:** Adult oncology medical-surgical ICU at a tertiary cancer center.

**Subjects:** 24 patients (10 with suspected severe sepsis or septic shock and 14 control subjects).

**Interventions and measurements:** Serum PCT (VIDAS Brahms PCT, Biomerieux) and plasma TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, and IFN- $\gamma$  (MSD electrochemiluminescence assay (Meso Scale Discovery, Gaithersburg, MD) levels were measured within 24h (Day 1) of ICU admission.

The samples were batched and the PCT and cytokine results were not available for clinical use. Receiver operating curves (ROC) for PCT and the 5 cytokines and their relationships to the Sequential Organ Failure Assessment (SOFA) scores on Day 1 and patient outcomes were analyzed.

**Results:** The mean SOFA score on Day 1 of the septic patients was 8.9 (range 2-14). The AUC for PCT, TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, IFN- $\gamma$  on Day 1 were 0.871, 0.806, 0.51, 0.889, 0.722, and 0.833, respectively. The highest AUC was demonstrated when IL-6 was coupled with PCT (0.9) and was lowest with IL-8 and PCT. 50% of the septic patients died. Nonsurvivors had higher levels of PCT, IL-6 and IL-8 on Day 1.

**Conclusions:**

Our preliminary findings suggest that plasma levels of IL-6 augment PCT in diagnosing severe sepsis/septic shock in cancer patients admitted to the ICU. A larger, more comprehensive study is needed to substantiate these findings.

### A-035

#### Utility Of A.D.A. Levels In Body Fluids From Peri urban Locality-India

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**BACKGROUND-**Adenosine deaminase (ADA )is rapid sensitive inexpensive diagnostic biomarker in body fluids for diagnosis of tuberculosis.

**AIM-** To assess the specificity and sensitivity of ADA levels in body fluids for diagnosis of tuberculosis.

**Material and Method-** Adenosine deaminase (ADA ) in 111 body fluids- 72 pleural fluids, 13 ascitic fluids, 26 cerebrospinal fluids and 3 serum samples was estimated by Gisti G Galanti method using kit manufactured by Tulip diagnostics.

Negative and positive were classified using cut of limits as per the kit reference.

These results were correlated with final diagnosis achieved by radiological, cytological, fluid protein level, ESR, and clinical correlation.

**Results-** Pleural fluids, out of 72, 62 were true positive with sensitivity 92 % specificity 100 %.

Limitation of the study \_TB culture, molecular methods were not used.

**CONCLUSION -** ADA is rapid sensitive and inexpensive diagnostic biomarker for tuberculous pleural effusion.

### A-036

#### The ALaRMS Score: Validation of Lab-based Mortality Prediction in a Swiss Population

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**Background:**

ALaRMS is an inpatient mortality predictive model (Acute Laboratory Risk of Mortality Score, published in 2013) based on additive scoring of routine laboratory measurements. This model was assumed to yield accurate mortality predictive information with an AUC of 87% in an U.S. population. In our study, we validated this model in a swiss tertiary hospital cross-sectional cohort.

**Methods:**

The laboratory data included the years 2012 and 2013 with a total number of 56101 cases. 54418 patients survived hospitalization. As the Inselspital uses troponin T testing and ICD-10 classification, the scoring had to be adapted accordingly. We

computed ALaRMS scores for all cases, added the information about survival, and generated ROC curves and AUROCs with bootstrapped confidence intervals.

**Results:**

In our cohort, we found a slightly lower, but comparable AUC of 83.04% (95% CI 82.06 - 84.03) for the ALaRMS model alone.

**Outlook:**

In a subsequent step, we aim to optimizing the ALaRMS model by penalized logistic regression modeling to take full advantage of the quantitative nature of our laboratory data and to narrow down the number of laboratory tests needed for efficient and effective mortality prediction.

### A-037

#### Obesity and Oxidative Stress

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**Background:**

Obesity is become one of the most common risk factor of metabolic syndrome. Obesity and its related conditions are lead to oxidative stress and inflammation. The aim of this study was to investigate the relationship between inflammatory parameters and obesity.

**Methods:**

37 obese adolescents (19 boys and 18 girls, median age:11, age range 6-16) were randomly select from obese children who were received to Bezmialem Vakif University Pediatric Endocrinology Clinic in Turkey. The control group consisted of 37; age- and gender- matched healthy children. All children's weight and height measurements were performed by the same person who used same equipments. BMI was calculated that body weight (kg) divided by height in meters squared.

After these measurements, HOMA-IR, types of cholesterol, CRP, total antioxidant activity (TAS), total oxidant status (TOS), thiol, catalase and paroxanase (PON) were assayed in serum samples. The SPSS software (ver. 11.5 for Windows; SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

**Results:**

Differences between groups were evaluated by Mann Whitney U test. BMI (P<0,001), HOMA-IR (P<0,001), total cholesterol (P<0,001), HDL cholesterol (P<0,001), LDL cholesterol (P<0,001), triglyceride (P<0,001), CRP (P=0,034), TAS (P<0,001), TOS(P=0,006), thiol (P=0,001) are significantly higher in obese group. There were no difference in catalase(P=0,152) and PON (P=0,273) between two groups.

**Conclusion:**

This study suggests that obese children are exposed to more oxidative stress than normal-weight children. Their lipid profiles are more abnormal than control group. Therefore, obese children are more prone to cardiovascular disease than normal-weight children.

### A-038

#### Aldosterone Status in Patients with Obstructive Sleep Apnea and Resistant Hypertension.

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**Background:** There is a strong association between Obstructive Sleep Apnea (OSA) and Resistant Hypertension (RH) and also between RH and hyperaldosteronism. Previous studies have shown controversial results about aldosterone and renin measurements related to OSA severity in patients with RH. The objective of this study was to evaluate the relationship between OSA and aldosterone status in patients with RH. **Methods:** We evaluated patients with RH and OSA (determined for polysomnography with apnea / hypopnea index - AHI). It was considered moderate apnea AHI > 15, and severe when AHI > 30. All patients were evaluated with 24-hour Ambulatory Blood Pressure Monitoring (ABPM); laboratory tests including plasma renin activity and serum aldosterone (in a first visit) and aldosterone measured in 24-hour urine (in a second visit). Patients were instructed to withdraw spironolactone four weeks before blood tests; 24-hour urine was obtained in use of all antihypertensive scheme including diuretics and spironolactone. Aldosterone was determined by Radioimmunoassay (Siemens, Los Angeles, CA); renin was determined by Chemiluminescence using Liaison Direct Renin kit (DiaSorin, Saluggia, Italy), the results were converted to renin activity and after used to calculate aldosterone-to-

renin ratio (ARR). Statistical analysis was performed with SPSS 17.0; we compared severe and moderate OSA in a bivariate form; continuous variables were analysed with T test for normal distribution or Mann Whitney for abnormal;  $\chi^2$  test was used for categorical variables. **Results:** 122 patients were evaluated, 48 (39%) men, the mean age was  $62 \pm 7$  years; AHI average was  $40 \pm 20$ . Patients with AHI  $> 30$  (severe OSA) had increased serum aldosterone ( $11.6 \pm 7.4$  ng/dL vs  $8.5 \pm 5.2$  ng/dL,  $p = 0.042$ ) and plasma renin activity ( $8.0 \pm 11.2$  ng/mL/h vs  $2.9 \pm 6.7$  ng/mL/h,  $p = 0.008$ ) when compared to group with moderate OSA. ARR and Urinary aldosterone were similar in both groups ( $10.9 \pm 17.1$  vs  $14.3 \pm 22.6$ ,  $p = 0.42$  and  $8.9 \pm 5.1$  mcg/24h vs  $7.7 \pm 6.6$  mcg/24h,  $p = 0.24$ , respectively). **Conclusions:** Severity of OSA was associated to higher serum aldosterone and higher plasma renin activity in patients with RH. There is no association with hyperaldosteronism based on ARR. Similarly, there was no statistical difference in Urinary Aldosterone levels based on severity of apnea, what probably was associated to use of antihypertensive drugs.

### A-039

#### The Levels Of Vaspin And Chemerin Levels And Correlation Between Cardiac Parameters In Patients With Psoriasis Vulgaris

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**BACKGROUND:** Significant associations between psoriasis and obesity or being overweight have been observed. Adipokines are involved in the pathogenesis of psoriasis and they are biomarkers of obesity-related inflammation. Chemerin is a newly identified adipokine and high systemic chemerin level was found as an independent marker of the metabolic syndrome. Vaspin is the anti-inflammatory adipokine, is discussed as a new link between inflammation and obesity. This study investigated vaspin and chemerin levels in the serum of psoriatic patients and healthy controls. and an association between vaspin-chemerin levels with predictors of subclinical cardiovascular disease in patients with psoriasis.

**METHODS:** A total of 56 patients suffering from psoriasis and 32 age-matched controls were included in the study. Vaspin and chemerin serum levels were analysed by ELISA. All patients were evaluated by transthoracic Doppler echocardiography. The psoriasis area severity index (PASI) was calculated in all psoriatic patients.

**RESULTS:** The serum concentration of soluble chemerin was significantly higher in psoriatic patients compared to healthy controls ( $330.9 \pm 70.1$  ng/mL,  $300.8 \pm 59.6$  ng/mL, respectively;  $p = 0.04$ ). There was no significant difference in the serum concentration of soluble vaspin between psoriatic patients and the control group ( $129.9$  pg/mL,  $126.4$  pg/mL, respectively;  $p > 0.05$ ). The epicardial fat tissue (EFT) was significantly increased ( $0.33 \pm 0.13$  cm vs.  $0.25 \pm 0.12$  cm;  $p = 0.04$ ) in patients with psoriasis compared with the controls. Flow mediated dilatation (FMD) was lower in psoriatic patients compared to the control group ( $6.66 \pm 2.44$ ,  $11.77 \pm 3.28$ , respectively;  $p = 0.000$ ). It was found the ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity ( $E/E'$ ) for the psoriatic group to be higher than the control ( $5.59 \pm 1.98$ ,  $4.69 \pm 0.94$ , respectively;  $p = 0.032$ ). The ratio of early diastolic mitral annular velocity ( $E'$ ) to late diastolic mitral annular velocity ( $A'$ ) was lower in psoriatic group than the control ( $1.05 \pm 0.4$  vs.  $1.32 \pm 0.47$ ,  $p = 0.014$ ). The myocardial performance index (MPI) was found lower in psoriatic patients than the control ( $0.54 \pm 0.06$  vs.  $0.60 \pm 0.09$ ,  $p = 0.009$ ). There was no correlations between vaspin with FMD, EFT and other echocardiography parameters. Chemerin correlated with ratio of mitral peak velocity of early filling (E) to mitral peak velocity of late filling (A).

**CONCLUSIONS:** Patients with psoriasis have higher blood levels of chemerin. In psoriatic patients there was subclinical cardiac dysfunction. There was a correlation between serum chemerin level and cardiac diastolic dysfunction that was not previously shown. These findings suggest that chemerin may play a role in the pathogenesis of psoriasis and can be used as markers of the disease. Further studies, investigating the interplay between vaspin, chemerin, inflammation, and psoriasis are needed.

### A-040

#### A prospective multi-site evaluation of the intra-menstrual cycle variability of anti-müllerian hormone (AMH) using an automated AMH immunoassay

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**Background and Objective:** Access AMH<sup>1,2</sup> is a biomarker that is being developed for evaluating response to controlled ovarian stimulation in women undergoing in vitro fertilization procedures. Published results for intra-menstrual cycle variability lack agreement. The purpose of this study is to determine whether or not AMH levels vary significantly across the normal menstrual cycle.

**Methods:** 24 apparently healthy women were prospectively enrolled from 2 sites with IRB-approved informed consent. Blood samples were collected 2 times per week throughout each complete menstrual cycle (21 to 35 days) starting with baseline (day 2 to 4). Eligibility criteria:  $\geq 18$  years to  $\leq 45$  years, both ovaries present, no polycystic ovary syndrome (PCOS), no history of ovarian surgery, no exposure to cytotoxic drugs or pelvic radiation therapy, no recent contraceptive use, and no other recent hormonal therapy. Serum samples were tested on the Beckman Coulter Access 2 immunoassay analyzer<sup>3</sup>. Age-adjusted mixed-effects models were constructed to estimate intraclass correlation (ICC) and within-subject variability across the menstrual cycle.

**Results:** 191 specimens were collected from 24 women (mean age 35 years; range 24 to 45 years). Older age was significantly associated with lower mean AMH values ( $p$ -value = 0.004). There was no evidence of a linear trend in AMH levels across cycle days ( $p$ -value = 0.409). AMH showed more variability for levels  $\geq 3$  ng/mL and less variability for levels  $< 3$  ng/mL. The estimated ICC was 0.94 (95% confidence interval, 0.89-0.96), indicating that 6% of the overall variability in AMH was due to within-subject variability.

AMH Category	N		Mean AMH (ng/mL)	Within Subject		Between Subject		ICC
	Subjects	Samples		SD	CV	SD	CV	
All	24	191	3.9	0.76	19.4%	3.06	78.3%	0.94
$\geq 3$ ng/mL	12	96	6.6	1.06	15.9%	2.93	44.1%	0.89
$< 3$ ng/mL	12	95	1.1	0.22	19.3%	0.79	69.3%	0.93

**Conclusion:** No trend in AMH results was observed throughout a normal menstrual cycle. Fluctuations in AMH results during the menstrual cycle accounted for only 6% of the overall variability.

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### A-041

#### Unexpected karyotype: Down syndrome with a de novo (dup21q) with a mother carrier of a rob(14;21)

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**Introduction:** Down syndrome, the most frequent form of mental disability caused by a microscopically demonstrable chromosomal aberration, is characterized by a well defined and distinctive phenotypic features and natural history. Most individuals (95%) with trisomy 21 have 3 free copies of chromosome 21; in about 5% of patients, 1 copy is translocated to another acrocentric chromosome, most often chromosome 14 or 21. In 2 to 4% of cases with free trisomy 21 there is recognizable mosaicism for a trisomic and a normal cell line. **Objective:** Here we describe a patient with classical features of Down Syndrome with a (dup21q) and her mother carrier of a rob(14;21). **Methods:** The cytogenetic study was held after chromosome analysis of metaphases obtained from culture of peripheral blood lymphocytes PHA-stimulated, Giemsa Banding and karyotyping according the ISCN 2013. **Results:** The cytogenetic analysis demonstrated a 45,XX,rob(14;21)(q10;q10) (fig.1) and 46,XX,+21,rob(21;21)(q10;q10) (fig.2). **Discussion:** Most de novo t(14;21) trisomies originate in maternal germ cells. The mean maternal age is 29.2 years. In de novo t(21;21) Down Syndrome the situation is different, in most cases the t(21;21) is an isochromosome (dup21q) rather than the result of a Robertsonian translocation caused by a fusion between 2 heterologous chromatids. About half were of paternal and half of maternal origin. In de novo t(21;21) true Robertsonian trisomy 21 cases, the extra chromosome 21 was maternal. In this case the expected karyotype would be the presence of the translocated

chromosome rob(14;21) maternally inherited but a de novo event : a (dup21q) happened leading to the same diagnosis of Down syndrome. We hypothesized that in this case the (dup21q) is an isochromosome probably of maternal origin as she is a carrier of a translocation with altered recombination patterns and nondisjunction enabling the formation an isochromosome.

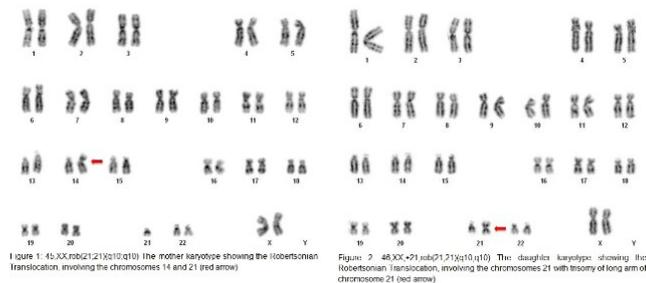


Figure 1: 46,XX,rob(21;21)(10;10) The mother karyotype showing the Robertsonian Translocation, involving the chromosomes 14 and 21 (red arrow)  
 Figure 2: 48,XX,+21,rob(21;21)(10;10) The daughter's karyotype, showing the Robertsonian Translocation, involving the chromosomes 21 with trisomy of long arm of chromosome 21 (red arrow)

**A-042**

**Double aneuploidy with a karyotype 48,XXY,+21**

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**Introduction:** A chromosome abnormality reflects an atypical number of chromosomes or a structural abnormality in one or more chromosomes including autosomes and sex chromosomes. Double aneuploidy is the presence of two different chromosomal abnormalities in the same individual and it's a relatively rare condition. Trisomy 21, also named Down Syndrome (DS) is caused by the presence of an additional autosome, affecting 1 to 700 live births. Klinefelter Syndrome (KS) is a genetic condition characterized by an extra X chromosome resulting in a 47,XXY karyotype. This karyotype exists in roughly between 1 to 500-1000 live male births. Though trisomy 21 and numerical sex chromosomes anomalies are both common disorders, the co-occurrence of both is rare. A high percentage of double and multiple chromosomal aneuploidies were observed in spontaneous abortion and mostly involving acrocentric chromosomes. Only a few cases of double aneuploidy (DS+KS) have been reported in the literature since its first report by Ford et al in 1959. **Objective:** Here we present a case of postnatal diagnosis of double aneuploidy DS +KS. **Methods:** The cytogenetic study was held after chromosome analysis of metaphases obtained from culture of peripheral blood lymphocytes PHA-stimulated, Giemsa Banding and karyotyping according the ISCN 2013. **Results:** The cytogenetic analysis demonstrated a 48,XXY,+21 karyotype (Fig.1). **Discussion:** Double aneuploidy usually are associated with advanced maternal age, caused possibly by non-disjunction during meiosis, which may cause chromosomal changes sexual or autosomal in offspring. The patient with double aneuploidy can present characteristics of both chromosomal anomalies. The occurrence of double aneuploidy +21 and XXY is rare, published data are scarce, and yet, the incidence and risk of recurrence are difficult to determine. This case report may add to other cases in order to improve the study of the incidence and recurrence of this rare finding.

**A-043**

**Comparison of Performance: Siemens CLINITEK Novus Urine Analyzer and CLINITEK Advantus Urine Analyzer**

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**Background:** The ability to offer a full set of solutions to accommodate different testing volumes or sites with high correlation of results between analyzers is imperative for all healthcare networks. As patients move between care environments (physician office to a specialized clinic, hospital emergency department, or inpatient setting), clinicians need consistent results to ensure that the test result information leads to the same clinical decision. This requirement for end-to-end solutions is not new but has recently become more urgent in discussions between clinicians and laboratory management.

Comparable performance among urine analyzers, whether used in a centralized lab, a point-of-care testing site, or a backup situation, is essential in the clinical environment. This is particularly true in the instance where one instrument is unavailable and another must match its level of performance in terms of sensitivity, specificity, and reliability to ensure consistent test outcomes. The objective of this study is to compare the performance of three strip types on the CLINITEK Advantus<sup>®</sup> instrument to the CLINITEK Novus<sup>®</sup> PRO 12 cassette on the CLINITEK Novus instrument, using contrived urine samples.

**Methods:** The study analyzed the CLINITEK Novus urine analyzer using the CLINITEK Novus PRO 12 reagent cassette and the CLINITEK Advantus urine analyzer using MULTISTIX<sup>®</sup> 10SG, MULTISTIX 10LS, and CLINITEK<sup>®</sup> Microalbumin 9 reagent strips. Testing was conducted on two lots of each reagent with two instruments of each type. Clinical specimens were contrived to each of the CLINITEK Novus PRO 12 cassette block outputs for each analyte using a single instrument.

**Results:** Excellent performance was observed with albumin, bilirubin, ketone, protein, and nitrite tests across the entire reporting range. 99.0% of all results for all analytes fell within 1 target block output. A false-negative rate of 1.8% and a false-positive rate of 0.2% were observed when removing pH and specific gravity testing. 93% of pH results were within 0.5 pH units and 100% of specific gravity results were within 1 block when rounding CLINITEK Novus system quantitative results to CLINITEK Advantus system block outputs.

**Conclusion:** Providing an end-to-end solution for urine analyzers requires comparable performance of systems, whether used in a centralized lab, a point-of-care testing site, or a backup situation. This study demonstrates that the CLINITEK Novus analyzer and CLINITEK Advantus analyzer provide strong result agreement allowing for consistent clinical decision making.

**A-044****High “Normal” Potassium Poses Mortality Risk for All Patients**

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**Background:** Recent studies show increased mortality in acute myocardial infarction (AMI) patients with serum potassium levels of 4.5-5.0 mEq/L, which is within the reference interval used by most laboratories. These findings have created an unresolved controversy challenging established potassium repletion therapeutic targets. We hypothesize this higher risk is applicable generally, not just to AMI patients.

**Methods:** Retrospective cohort study of 375,747 hospital visits at Sarasota Memorial Hospital for years 1998-2014; and for years 2012-2014 at a major academic medical center in the northeast and a regional hospital in the southwest. Primary outcomes were in-hospital and one-year mortality. Models of mortality were generated and fit by logistic regression, yielding multivariate adjusted odds ratios for potassium-linked mortality.

**Results:** Utilizing logistic regression with adjustment for possible confounding factors, our analysis for all patients, independent of diagnosis, yields lowest mortality at potassium values from 3.5 to 4.5 mEq/L, with significantly higher risks beyond 4.5 mEq/L. For both the AMI cohort and the non-AMI cohort, in-hospital all-cause mortality odds ratios were above 1.8 ( $p < 0.001$ ) for potassium between 4.5 and 5.0 mEq/L (within the usual reference interval); and were above 3 ( $p < 0.001$ ) for potassium between 5.0 and 5.4 mEq/L (often considered within the reference interval). Adjusting for serum Creatinine levels  $> 2.0$  mg/dL produced the same high “normal” mortality risks. Our findings hold for one-year post-discharge mortality, as well as in-hospital mortality. While the risk functions differ in detail between AMI and other patients, we find that both show minimum risk within the same cut-points, with substantial increased risk above 4.5 mEq/L.

**Conclusions:** Our analysis extends the AMI finding: all patients have an increased mortality risk for serum potassium levels above 4.5 mEq/L. The etiology of death associated with mild hyperkalemia remains unclear. Presence of renal insufficiency appears not to account for this increased mortality. Without prospective studies, our findings cannot establish safety or danger of potassium repletion therapeutic targets. Finally, we point out that standard reference intervals are not based on patient risk, but are defined as the central 95% of test results for a “healthy” cohort. Reference interval cut-points would be more meaningful with a risk-based methodology.

**A-045****Assessment of Hyperkalaemia in the Medical Emergency Unit**

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**Objective:** To assess the prevalence, severity and risk factors of Hyperkalaemia and its effect on mortality and length of hospital stay of patients requiring emergency medical care.

**Methods:** A retrospective analysis was carried out on the first potassium level on admission of all patients admitted through the Medical Emergency Unit (ward F1), from January 2013 to March 2014, of Tygerberg Hospital, a tertiary health center in Western Cape Province, South Africa. Using the computerised hospital database we retrieved information on the following: (1) Number of patients that presented with Hyperkalaemia on admission (2) Severity of Hyperkalaemia classified as mild, moderate and severe (3) Risk factors; age, sex and diagnosis on admission (4) Clinical impact; length of hospital stay and hospital mortality. Hyperkalaemia was considered at serum potassium  $> 5.2$  mmol/l while critical hyperkalaemia  $> 6.0$  mmol/l according to established cut-offs for the reference population.

**Results:** Over a period of 15 months One hundred and thirty nine thousand one hundred and fifty three (139,153) requests for serum potassium was received by the laboratory out of which thirteen thousand one hundred and sixty four (13164) accounting for ten percent (10%) of the total request was from the medical emergency unit. 1 out of every 5 of the serum potassium result from the medical emergency unit was abnormal. The overall prevalence of hyperkalaemia was 8.1% and 12.3% of this was within the critical range. Gender was not a significant risk factor (M:F, 1.1;1) while mean age of presentation was  $52 \pm 2.6$  years. Diagnosis on admission was related to the Genitourinary (25.8%), Cardiovascular (15.3%), Pulmonary (14.2%), Endocrine (11.9%), Central Nervous system (7.3%), Sepsis (6.5%), Cancer (5.3%), Haematological (4.3%), Gastrointestinal system (4.3%), others (5.8%). In hospital mortality and length of hospital stay was higher ( $p < 0.05$ ) among patients with hyperkalaemia (38%, 9 days) than in patients with normal serum potassium (6%, 7 days).

**Conclusions:** Hyperkalaemia is a common problem among patients requiring emergency medical care. It results from various medical conditions and it is associated with high In-hospital mortality and longer length of hospital stay. It is therefore important to recognize this problem early and institute early treatment measures in order to improve the prognosis.

**A-049****SERUM SALUSIN-ALPHA IS INCREASED IN PATIENTS WITH PSORIATIC ARTHRITIS**

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**Introduction:** Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized with skin lesions and joint involvement. Mechanisms of developing early atherosclerosis in PsA patients is not elucidated yet. Salusin- $\alpha$  and salusin- $\beta$  are two new bioactive molecules. Salusin- $\beta$  has been reported to have pro-atherosclerotic effects, but salusin- $\alpha$  has anti-atherosclerotic effects. Mechanisms of atherosclerosis developing in PsA patients may be associated with salusins.

**Aim:** The purpose of this study was to identify the serum salusin- $\alpha$  and salusin- $\beta$  levels in patients with PsA and to determine the possible relationship with the disease findings.

**Material and methods:** Forty patients diagnosed with PsA according to CASPAR classification criteria and 40 healthy volunteers were included in the study. Demographic, clinical, laboratory and radiological data were recorded in all patients. Disease activity indexes (PASI, BASDAI, BASFI, HAQ) were recorded. Serum salusin- $\alpha$  and salusin- $\beta$  level were measured by ELISA method.

**Results:** Among 40 PsA patients 13(32.5%) were males and 27(67.5%) were female, mean age was 48.5 year and mean disease duration was 2.4 year. Demographic and clinical assessment of patients were as follows: 20(50%) patients had family history, 18(45%) patients were smoker, 19(47.5%) patients had HLA-B27 positivity, 33(82.5%) had sacroiliitis, 36(90%) had enthesitis, 23(57.5%) had DIP joints and nail involvement, 26(65%) had wrist involvement, and 11(27.5%) had ankle involvement. 20 (50%) patients had elevated CRP level and 25(62.5%) patients had elevated ESR level. Compared with the control group PsA patients had elevated serum salusin- $\alpha$  level ( $p = 0.004$ ). The relationship between serum salusin- $\alpha$  level and ankle arthritis and dactylitis were determined ( $p = 0.04$ ,  $p = 0.03$ ). Serum levels of salusin- $\beta$  were similar in PsA patients and controls ( $p = 0.285$ ). Serum salusin- $\beta$  level were correlated with ankle arthritis ( $p = 0.02$ ).

**Conclusion:** We found elevated serum salusin- $\alpha$  and normal serum salusin- $\beta$  levels in PsA patients. Salusins may play an important role in the pathogenesis of early atherosclerosis development in patients with PsA. In this regard, there is a need for multicenter prospective studies.

**A-051****Performance evaluation of the cobas u 701 urine analyzer**

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**Background:** The cobas u 701 (Roche Diagnostics) system provides an automated solution for sediment microscopy using imaging analysis intended for the in vitro quantitative determination of erythrocytes (RBC) and leukocytes (WBC); the semi-quantitative determination of squamous (SEC) and non-squamous (NEC) epithelial cells, bacteria (BACT), and hyaline casts (HYA); and the qualitative determination of pathological casts, crystals, yeasts, mucus, and sperm in urine. This study evaluated the analytical performance of this system including experiments for precision, recovery of semi-quantitative range borders, carry-over and method comparison versus other automated systems (IRIS IQ 200), and conventional microscopy using Kova chamber technology.

**Methods:** This study tested 315 remnant, de-identified urine samples for method comparison. Each methodology was performed according to CLSI guidelines and manufacturer's package insert instructions. In addition, the operability was verified by routine simulation runs (including system stress runs) and completion of a detailed

questionnaire. Precision was assessed by calculation of standard deviations (SD), or coefficient of variance (CV %) within acceptable agreement rates. Recovery of defined concentration ranges was assessed for HYA, BACT, SEC, NEC by diluting high positive samples and measuring in triplicate on cobas u 701 system and the predicate methods. The cobas u 701 system was tested for sample carryover using the Broughton model with subsequent measurements of high positive and negative samples.

Results: Repeatability and intermediate precision were all within the manufacturer's acceptance limits. SDs for RBCs and WBCs in low concentration samples were well within < 2 cells/ $\mu$ L and < 1 cell/ $\mu$ L limits respectively. Intermediate CVs were < 10% for the QC in the low pathological range (at about 220 and 450 cells/ $\mu$ L for RBC and WBC respectively). Repeatability experiments for semiquantitative and qualitative parameters confirmed reproducible recognition of negative and positive samples (distributed over 2 concentration ranges).

Results obtained for HYA, BACT, SEC, and NEC were within the expected concentration ranges.

No significant deviations for sample carryover were found for any parameter tested.

Method comparison of cobas u 701 system results versus conventional microscopy provided regression slopes of 1.04 and 0.98 for RBC and WBC respectively (specificity results of 81% - 97% and sensitivity results between 51 - 100%). The cobas u 701 system versus the Iris IQ 200 results for method comparison yielded a lower agreement for RBC (slope of 1.26, higher scattering) and sensitivity ranged from 32 - 97%. However, reclassification for all results on Iris IQ 200 improved the results in the statistical calculation.

User interface, availability of maintenance wizards, throughput, and imaging technology are beneficial as documented by the detailed questionnaires completed by each operator.

Conclusions: The analytical performance of the cobas u 701 system met our expectation for a new urinalysis system. The agreement with visual microscopy without requiring reclassification provides improvement for routine workflow. The imaging technology is a useful system for microscopic urine testing. The cobas u 701 urine analyzer standardizes the entire urine testing procedure for microscopy, reduces operator intervention and offers centralized result management.

Disclaimer: cobas u 701 is not cleared or approved for use in the USA

### A-052

#### Associations of single nucleotide polymorphisms in precursor-microRNA (miR)-125a and the expression of mature miR-125a with the development and prognosis of autoimmune thyroid diseases.

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**Background:** It is important to search the biomarker to predict the development and prognosis of autoimmune thyroid diseases (AITDs) such as Hashimoto's disease (HD) and Graves' disease (GD). MicroRNA (miR) bind directly to the 3' untranslated region of specific target mRNAs to suppress the expression of proteins, promote the degradation of target mRNAs and regulate immune response. miR-125a is known to be a negative regulator of regulated upon activation normal T cell expressed and secreted (RANTES), interleukin (IL)-6 and transforming growth factor (TGF)- $\beta$ ; however, its association with AITDs remains unknown.

**Methods:** To clarify the association between AITDs and miR-125a, we genotyped the rs12976445 C/T, rs10404453 A/G and rs12975333 G/T polymorphisms in the MIR125A gene, which encodes miR-125a, using direct sequencing and polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods in 155 patients with GD, 151 patients with HD and 118 healthy volunteers. Among GD patients, 60 GD patients had been treated with methimazole for at least five years and were still positive for anti-thyrotropin receptor antibody (TRAb) (intractable GD) and 45 GD patients had maintained an euthyroid state and were negative for TRAb for more than two years without medication (GD in remission) and 50 patients who could not be categorized to intractable GD or GD in remission groups at the time of analysis. All patients with GD had clinical histories of positive TRAb and thyrotoxicosis. Among HD patients, 59 HD patients had developed moderate to severe hypothyroidism before 50 years of age and had been treated with thyroxine (severe HD) and 41 untreated, euthyroid HD patients were over 50 years of age (mild HD) and 51 patients who could not be categorized to severe HD or mild HD groups at the time of analysis. All patients with HD were positive for anti-thyroid microsomal antibody (McAb) and/or anti-thyroglobulin antibody (TgAb) and all patients with mild HD had a palpable diffuse goiter. All healthy volunteers were euthyroid and negative for

thyroid specific autoantibodies (control subjects). All patients and control subjects are Japanese and unrelated.

**Results:** We determined that the CC genotype and C allele of the rs12976445 C/T polymorphism were significantly more frequent in patients with HD compared with control subjects ( $P < 0.05$ ) and in intractable GD compared with GD in remission ( $P < 0.05$ ). The expression of miR-125a was correlated negatively with age ( $P = 0.0010$ ) and down-regulated in patients with GD compared with control subjects ( $P = 0.0249$ ).

**Conclusion:** miR-125a expression in PBMCs and the rs12976445 C/T polymorphism were associated with AITD development and prognosis.

### A-053

#### Severe acute pancreatitis and serum C-Reactive Protein

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**Background:** Severe acute pancreatitis (SAP) is associated to high mortality rates. Elevated serum C-Reactive Protein (CRP) levels in patients with acute pancreatitis have been proposed as a prognostic marker of the disease. The aim of this study was to assess the quantification of CRP in serum of patients with acute pancreatitis, through its monitoring during the first 72 hours and determine their relationship with SAP.

**Methods:** We studied patients with acute pancreatitis. Serum CRP levels were measured initial, 24, 48 and 72 hours after admission in the emergency room. Acute pancreatitis was established in patients with acute abdominal pain and serum amylase > 300 IU/L (reference values: < 100 IU/L). Serum CRP was determined by turbidimetric immunoassay in Dimension EXL (Siemens®) with reference values: < 0.5 mg/dl. Patients were classified into two groups according to the type of acute pancreatitis: edematous acute pancreatitis (EAP) and SAP. Statistical analysis was determined using receiver operating characteristic (ROC) techniques by analysing the area under the ROC curve (AUC) using the software MEDCALC®.

**Results:** We studied 17 patients with ages between 17 and 86 years old (mean = 56.4), 7 women and 10 men. Twelve patients were EAP and 5 were SAP. No statistically significant differences were found between EAP and SAP according to the serum CRP levels initial and 24 hours ( $p > 0.05$ ). The AUC of serum 48 hours CRP levels for diagnosis of SAP was 0.955 ( $p < 0.0001$ ), optimal cut-off value was 3.3 mg/dl exhibiting 100% sensitivity and 81.8% specificity. The AUC of serum 72 hours CRP levels was 0.970 ( $p < 0.0001$ ), optimal cut-off value was 3.3 mg/dl exhibiting 100% sensitivity and 90.9% specificity.

**Conclusions:** Serum CRP levels measured after 48 hours of evolution of the disease showed high diagnosis efficacy to predict whether an acute pancreatitis is edematous or severe.

### A-054

#### Comparison of robust and traditional statistical methods for evaluation of blood glucose measurements in an external quality assessment program

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**Objectives:** External quality assessment (EQA) evaluates the performance of laboratories by means of interlaboratory comparisons, and is an important measure for accuracy and reliability of the laboratory results. Parametric statistics are the more commonly known approach in an external quality assessment program. However, due to the variability of laboratory performances, the distribution of data is often abnormal, including some outlying values. Robust statistical methods, which are based on weighted data and are resistant to the presence of outliers can be used alternatively for EQA evaluation.

**Design & methods:** In this study, we compared the performance scores obtained by using different statistical methods: Parametric statistics (arithmetic mean and standard deviation) and non-parametric robust statistics (median and robust standard deviation). A total of 1008 glucose results of three lots at different concentrations, submitted through the Kbudek-EQA reporting system, were collected and analyzed by Kbudek-EQA evaluating system and SPSS 17.0. Participants were evaluated in their peer groups.

The data distributions of three sets were tested by Kolmogorov-Smirnov Z test. The distribution of results was not Gaussian. "Consensus of Participants' Results" approach was used to determine the assigned value for a test material. z-scores were calculated using both standard deviation and robust standard deviation. The z-score values outside the  $\pm 3$  standard deviation (SD) were evaluated as a procedure that needs investigation. These were considered unsatisfactory, while the values inside the  $\pm 2$  SD limits were considered satisfactory, and z-scores outside the  $\pm 2$  SD limit but inside the  $\pm 3$  SD limits were considered questionable.

**Results:** We found the rate of the unsuccessful and questionable performance scores of the three lots to be 4.9%, 10.1%, 11.1% respectively, by using robust statistics and 2.1%, 6.8%, 7.9% by using parametric statistics. Two methods of evaluation of performance didn't show statistically very good agreement (McNemar's test,  $P < 0.05$  for all the three lots).

**Conclusion:** External quality assessment including extensive participants often result in abnormal distribution. Robust statistical methods are insensitive to slight deviation for a given probability model and can estimate the population parameters utilizing robust algorithm. We can conclude that robust statistical method may be more appropriate for EQA result analysis in selected cases.

### A-055

#### Molecular Epidemiology Analysis of *Klebsiella pneumoniae* Carbapenemase-2 in Regional Hospital in Taiwan

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**Background:** Carbapenems are important last-line  $\beta$ -lactams antibiotics for treatment of multidrug resistant bacteria. *Klebsiella pneumoniae* carbapenemases (KPCs) are serine  $\beta$ -lactamases that have become a major cause of multidrug resistant nosocomial infection worldwide because they confer on the bacteria which resistant to most of  $\beta$ -lactams antibiotics including penicillins, cephalosporins, monobactams and carbapenems. *Enterobacteriaceae* (mainly in *Klebsiella pneumoniae*) with carbapenems resistance conferred by  $bla_{KPC}$  are rapid spread which may result in major global health problems. Consequently, the prevalence monitoring of KPC-producing *Klebsiella pneumoniae* becomes an inevitable task in the clinical workplace. In this study, we investigated the expression of  $bla_{KPC-2}$  by polymerase chain reaction (PCR) method and established genotype profile by pulse-field gel electrophoresis (PFGE) in carbapenem-resistant *Klebsiella pneumoniae* (CRKP).

**Methods:** According to Clinical and Laboratory Standards Institute (CLSI) guidelines (M100-S21), the clinical specimens collected from August 2011 to November 2014 were tested for drug susceptibility to imipenem (IPM), meropenem (MEM), and ertapenem (ETP) using disk diffusion method. The production of carbapenemase was detected by the modified Hodge test (MHT), and confirmed  $bla_{KPC-2}$  gene expression by PCR. The genetic relationship among isolates was analyzed by PFGE using restriction enzyme *Xba*I.

**Results:** The 109 CRKPs clinical specimens were isolated and analyzed from En Chu Kong hospital of Taiwan. Of which, seventeen (15.6 %) isolates showed carbapenemase activity, and twelve (11 %) isolates contained KPC-2 gene. PFGE analysis showed two patterns for  $bla_{KPC-2}$  positive isolates. Five isolates were positive to MHT, but showed negative result by PCR. This is likely due to the presence of other carbapenemases.

**Conclusion:** This study reveals KPC-2-producing *Klebsiella pneumoniae* have become a significant concern in our hospital. Together, we have established PFGE method which helps differentiate infectious strains efficiently while controlling the outbreak of nosocomial infection.

### A-057

#### Evaluation of Performing Immunology Tests with the Lithium-heparin Tube

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##### Background:

Nowadays, integration of chemistry and immunoassay analyzers is the trend to reduce the cost in most medical laboratories. Therefore, the study aimed to assess the appropriateness of performing immunoassay tests with the Li-heparin tube.

The study analyzed 24 immunoassay items, including 12 qualitative and 12 quantitative items. Eight of the 24 items on the package inserts do not show whether the Li-heparin tube is applicable.

##### Methods:

Paired venous blood samples from OPD patients, 10 males and 10 females, were collected in the serum separating tubes (SST) and Li-heparin tubes simultaneously. After clotting in the SST tubes for 30 minutes, paired samples were centrifuged for 10 minutes at 2851 relative centrifugation force (RCF). Immunoassay items, 24 tests totally, were performed on ABBOTT ARCHITECT i2000 autoanalyzer, and data were compared based on two different tubes. Desirable bias of within subject biological variation (CVw%) were used as an indicator of error allowances.

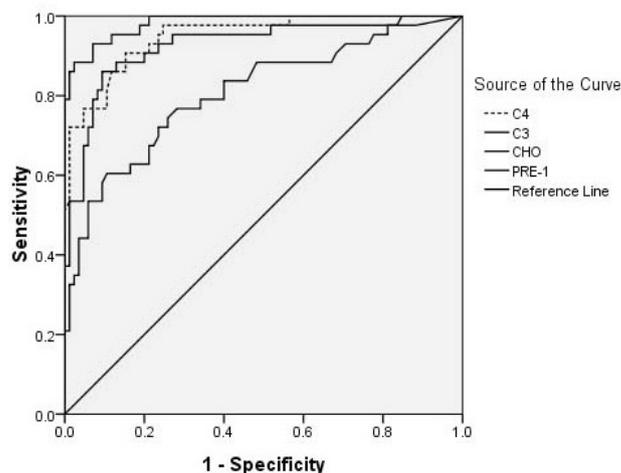
##### Results:

Sensitivity and specificity of both tubes for 12 qualitative tests reached consistently. Statistically significant differences ( $p < 0.05$ ) between two tubes were shown on E2 and FSH, and the correlations were 0.995 and 0.993 respectively. The mean difference of both tubes were 7.9% for E2 and 17.3% for FSH; however, the error allowances defined from within subject biological variation were 18.1% for E2 and 8.7% for FSH. According to the error allowances from the within subject biological variation, this study showed the bias of both tubes on E2 were acceptable, but the bias for FSH did not meet the acceptable criteria.

##### Conclusion:

The study indicated that verifying the information from package inserts was a must. Among the 24 tests, FSH could not be analyzed with the Li-heparin tube, and it was not complied with the manufacture recommendations. The findings from this study were expected to be applied in the resources integration and auto barcode-labeling machine implementation in the modern clinical laboratory in the future.

### ROC Curve



### A-059

#### The Comparison Of Low Flow Vs. High Flow Anesthesia On Oxidative Stress During Pnoperitoneum Performed In Laparoscopic Cholecystectomy

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Pneumoperitoneum performed in laparoscopic surgery can be defined as a specific case/model of ischemia/reperfusion injury. We wanted to compare the effects of low gas flow anesthesia to high gas flow anesthesia on oxidative stress and inflammation parameters in laparoscopic cholecystectomy in which oxidative stress is triggered by pneumoperitoneum.

55 patients aged between 18-70 years with an ASA status of I or II, scheduled to undergo elective laparoscopic cholecystectomy were enrolled in the study. The patients were randomized into two groups as high flow (HF) group and low flow (LF) group. Gas flow was 4L/dk (50% O<sub>2</sub>, 50%air) in HF group (n=28) and 1L/dk (50% O<sub>2</sub>, 50%air) in LF Group (n=27). ECG, NIBP, SpO<sub>2</sub>, etCO<sub>2</sub>, and BIS monitoring were applied to every subject and inhalational anesthetic concentration was set to maintain a BIS value between 40-60. All patients' O<sub>2</sub>, inspiratory and expiratory concentrations of inhalation agent desflurane, BIS, blood pressure, pulse, peripheric oxygen saturation values were recorded during the operation. Venous blood samples were taken after the induction of anesthesia, during the termination of pneumoperitoneum and postoperative 24<sup>th</sup> hour for MDA, nitrotyrosine, CRP, cortisol, IL-6 analyses.

Serum MDA levels were measured by HPLC (Ultimate3000,ThermoDionex, USA) with a fluorescence detector. Within-run precision values were 1.8-5.5% and between-run precision values were 6.5-9% for 0.40-1.55 umol/L MDA, according to manufacturer's claim. The lower detection limit was 0.02 umol/L. Serum nitrotyrosine (SunRed, China) and IL-6 (Assaypro, USA) levels were measured by sandwich enzyme immunoassays. Cortisol levels were measured with a chemiluminescent immunoassay (Dxi,BeckmanCoulter, USA). Serum CRP levels were measured immunoturbidometrically (Integra400, RocheDiagnostics, Germany).

MDA and nitrotyrosine levels were not significantly different when HF and LF groups are compared according to their sampling times; induction, during the termination of pneumoperitoneum and postoperative 24<sup>th</sup> hour. There were significant decreases in MDA levels between pneumoperitoneum termination vs. postoperative 24<sup>th</sup> hour and induction vs. postoperative 24<sup>th</sup> hour in HF and LF groups (47,97 umol/L vs 32,42 umol/L, P=0.000 and 47,97 umol/L vs 42,03 umol/L, P=0.000, respectively for HF group; 49,99 umol/L vs 35,37 umol/L, P=0.002 and 46,53 vs 35,37 umol/L, P=0.000, respectively for LF group).

The increase observed in nitrotyrosine levels between pneumoperitoneum termination vs. postoperative 24<sup>th</sup> hour and induction vs. postoperative 24<sup>th</sup> hour in HF and LF groups were not significant. When MDA and nitrotyrosine levels were compared according to the duration of operation (<60minutes and >90minutes), no significant difference was observed. There was no significant difference of CRP, cortisol and IL-6 levels among Group HF and Group LF.

Ischemia/reperfusion injury occurring during pneumoperitoneum performed in laparoscopic operations exhibit a timewise decrease in MDA levels, which could be explained by activation of antioxidant systems. As for the possible protective effect of LF anesthesia vs. HF anesthesia, no protective effect of LF anesthesia was observed with regards to oxidative stress and inflammatory markers in our group. Further research with greater number of subjects is required to confirm the changes observed which have not reached statistical significance.

#### A-060

#### MEASUREMENT OF PRO- AND ANTI-INFLAMMATORY CYTOKINES IN ACUTE STROKE. HOW USEFUL ARE FOR THE PREDICTION OF PATIENTS SUSCEPTIBLE TO INFECTIONS?

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**BACKGROUND:** Stroke affects the normally well-balanced interplay of two supersystems: the nervous and the immune system. Immunodepression after stroke increases the susceptibility to infection, the most relevant complication in stroke patients. Stroke-associated infections (SAI) have been reported in 21-65% of patients with stroke. The pathophysiology of SAI is not clearly understood yet. The incidence of SAI as well as the cytokine profiles were assessed in patients with acute stroke.

**METHODS:** In a prospective study 100 patients with acute stroke were enrolled. Interleukin-6 (IL-6), Interleukin-8 (IL-8), Interleukin-10 (IL-10) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) were measured upon admission and at 24, 48, 72 hours thereafter, with a final measurement on day-7. Stroke severity was measured at the time of admission and during hospitalization with the Scandinavian Stroke Scale (SSS). Eighty healthy subjects served as controls. All cytokine levels were quantified in EDTA plasma samples employing a biochip array kit on the Evidence Investigator analyzer (Randox).

**RESULTS:** Mean age(SD) of the patients was 75.2(9.4) years. The mean time(SD) between the onset of neurological symptoms and hospital admission was 3.22(1.58) hours. SAI were diagnosed in 46 (46%) patients (urinary tract infections=13, respiratory tract infections=29, both=2, sepsis=2). Mean SSS(SD) was significantly lower in patients with SAI compared to those without SAI, upon admission 22.08(15.48) vs 40.68(13.65), p=0.0001 and during hospitalization 21.80(25.52) vs 51.18(13.01), p=0.0001.

Upon admission, we observed significant increases in patients with SAI compared to those without SAI (mean $\pm$ SE), in IL-6 (24.27 $\pm$ 8.32 vs 6.03 $\pm$ 1.61, p=002), IL-8 (15.39 $\pm$ 3.49 vs 3.54 $\pm$ 0.50, p=0.001) and IL-10 (5.35 $\pm$ 2.16 vs 1.51 $\pm$ 0.39, p=0.015) whereas TNF- $\alpha$ /IL10 ratio was significantly decreased(2.94 $\pm$ 0.98 vs1.63 $\pm$ 0.18, p=0.043). The diagnostic accuracy of a single measurement of IL-6 [AUC=0.853 (95%CI 0.794-0.913), P<0.0001], IL-8 [AUC=0.822 (95%CI 0.754-0.890), P<.00001] and IL-10 [AUC=0.762 (95%CI 0.680-0.843), P<0.0001] upon hospital admission, for diagnosis of SAI was high. Logistic regression analysis where SSS-score, IL-6, IL-8, IL-10 and TNF- $\alpha$ /IL-10-ratio upon admission were inserted as

variables, revealed IL-6 (OR=1.10, 95%CI 1.01-1.24), IL-8 (OR=1.24, 95%CI 1.12-1.31) and IL-10 (OR=1.08, 95%CI 1.04-1.15) as independent predictors of SAI.

**CONCLUSION:** Measurement of IL-6, IL-8 and IL-10 upon admission can reveal patients, candidates for subsequent SAI

#### A-061

#### Analysis of allergens in patients with allergic skin diseases in South China

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**Objective:** To investigate the levels and types of allergen-specific IgE antibodies in the serum of patients with allergic skin diseases and provide relevant basis for the clinical diagnosis,treatment and prevention of allergic skin diseases.

**Methods:** 822 patients of allergic skin diseases including 136 cases of atopic dermatitis, 172 cases of eczema and 514 cases of urticaria, who were treated in Peking University Shenzhen Hospital in 2014, were recruited. Western blot was used to detect the specific IgE antibodies in serum.

**Results:** The allergic skin diseases included atopic dermatitis, eczema and urticarial and their total positive rates of allergen-specific IgE allergen antibody in serum were 49.3%, 45.1%, 49.4%, respectively. The result was no significantly different. The positive rates of allergen-specific IgE were 75.0%, 80.8%, and 67.4% for the above-mentioned three allergic skin diseases in children respectively, and these rates were significantly higher than in the adult group (47.0%, 41.8%, 46.5%). In patients with three allergic skin diseases, the allergen species with a higher positive rate were the same, which were dust mites (23.5%, 20.3%, 22.0%), crab (17.6%, 15.7%, 22.2%) and marine fish combinations (14.0%, 15.1 %, 12.1%). In patients with three allergic skin diseases, the content of allergen-specific IgE antibody was mainly level 1 in density (48.0%, 49.4%, 43.0%). The majority of patients were positive for two or more allergens.

**Conclusions:** Allergic skin diseases in children are closely related to the contact of allergens. The house dust mites group, crab and marine fish group are the main allergens in South China. Patients with allergic skin diseases should avoid contacting the related allergens in order to reduce the occurrence of allergic diseases.

#### A-062

#### A Study Of sdLDL-C And Insulin Resistance In Apparently Healthy Obese Young Adults Of Southern Part Of Indian Subcontinent

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#### Background:

Indian subcontinent is a land of diversities with not just 49 ethnic groups but wide regional variation in diet from one geographical area to another that decides the health status of the population. Unlike earlier times developing countries too are facing the challenge of obesity and the modern epidemics have a common root cause tapering to obesity. Obesity during adolescent and young adulthood usually persists to adulthood in almost 70-80% cases and gives rise to early onset of type 2 diabetes mellitus, cardiovascular disorders and metabolic syndrome insulin resistance being the common link to all. Not many studies have been done in India on young adult health which is the group that can be targeted for early prevention of such modern epidemics.

#### Objective:

The present study was taken up to study the prevalence of insulin resistance in apparently healthy young adult obese population and study its correlation with different cardiovascular risk factors like lipid profile and sdLDL-C.

#### Material and methods:

In a randomized control study 106 apparently healthy young adults in the age group of 21-34 years were chosen from the community out of which 45 were obese and 61 were age and gender matched non-obese controls. They were divided in obese and non-obese groups based on their BMI and cut-off BMI was 25Kg/m<sup>2</sup>. Along with physical parameters fasting plasma glucose, lipid profile and routine biochemical parameters were assayed by standard kit methods and plasma insulin was measured by ELISA kit. Different lipid ratios, atherogenic index and insulin resistance were calculated. Atherogenic index was measured by the formula Log (Triglycerides/ HDL-C). Insulin resistance was measured by HOMA-IR model and QUICKI index. Small dense LDL-C (sdLDL-C) was quantified by modified Tsutomu-Hirano method.

**Results:**

In the obese group BMI, waist circumference (WC) and waist-hip ratio (WHR) elevated significantly (p=0.0001) and TG, VLDL-C and sdLDL-C as well as atherogenic index elevated significantly (p<0.001). Significant Hyperinsulinaemia (p<0.0001) was found in the obese group and 50% of obese cases had hyperinsulinaemia. Insulin resistance calculated by HOMA-IR and QUICKI index was statistically significant (p<0.0001) in obese. Linear regression analysis showed sdLDL-C (R<sup>2</sup>=0.08, p=0.05 at 95% C.I.), hyperinsulinaemia (R<sup>2</sup>=0.089, p=0.054 at 95% C.I.) and insulin resistance (R<sup>2</sup>=0.099, p=0.03 at 95% C.I.) significantly dependent on WC and atherogenic index was significantly dependent on TG (R<sup>2</sup>=0.0036, p=0.05 at 95% C.I.) rather than any other lipid factors. On ROC analysis either method of insulin resistance showed equal efficacy (AUC for HOMA-IR= 80.3% and QUICKI = 80.14%; C.I. 95%) and atherogenic index turned out to be a better predictor than sdLDL-C (AUC for Atherogenic index= 76.14% and QUICKI = 71.46%).

**Conclusions:**

Carbohydrate-rich diet increases TG and hence protein rich diet is advisable. For Indian subpopulation WC and WHR should also be evaluated along with BMI. Insulin resistance should be identified early and interventional measures should be taken in terms of physical exercise and insulin receptor sensitizers for a short-term. sdLDL-C rises earlier than total cholesterol and hence a CVS risk predictor.

**A-063**

**Prognostic Utility of AFP in Acute Liver Failure**

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**Objective**

Higher alpha-fetoprotein (AFP) levels are indicative of liver regeneration but alone are not of minimal help in determining prognosis in patients with acute liver failure (ALF). The purpose of this study is to assess the utility of AFP concentration in combination with various severity of illness scores (SIS) [Sequential Organ Failure Assessment (SOFA) score, Model for End Stage Liver (MELD) score, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score] to determine if AFP will improve the predictions made by the SIS score(s) alone in the setting of ALF.

**Methodology**

This was a retrospective study with 810 ALF patients from the US Acute Liver Failure Study Group (ALFSG) who have AFP values that were determined from case report forms (CRF) or from sera collected on study day 1. The SOFA score, MELD score, and APACHE II score were calculated for each patient from available CRF data. We compared each severity of illness score to the severity score combined with the Log<sub>10</sub> AFP value to predict outcomes (transplantation, death, non-spontaneous survival [death or transplant 21 days or less from study admission]) for ALF from all etiologies and for ALF due to acetaminophen (APAP) toxicity alone (n = 306) using logistic regression; the Hosmer-Lemeshow (HL) test was used to evaluate the fit of the model to the data using the criteria p<0.15 for good model fit. Predictions from logistic regression were used to determine the area under the curve calculated using receiver operating characteristic (ROC) analysis.

**Validation**

Separate logistic regression models for each outcome were calculated for each of the SIS scores with and without AFP, for both All ALF etiologies and APAP alone, and for AFP alone. When all were examined, 5 combinations of both the SIS alone and the SIS plus the log<sub>10</sub> AFP were significant (p<0.05). These 5 pairs were examined using ROC analysis. The AUCs were calculated for 3 MELD scores, 1 SOFA score and 1 APACHEII score.

MELD/All Etiologies/Death: AUC for AFP = 0.590, MELD = 0.664, MELD + AFP = 0.689

MELD/All Etiologies/Non-SS: AUC for AFP = 0.563, MELD = 0.720, MELD + AFP = 0.727

MELD/APAP only/Non-SS: AUC for AFP = 0.587, MELD = 0.733, MELD + AFP = 0.748

SOFA/All Etiologies/Non-SS: AUC for AFP = 0.560, SOFA = 0.680, SOFA + AFP = 0.695

APACHEII/All Etiologies/Non-SS: AUC for AFP = 0.558, SOFA = 0.629, SOFA + AFP = 0.651

**Conclusion**

While AFP alone has been shown to be a limited prognostic indicator in ALF as seen with the low AUCs that were all less than 0.591, when it was added to severity of illness scores the prognostic ability of the SIS scores did show improvement,

particularly with MELD, with improvement from 0.007 to 0.025. The AFP improved the AUCs for the MELD, SOFA and APACHEII scores' ability to predict non-SS for all etiologies by 0.07, 0.015, and 0.022, respectively.

**A-064**

**Effects of Natural Opium on Atherosclerosis assessed by Carotid Ultrasound, hsCRP, Cholesterol, Glucose, BMI and Blood-Pressure studied on Opium-abusing and Non-abusing Indian Outpatients: A Cross Sectional Pilot Study**

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**Background:**

In developing countries including India and the middle east Natural Opium is currently the second most abused substance after tobacco. Decades of confusion exist about whether opium protects or harms the cardiovascular-system. Recent large Iranian Cohort studies suggest that Opium independently caused increased mortality risk (especially cardiovascular) after adjusting for Smoking, Age and Sex.

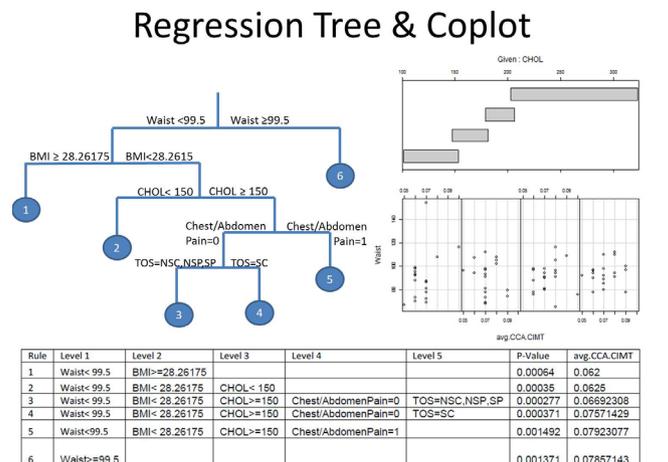
The population around Jodhpur harbors world's highest density of natural opium abusers. Most of the studies on effects of opium so far were done in Iran. We wanted to do a pilot study to see if the population around AIIMS Jodhpur has similar cardiometabolic associations with opium.

**Methods:**

A pilot cross sectional study is done on adult males out patients comparing Chronic Opium abusers with tobacco smoking and nonsmoking controls. We collected history of opium consumption, smoking, comorbidities and medications. We measured atherosclerotic predisposition directly by carotid intima-media thickness (CIMT), also hsCRP, Random Blood Sugar and total Cholesterol which could all be measured on nonfasting encounters. We also measured BP, BMI, and waist-circumference. Statistical Analysis done by "R" v3.1.1 and R-Studio: Average-Common-Carotid-CIMT used as the target variable and measure of atherosclerotic outcome; other variables were used a covariate.

**Results:**

Total 81 subjects subdivided according to Tobacco and Opium Status (TOS): Nonsmoking controls (NSC) 29, Tobacco Smoking control (SC) 27, Non Smoking OPium Abuser (NSP) 16, Tobacco Smoking Opium Abuser ( SP) 9. Results below.



**Conclusion:**

CIMT on opium population have so far rarely been published from anywhere in the world and is a novel part of our study. Preliminary statistical analysis of the result of this pilot is apparently showing some reversal of smoking mediated cardiometabolic effects eg mild reduction in blood pressure and CIMT to nonsmoking levels. However whether this is a sampling artifact or a real biological phenomena will need to be tested on well designed larger studies.

**A-065****Cardiovascular Risk Factors in first-degree relatives of young patient survivor of acute myocardial infarction**

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**Background:**

The premature coronary heart disease (CHD) is strongly associated with familiar component. Many studies have established the importance of a positive history family as an independent risk factor of CHD. The screening of risk factors must be considered in first-degree relative of any patient who develops CHD in young age. The aim of this study was compare the metabolic profile of first-degree relatives (FDR) of young patient survivor of acute myocardial infarction (AMI) with a group of healthy people without family history for precocious CHD.

**Methods:**

The study was conducted from November 2010 to January 2015 in a tertiary hospital. We excluded cases of familial hypercholesterolemia. A total of 167 first-degree relatives of patient with early onset AMI (age<45y) was matched for sex and age with a group enrolled by 267 persons of both sex and without familiar history of premature CHD. Laboratory analysis included fasting blood glucose, total cholesterol (TC), HDL cholesterol (HDL-C), LDL cholesterol (LDL-C), triglycerides and TSH. The patients were evaluated for the presence of metabolic syndrome. We defined metabolic syndrome using the 2007 International Diabetes Federation criteria.

**Results:**

There was a significant statistical difference between the FDR and control group for TSH ( $2,51 \pm 0,19$  vs  $1,84 \pm 0,10$  mU/L;  $p=0,004$ ); HDL-C ( $39,3 \pm 1,01$  vs  $49,4 \pm 1,3$  mg/dL;  $p=0,001$ ); triglycerides ( $163,1 \pm 9,9$  vs  $121,9 \pm 6,5$  mg/dL;  $p=0,001$ ); Body Mass Index ( $28,7 \pm 0,4$  vs  $26,8 \pm 0,4$ ;  $p=0,003$ ) and metabolic syndrome presence ( $46,5\%$  vs  $21,7\%$ ;  $p=0,001$ ). No statistically significance difference was found between the two groups for TC ( $190,1 \pm 4,1$  vs  $185,9 \pm 3,6$  mg/dL;  $p=0,463$ ); LDL-C ( $118,1 \pm 3,6$  vs  $111,4 \pm 3,4$  mg/dL;  $p=0,184$ ) and fasting blood glucose ( $95,5 \pm 2,4$  vs  $92,9 \pm 1,2$  mg/dL;  $p=0,448$ ).

**Conclusion:**

This study suggests that first-degree relatives of young patient with acute myocardial infarction have an unfavorable metabolic profile compared to those ones without family history for CHD ratifying the importance of early laboratorial evaluation in these people.

**A-341****Growth Differentiation Factor-15 in Patients with Light Chain (AL) Amyloidosis Has Independent Prognostic Significance and Adds Prognostic Information Related to Risk of Early Death and Renal Outcomes**

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**Background:** Growth differentiation factor-15 (GDF-15) has prognostic value in patients with cardiovascular disorders and adds prognostic information to other cardiac markers such as NT-proBNP and hs-TnT. Cardiac involvement is the most important determinant of prognosis in patients with AL-amyloidosis and cardiac biomarkers have major prognostic importance in AL. The aim of the study was to explore the value of GDF-15 in patients with AL-amyloidosis.

**Patients and Methods:** We measured the circulating levels of GDF-15, NT-proBNP and hs-TnT in 77 patients with newly diagnosed AL-amyloidosis, before and 3-months post frontline treatment. GDF-15 was measured by a novel pre-commercial immunoassay (Roche Diagnostics).

**Results:** Patients' median age was 68 years; most patients had cardiac (61%) or renal involvement (74%); 61% had NT-proBNP >1,284pg/ml and 46% had hsTnT >54ng/ml. Median levels of GDF-15 were 3,594pg/ml (range 626-71,475pg/ml); 95% of patients with AL had GDF-15 levels >1,200pg/ml. GDF-15 correlated with NT-proBNP ( $r=0,538$ ,  $p<0,001$ ), hs-TnT ( $r=0,447$ ,  $p=0,02$ ) and eGFR ( $r=-0,570$ ,  $p<0,001$ ). Patients with GDF-15 levels within the upper quartile (>7,575 pg/ml) had a very poor outcome (median overall survival (OS) 3-months) compared to patients with GDF-15 levels below the upper quartile ( $p=0,01$ ). Higher cut-off levels for NT-proBNP and hs-TnT did not discriminate patients at high risk for early death more accurately. In a multiple logistic regression model which included GDF-15, NT-proBNP and hs-TnT, only GDF-15 in the upper quartile (HR: 8.427, 95% CI 1.73-41.1,  $p=0,008$ ) was independently predictive of early death at 3-months. Similar results were obtained when these biomarkers were treated as continuous variables. Regarding OS, GDF-15 had independent prognostic significance in a multivariate model that included both NT-proBNP and hs-TnT. We also evaluated changes in the levels of GDF-15, NT-proBNP and hs-TnT in patients who received lenalidomide after 3-months of treatment. In these patients NT-proBNP often increases without obvious deterioration of cardiac function, thus complicating the assessment of cardiac response early, during the course of therapy. NT-proBNP levels increased substantially both in those with hematologic response ( $p=0,05$ ) and in those without hematologic responses ( $p=0,013$ ); similarly, hs-TnT levels increased in non-responders ( $p=0,006$ ), while GDF-15 levels did not change significantly in both cases.

As GDF-15 reflects heart and renal defects, we further evaluated whether GDF-15 could be associated with the risk of progression to ESRD and need for dialysis. Using ROC analysis, GDF-15 >median was identified to better discriminate patients with shorter time in dialysis (29-months vs not reached,  $p=0,001$ ; with 38% vs. 8% progressing to ESRD, respectively). eGFR <60ml/min/m<sup>2</sup> was also a strong predictor of ESRD ( $p=0,004$ ). However, in multivariate analysis which included GDF-15 >median, eGFR <60ml/min/m<sup>2</sup> and proteinuria >5g/day, only GDF-15 was independently associated with a higher risk of ESRD requiring dialysis (HR: 4.25, 95% CI 1.01-18,  $p=0,045$ ).

**Conclusions:** GDF-15 is a novel biomarker with prognostic implications for different outcomes in patients with AL-amyloidosis; it is associated with a high risk of early death, with OS and also with renal outcome. More importantly GDF-15 adds prognostic information independent of the traditional cardiac biomarkers and thus, its measurement in larger series of patients is recommended.