Tuesday, August 1, 9:30 am – 5:00 pm

Clinical Studies/Outcomes

A-100

Selected pro- and anti-inflammatory cytokine serum concentrations in different clinical forms of multiple sclerosis

A. Kost, L. Lapovets, U. Pidvalna. Danylo Haltsky National Medical University, Lviv, Ukraine

Background: Multiple sclerosis (MS) is an immune-mediated central nervous system disease characterized by inflammation, demyelination and axonal degeneration. The pathology of MS suggests an autoimmune cause involving cellular and humoral components of the immune system. Active MS lesions are characterized by T-cell and macrophage infiltration and the presence of immune mediators, including adhesion molecules, chemokines, and cytokines. Cytokines are proven mediators of immunopathological processes in MS. The aim of this study was to delineate the serum cytokine profile in patients with MS and the controls and to determine in different clinical forms of MS.

Methods: This study involved 62 consecutive MS patients—28 patients with progressive MS and 34 patients with relapsing-remitting MS (RRLMS). The control group consisted of 18, age and sex matched, non-immunological, neurological patients. The patients were evaluated using the Expanded Disability Status Scale (EDSS) and magnetic resonance imaging (MRI) with gadolinium. Serum samples for cytokine measurements were collected on admission. Plasma levels of proinflammatory T-helper (TH1) (interferon (IFN)-γ) cytokines, peripheral mononuclears (IL-1β, IL-6, TNF-alpha) and anti-inflammatory or down-regulatory TH2 cytokines (IL-4, IL-10) were determined by an enzyme-linked immunosorbent assay (ELISA) method.

Results: All patients with MS had significantly higher cytokine (IFN-γ, IL-1β, IL-6, TNF-α, IL-4, IL-10) concentrations compared with controls (p<0.001). Increased IL-1β, IFN-γ (p=0.032 and 0.041, respectively) and decreased IL-4, IL-10 (p=0.038 and 0.02, respectively) levels were found in progressive MS compared with RRMS. Patients with progressive MS with disease progression presented higher IL-1β, TNF-alpha, IFN-γ and IL-10 levels than those without disease progression (p<0.05). There was a significant inverse correlation between IL-10 levels and EDSS score in patients with progressive MS (R = -0.43, p < 0.05).

Conclusion: Profiling cytokines in multiple sclerosis may help to identify mechanisms involved in the pathogenesis of the disease, and, potentially, lead to new therapies directed at cytokines or their receptors. The level of IL-10 can serve as an additional diagnostic criterion for assessing the disability in patients with progressive MS.

A-104

Liver Fibrosis Biomarkers and Acoustic Radiation Force Impulse Imaging for non-invasive assessment of Non-Alcoholic Steatohepatitis in patients with morbid obesity before bariatric surgery

J. Cebreiro-López, J. A. Noguera Velasco, F. Guzmán Aroca, M. D. Frutos Bernal, J. A. Luján Monpám, A. Bas. Clinical University Hospital Virgen de la Arrixaca, Murcia, Spain

Background: There is a wide spread of liver histology in Non-Alcoholic fatty liver disease (NAFLD). Simple steatosis is generally considered benign and reversible, but steatohepatitis (NASH) can evolve to progressive fibrosis and liver cirrhosis in the long term. The early detection of NASH would make it possible to anticipate the natural course of the disease, allowing therapeutic action to be proposed before the appearance of fibrosis, therefore, identification of NASH patients is crucial. Obesity is a recognized risk factor for NAFLD. The prevalence of NAFLD in the general population ranges from 15 to 30% and increases with obesity. In overweight subjects, the prevalence of steatosis is at least two times greater than in lean subjects and in morbid obesity the prevalence of NAFLD and NASH is nearly 90% and 37% respectively. Liver biopsy is the standard for the diagnosis of NAFLD but has risks and limitations, so that non-invasive diagnostic tools such as serum biomarkers, imaging methods have been developed. The ELF test measures three markers of liver matrix metabolism in serum (hyaluronic acid, procollagen-III amino terminal peptide and tissue inhibitor of metalloproteinase-1) and the result becomes a score that indicates the level of fibrosis. Acoustic Radiation Force Impulse (ARFI) is a imaging technique that provides a quantitative measure of the tissue elasticity, shear wave velocity (SWV), that correlates with the degree of fibrosis. We aimed to develop a model that combines ELF and ARFI and to assess its feasibility for detecting NASH in morbid obese patients with suspected NAFLD.

Methods: We selected 57 morbid obesity patients who were to undergo bariatric surgery and were classed according to their biopsy findings. Group A (n=28): normal liver or simple steatosis; Group B (n=29): NASH and/or fibrosis. All patients were evaluated with ARFI before surgery and ELF test was calculated.

Results: Significant differences in ELF and SWV results were found between the two groups (p=0.002, p=0.003). AUROC for differentiating patients of both groups using ELF and SWV were 0.780 (p=0.002) and 0.729 (p=0.003). We developed a logistic regression model that combined clinical variables, biomarkers and the SWV and defined the probability of presenting NASH and/or fibrosis (group B). The variables included were age, body mass index, metabolic syndrome, mean corpuscular volume, AST, ALT, SWV and ELF. The AUROC of the model was 0.890 (p=0.044) and was significantly higher than any of the individual variables.

Conclusion: The combination of the ELF and the ARFI represents a efficient option for the identification of obese patients with NAFLD and signs of NASH and fibrosis. Using complementary methods together with different biological bases is an advantage over the use of individual techniques and increases confidence in diagnosis. In the case of patients who are going to be subjected to bariatric surgery, the use of this model would make it possible to presurgically identify those patients with more severe hepatopathy, thus establishing a population at risk in which surgery could be prioritized, and to propose prior therapeutic actions to reduce postsurgical morbidity and mortality related to hepatopathy.

A-109

Evaluation of Glycated Albumin as a Useful Indicator for Renal Dysfunction in Diabetic and Nondiabetic Population

N. Duan, H. Li, L. Pang. Peking University First Hospital, Beijing, China

Background: Glycated albumin (GA) reflects serum glucose of preceding 2-3 weeks and plays an important role in diabetes mellitus (DM). This study aimed at investigating whether GA can assess renal dysfunction in population.
Clinical Studies/Outcomes

PREVALENCE OF METABOLIC SYNDROME IN GRANITE WORKERS

S. Panakala1, R. Kondreddy1, K. Kumar2, A. Rawal1, J. R. Peela1, J. R. Kooriyi1, M. Prasad1, M. G. I. El Fituri1, 1Department of Biochemistry, 2Mamatha Medical College, Khammam, India, 1Department of Biochemistry, 3Varan Arjun Medical College and Rothikhandl Hospital, Bantha, Shahjahanpur, UP, India, 1Department of Biochemistry and Medical Genetics, School of Medicine, St. Matthews University, Grand Cayman, Grand Cayman, Cayman Islands, 1Department of Physiology, School of Medicine, St. Matthews University, Grand Cayman, Grand Cayman, Cayman Islands, 1Narayana Medical College Hospital, Nellore, Andhra Pradesh, India, 1Department of Global Health, College of Global Public Health, New York University, New York, NY

BACKGROUND: The prevalence of the metabolic syndrome (MS) has significantly increased over the last few decades and has become a main health challenge worldwide. Prevalence of MS is quickly rising in developing countries due to changing lifestyle. It was considered worthwhile to study MS and its components in granite workers since granite factories are situated in and around Khammam area. Moreover, no studies of MS in granite workers have been reported in literature.

OBJECTIVES: Aim of our study is to assess the prevalence of metabolic syndrome and its components in granite workers.

MATERIALS AND METHODS: 210 male workers in the age group of 20-50 working in granite industries located in and around the Khammam town of Telangana State are selected for the present study. Blood pressures (BP), waist circumference (WC) were measured. Fasting blood samples were collected for the estimation of glucose and lipids.

RESULTS: 69 subjects out of 210 were identified as having MS based on updated National cholesterol education program- Adult Treatment Panel III (NCEP-ATP III) guidelines.

CONCLUSION: MS should be identified and remedial measures may be suggested, so that the risk of hypertension, cardiovascular risk, diabetes and the resultant morbidity is minimized and can be delayed.

PREV ALENCE OF METABOLIC SYNDROME IN GRANITE WORKERS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No Of Granite Workers</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevate BP</td>
<td>85</td>
<td>49</td>
</tr>
<tr>
<td>Elevate waist Circumference</td>
<td>61</td>
<td>29</td>
</tr>
<tr>
<td>Elevated TG</td>
<td>52</td>
<td>25</td>
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<tr>
<td>Reduced HDL</td>
<td>72</td>
<td>34</td>
</tr>
<tr>
<td>Elevated Glucose</td>
<td>42</td>
<td>20</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>69</td>
<td>33</td>
</tr>
</tbody>
</table>

Evaluating neonatal minimum volumes with Abbott Architect c8000 and Sysmex XN

P. Delphy1, J. Baker1, R. Wonderling2. 1MultiCare Health System, Tacoma, WA, 2Abbott Diagnostics, Abbots Park, IL

BACKGROUND: Our neonatologists approached the laboratory to find a solution to reduce neonatal blood collection volumes. Nurses draw specimens in wide bore BD Microtainers (Cat # BD 365967) which can potentially reduce the amount of blood drawn from neonates, but short collections lead to high rates of QNS and redraws. Nurses frequently collected whole blood in spun hematocrit tubes and phase platelet devices in situations of previous QNS or other collection issues. We wanted a solution that was efficient and productive for both nursing and the laboratory that would maximize quality and safety for the neonates.

METHODS: We started by reviewing actual patient hematocrit values to assess the number (%) of high/low hematocrit specimens. 155 specimens in one month showed 87% of neonates with a hematocrit ≤50 and 60% of neonates ≤40. Based on this population, we conservatively based the study on a hematocrit of approximately 60% to establish extreme minimum volumes. We selected 20 most frequently ordered chemistry tests and included the volume of each test. We selected a Microtainer® (Cat # BD 365967) which can potentially reduce the amount of blood drawn from neonates, but short collections lead to high rates of QNS and redraws. Nurses frequently collected whole blood in spun hematocrit tubes and phase platelet devices in situations of previous QNS or other collection issues. We wanted a solution that was efficient and productive for both nursing and the laboratory that would maximize quality and safety for the neonates.

RESULTS: The Abbott Architect c8000 Sampling Dead Volume + Over Aspiration Volume (DV/OAV) is 0.058 mL. This DV/OAV plus the accumulation aspiration volumes (calculated from the Abbott Architect Sample volumes) ranges from 0.083 mL (minimum 4 assay panel + HIL) to 0.1337 mL (maximum 20 assay panel plus

A-112

Effects of laboratory results and lifestyle parameters on the development of non-alcoholic fatty liver disease: The Korean National Health Insurance Service-National Sample Cohort 2009-2013

J. Rim1, T. Youk2, J. Cho3, H. Gee4, J. Yoo1. 1Yonsei University College of Medicine, Severance Hospital, Seoul, Korea, Republic of; 2National Health Insurance Service Ilsan Hospital, Goyang, Korea, Republic of; 3Yonsei University College of Medicine, Seoul, Korea, Republic of

BACKGROUND: The purpose of this study was to investigate the effects of anthropometric, laboratory, and lifestyle factors on the development of non-alcoholic fatty liver disease (NAFLD) in a nationwide, population-based, 4-year retrospective cohort.

METHODS: The propensity score-matched study and control groups contained 1,474 subjects (940 men and 534 women) who had data in the Korean National Health Insurance Service-National Sample Cohort 2009-2013. Cross-sectional study and divided into 5 groups: healthy subjects (n = 3238), impaired fasting glucose (n = 83), DM without renal complications (n = 317), DM with albuminuria (n = 60) and non-diabetic chronic kidney disease patients (n = 116). All analyses were conducted using the subjects with fasting venous blood and morning urine samples. Statistical analysis was done by SPSS 16.0.

RESULTS: Among all groups, mean GA, hemoglobin A1c, fasting plasma glucose, serum creatinine were the highest and estimated glomerular filtration rate (eGFR) was the lowest in DM with albuminuria group. When eGFR was 90-105 mL/min/1.73 m2 or mildly decreased to 60-90 mL/min/1.73 m2, GA increased significantly with elevating albumin-to-creatinine ratio (ACR) from 0-10 mg/g to 10-30 mg/g to > 30 mg/g (P < 0.01 and P < 0.001). GA increased further when eGFR decreased moderately to severely as renal function continuing to deteriorate (eGFR ≤ 60 mL/min/1.73 m2). When ACR ≤ 30 mg/g and eGFR ≤ 60 mL/min/1.73 m2, more than 50% were DM patients and had significant higher GA levels than other subjects with eGFR > 105 mL/min/1.73 m2. After adjusting demographics (age at enrollment, gender and body mass index [BMI]), every 5% rise of GA levels showed a 1.778-fold increased risk in all subjects (adjusted odds ratio [OR], 1.778; 95% confidence interval [CI], 1.373-2.302; P < 0.001) and 1.737-fold risk in DM subjects (adjusted OR, 1.737; 95% CI, 1.221-2.471; P = 0.002) for occurrence of ACR > 30 mg/g in contrast to ACR ≤ 30 mg/g. Compared to eGFR > 90 mL/min/1.73 m2, 5% rise of GA levels showed a 1.482-fold risk for eGFR 60-90 mL/min/1.73 m2 (adjusted OR, 1.482; 95% CI, 1.112-1.975; P = 0.007) and 1.996-fold risk for eGFR ≤ 60 mL/min/1.73 m2 (adjusted OR, 1.996; 95% CI, 1.366-2.916; P < 0.001).

CONCLUSIONS: Increased GA serves as a risk marker for renal dysfunction and an effective complement to ACR for DM patients. GA combined with eGFR and ACR can reflect renal function changes in population, especially those DM and early diabetic kidney disease subjects whose eGFR might be in normal values.
Growth Differentiation Factor-15 is a New Biomarker with Independent Prognostic Significance for Survival and Renal Outcomes in Different Cohorts of Patients with Light Chain (AL) Amyloidosis

I. Papassotiropoulos, G. Merlino, E. Terpos, A. Akalestos, F. Apostolakou, P. Milani, M. Basset, F. Russo, E. Psimennou, M. Roussou, M. Guvriatopoulou, D. Fotiou, D. Zografos, C. Pamboucas, E. Papapapopoulos, M. A. Dimopoulos, G. Palladini, E. Kastritis, Department of Clinical Biochemistry, “Aghia Sophia” Children’s Hospital, Athens, Greece, Amyloidosis Center, University Hospital Policlinico San Matteo, Pavia, Italy, Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Background: Growth differentiation factor-15 (GDF-15), a member of TGF-beta family, is involved in several pathological conditions, which include inflammation, cancer, cardiovascular, pulmonary and renal diseases. Serum GDF-15 levels add prognostic information to conventional prognostic factors, such as NT-proBNP and troponins, in cardiovascular disorders and also have shown to be associated with renal damage and risk of end stage renal disease in patients with diabetes. Based on the above data, we evaluated the prognostic value of GDF-15 levels in patients with AL amyloidosis and showed that in a cohort of 77 patients GDF-15 was associated with early death, shorter survival and progression to dialysis, independently of the cardiac biomarkers and renal stage. In order to validate the prognostic value of serum levels of GDF-15, we evaluated GDF-15 in two independent cohorts of patients treated in two different centers (Pavia Amyloidosis Center and Department of Clinical Therapeutics, Athens). Methods: Cirulating levels of GDF-15 were measured by a novel pre-commercial immunoassay (Roche Diagnostics), along with measurements hs-Troponin-T and NT-proBNP in more than 800 serial stored samples using electrochemiluminescence techniques. The Pavia cohort included 202 and the Athens cohort included 107 patients with AL amyloidosis. Standard criteria were used for the diagnosis, evaluation of organ involvement and cardiobiomarker-based risk stratification. Renal staging was based on baseline proteinuria (>5g/day and eGFR<50mL/min). Median age and involved FLC levels were similar between the two cohorts but there were differences in other baseline characteristics including heart involvement and Mayo stage Median follow up for the Pavia cohort was 18-months and for the Athens cohort was 45-months (p<0.001), while survival at 2 years was identical. Results: Median GDF-15 levels was 3.027pg/ml in Pavia (range 624-1000,000pg/ml) and 3.854pg/ml (range 626-71,475pg/ml) in Athens cohort (p=0.09); the upper quartile of GDF-15 levels however was ≥5,655pg/ml for the Pavia and ≥7,553pg/ml for Athens cohort, while 90% and 94% of patients in the two cohorts had GDF-15 levels >1,200pg/ml (the upper limit of normal for individuals without cardiovascular disease). We then evaluated the prognostic significance of GDF-15 levels in the two cohorts by applying the previously identified cutoff of 7,575pg/ml. GDF-15 above cutoff was associated with significantly shorter survival both in Pavia (17 months vs not reached, p=0.003) and in Athens cohort (13 vs 47 months, p=0.03). We then evaluated the prognostic significance regarding renal outcomes (dialysis): GDF-15 >4,000pg/ml was associated with a HR of 6.95% CI 2015.6, p<0.001) in Athens cohort (progression to dialysis within 2 years in 7% vs 47%); however, very few events have occurred in Pavia cohort and analysis was inconclusive. Although renal stage discriminated 3-groups in univariate analysis (p=0.03), in multivariate analysis, GDF-15 >4,000pg/ml outperformed renal stage and was the only independent prognostic factor for dialysis risk. Conclusion: This study validated and confirmed in two independent cohorts, with differences in their characteristics, the prognostic value of GDF-15, which emerges as a novel biomarker with prognostic implications for different outcomes in patients with AL amyloidosis. Importantly, GDF-15 emerges also as a new biomarker for renal outcomes in patients with AL-amyloidosis.
The dibucaine number is required to accurately predict pseudocholinesterase phenotypes

K. Volzling, T. L. Kauttainen, J. Ulloor, O. K. Ndimbie, M. A. Beischer, K. B. Sidker. Abbott Laboratories, Irving, TX

OBJECTIVE: The relationship between pseudocholinesterase (PChE) phenotypes and dibucaine numbers (DNs) is used to identify individuals who may experience prolonged effects of neuromuscular-blocking general anesthetics administered during surgery (Table 1). The objective of this study is to determine if uninhibited or dibucaine-inhibited PChE activity sufficiently predicts enzyme phenotype.

METHODS: Pairs of uninhibited and dibucaine-inhibited PChE activity data were analyzed for 39,719 patient samples across 43 laboratories. DNs were calculated for each sample from this paired data (Equation 1). The uninhibited and dibucaine-inhibited PChE activity of each sample was then evaluated relative to its corresponding DN to determine if a correlation exists between enzyme activity and DN.

Equation 1: 
$$DN = 100 \times \left(1 - \frac{PChE \text{ activity}}{PChE \text{ activity} \times \text{dibucaine-inhibited activity}} \right)$$

RESULTS: Wild-type, heterozygous, and homozygous atypical PChE phenotypes were present in the data set as indicated by the DN calculation (Table 1).

<table>
<thead>
<tr>
<th>DN</th>
<th>PChE Phenotype</th>
<th>Recovery from general anesthesia</th>
<th>Frequency - this study</th>
</tr>
</thead>
<tbody>
<tr>
<td>DN&lt;72</td>
<td>Wild-type (E1, E1)</td>
<td>Normal</td>
<td>94.2% (34,565)</td>
</tr>
<tr>
<td>35≤DN&lt;72</td>
<td>Heterozygous atypical (E1, E1')</td>
<td>Prolonged</td>
<td>5.6% (2083)</td>
</tr>
<tr>
<td>DN&gt;35</td>
<td>Homozygous atypical (E1', E1')</td>
<td></td>
<td>0.2% (71)</td>
</tr>
</tbody>
</table>

Consistent with literature, over 90% of PChE samples in this study were wild-type (DN<72) and less than 0.5% were homozygous atypical (DN>72). 100% of uninhibited and homoyzogous atypical PChE samples displayed activity <18,000 U/L, as did 97.1% of uninhibited heterozygous, and 98.5% of uninhibited wild-type samples. Despite the small fraction of homozygous and wild-type samples with uninhibited PChE activity >15,000 U/L, there was no overall correlation between uninhibited activity and phenotype or DN.

Dibucaine-inhibited PChE activity for all phenotypes did not exceed 16,000 U/L and did not correlate with phenotype or DN.

CONCLUSIONS: The DN calculation is essential for accurate PChE phenotyping. Taken in isolation, neither uninhibited nor dibucaine-inhibited PChE activity correlates with enzyme phenotype. These data may be used to determine the DN for a patient receiving general anesthesia if they have previously suffered a prolonged recovery from anesthesia or have a family history of atypical phenotypes. Application of DN to management of these patients may prevent unexpected postoperative respiratory muscle paralysys that lasts hours to days and necessitates mechanical ventilation.

An observational prospective single center study to assess utility of serum cystatin C and its estimated GFR among various subgroups of patients' experience in semi urban locality

M. S. Patwardhan1, H. Shah2, A. Ahuja3, S. Babu4. Dr Patwardhan's Pathology Laboratory, Ulhasnagar, India, 2Bombay Hospital & Research Centre, Mumbai, India, 3Shivneri Hospital, Ulhasnagar, India, 4Agape Diagnostics, Kochi, India

Background: Serum creatinine and cystatin C are complementary markers of GFR. Whereas serum creatinine is affected by age, race, sex and muscle mass, cystatin C remains unaffected. Cystatin C has been used extensively as a research tool but it is not commonly done in routine laboratories in India because of its cost. Study aims to assess the subgroups of patients with nephropathy who get additional benefit from cystatin C test over creatinine.

Methods: Inclusion criteria: Consecutive 131 subjects seen and referred by nephrologist and physician. Exclusion criteria: Patients with age greater than 75 years, those suffering from hypo or hyperthyroidism, patients taking steroids. Normal male: 20 normal female: 20 (for comparison). 2Hypertensive patients (s. creatinine: >1.5 mg/dl in males, >1.3 mg/dl in females): 21 3Chronic glomerulonephritis (urine protein ++): 15 4Diabetic nephropathy (s. creatinine >1.5 mg/dl in males, >1.3 mg/dl in females): 55

We estimated s. creatinine and urine creatinine by Jaffe kinetic. Cystatin C estimated by turbidimetry method. Microalbumin done by turbidimetry method (Agappe India) Urine protein done by sputhosaliclyc turbidimetry method. Tests done on semiautomated instrument. EGFR estimation from creatinine calculated from Cockcroft-Gault equation, and from cystatin C by Hoek formula $GFR = 4.32 \times (1/cystatin C \text{ mg/dl})$.

Results: We report good correlation in healthy male & female subjects between values of creatinine, cystatin C, GFR estimated from the above and albumin/creatinine Ratio. Reference range of cystatin C: (male) 0.78 to 1.2 mg/l, (female) 0.4 mg to 0.8 mg/l. Out of 21 Hypertensive patients (mean age 50 years), mean for creatinine eGFR was 52±18 ml with 4 patients in mild/stage 2 and rest 17 in moderate/stage 3 whereas cystatin C eGFR was reported mean of 83±40ml with 2 patients in mild reduction, 8 in moderate reduction and 11 patients within normal range. Therefore only 50% of hypertensive patients showed eGFR values in abnormal range with cystatin C as compared to creatinine as verified by normal urine microalbumin. This variation in creatinine results might be due to above mentioned factors. Out of 15 patients of glomerulonephritis mean for age was 41±15 years. About 40% of these patients had borderline creatinine values (mean 1.64 mg/dl) while all cystatin C values are in pathological range (mean 2.5 mg/dl). In 55 patients suffering from diabetic nephropathy, all values show good correlation between creatinine and cystatin C. Mean for creatinine was 2.21±0.9 mg/dl with eGFR with 37±24 ml; mean for Cystatin C was 2.19±2.9 mg/l with eGFR 37±25 ml. All the above patients had albuminuria.

Conclusion: Above study results show the importance of cystatin C and its eGFR in hypertensives and patients suffering from glomerulonephritis. It can be used as a complementary test in patients suffering from diabetic nephropathy.

Graft-derived cell-free DNA - a promising rejection marker in cardiac transplantation - Results from a prospective observational trial

E. Schürz1, L. Reinhard2, F. Knüttgen1, J. Beck1, U. Schulz1, M. Harden1, U. Fuchs3, N. Mettmenmeyer2, C. Knabbe1, A. Zittermann1, J. Gummet2, I. Birschmann1, M. Oellerich1. 1Chronis Biomedical, Göttingen, Germany, 2Dept. Clinical Pharmacology University Medical Center, Göttingen, Germany, 3Inst. for Laboratory and Transfusion Medicine, Heart and Diabetes Center NRW, Bad Oeynhausen, Germany, 4Clinic for Thoracic and Cardiovascular Surgery, Heart and Diabetes Center NRW, Bad Oeynhausen, Germany, 5Dept. of Medical Statistics, University Medical Center Göttingen, Göttingen, Germany

Background: Reliable noninvasive markers for early detection of rejection after heart transplantation are lacking. Immunosuppressant therapeutic drug monitoring is more useful to prevent toxicity rather than to predict efficacy. Graft-derived cell-free DNA (GcfDNA) has shown promise as a biomarker for the early detection of graft injury.

Methods: In a prospective observational trial, GcfDNA was monitored in 84 adult cardiac transplant recipients followed over at least one year post transplantation. GcfDNA was determined as described elsewhere (Clin Chem 2013; 59: 1732-1741). The turnaround time for an initial sample is about 2 days and one working day for any consecutive sample. Biopsies were done upon clinical suspicion of acute rejection and compared to GcfDNA test results.

Results: GcfDNA percentage was highly elevated (>5% of total cfDNA) on the first day after transplantation, evaluated in a subset of 15 patients, presumably due to ischemia/reperfusion damage. The median GcfDNA percentage decreased in stable patients with no signs of graft injury within the first week to a baseline value <0.5%, which it remained throughout the one year observation period. In 19 patients with samples drawn during biopsy-proven acute rejection periods (n=25), values were about 5-fold higher (median: 0.10%, 95%-CI 0.08-0.12%). In comparison to 23 patients with negative biopsy (n=23 samples; median: 0.19%, 95%-CI 0.16-0.26%), the median observed in samples (n=208) from 67 stable patients without rejection was (median: 0.10%, 95%-CI 0.08-0.12%). In 19 patients with negative biopsy (n=23 samples; median: 0.19%, 95%-CI 0.16-0.26%), the median observed in patients with biopsy-proven rejection was 2.7-fold. In 14 otherwise clinically stable patients with samples available 9 to 30 days prior to diagnosis of biopsy-proven acute rejection (n=22), 5-fold elevated GcfDNA values (median: 0.47%, 95%-CI 0.26-0.63%) compared to stable patient samples were observed. Isotoprimod showed only a moderate correlation with GcfDNA (Spearman correlation coefficient (R): 0.51, 95%-CI 0.40-0.60, n=222).

Conclusion: Plasma GcfDNA determinations allowed for early detection of cardiac transplant patients with acute rejection and may be helpful to personalize post-HTx immunosuppression.
Clinical Studies/Outcomes

Reproducibility among the four sites was greater than 95% for all read methods for both the turbidity and Prompt® inoculation methods.

Conclusion: This multicenter study showed that reformulated imipenem MIC results for gram-negative bacilli obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels. *Prompt® is a registered trademark of 3M.

Beckman Coulter, the stylized logo and the Beckman Coulter product and service names mentioned herein are trademarks or registered trademarks of Beckman Coulter, Inc. in the United States and other countries.

Pending clearance by US FDA, CE compliance, and other regulatory registrations.

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Evaluation of the Bio-Rad D-100™ Hemoglobin Testing System

B. Eichells, W. J. Candelaria. Maricopa Integrated Health System, Phoenix, AZ

Background: The D-100 is a high throughput automated test system used to quantify hemoglobin Alc (A1c) in whole blood samples. The D-100 uses High Performance Liquid Chromatography (HPLC) to separate hemoglobin fractions and obtain an HbA1c result that is expressed in NGSP or IFCC units. The D-100 also utilizes a bi-directional LIS interface and offers the capability of automatically reviewing (Bagging or releasing) the A1c results on the system.

Objective: The purpose of this study is to verify and validate the manufacturer claims of 10,000 tests (injections) per analytical cartridge with prefilter change every 2,000 tests on a single calibration. This testing included precision and accuracy checks, sample throughput, hemoglobin variant detection with no interference from heterozygous hemoglobins S, C, D and E, and workflow studies.

Methods: Beginning January 4, 2017 a new analytical cartridge and prefilter were installed on a D-100. Calibration and QC were run per guidelines. During the 10,000 test sample run study, 4 patient EDTA whole blood samples at ~ 5, 6.5, 8 and 12 % A1c were selected and run as precision samples in duplicates, twice a day for 10 days. Additionally, 40 samples whose NGSP values were pre-assigned by SRL % A1c were selected and run as precision samples in duplicates, twice a day for 10,000 tests on a single calibration. This testing included precision and accuracy calculations for the 4 precision samples were 0.86, 0.73, 0.87, and 0.86%. The sample throughput was confirmed to be 45 seconds per sample. The “Time to first result” was confirmed to be 2 minutes 15 seconds, where the 45 second assay of the first sample in the run follows a 1 minute 30 second system flush. Each successive sample of the run is 45 seconds.

Conclusion: The performance of the Bio-Rad D-100 met all of the manufacturers stated claims. The D-100 saves ~80% in tech time over our previous system, the Bio-Rad VARIANT™ II TURBO. With the built-in result review criteria and the bi-directional LIS interface, >90% of our patient samples are run and verified with no tech intervention.

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S35
Liver injury and endotoxemia in male and female alcohol-dependent individuals admitted to an alcohol treatment program

I. Kirpich, V. Vatsalya, K. Falkner, C. McClain, J. Umhau
University of Louisville, Louisville, KY, Food and Drug Administration, Silver Spring, MD

Background: Interactions between the liver, the gut, and the immune system are critical components of alcoholic liver disease (ALD). The aim of this study was to explore the interactions between alcohol-induced liver injury, endotoxemia, and inflammation at admission and over time during abstinence; and to examine the sex-related differences in these parameters in alcohol-dependent individuals admitted to an alcohol treatment program. Methods: A cohort of 48 otherwise healthy participants with alcohol use disorder, but no clinical signs of alcoholic liver injury (34 males (M)/14 females (F)) admitted to an alcohol detoxification program, was stratified into two groups based on baseline plasma ALT levels (as a marker of liver injury). Group 1 (ALT < 40 U/L, 7M/8F) and Group 2 (ALT ≥ 40 U/L, 27M/6F) were identified. Plasma biomarkers of liver damage, endotoxemia and inflammation were examined at baseline (T1), day 8 (T2) and day 15 (T3) of the admission. The drinking history was also evaluated. Results: Sixty-nine percent of patients had elevated markers of liver damage, including ALT (98.55±9.82 vs 26.47±2.28 U/L), AST (130.7±17.49 vs 34.53±25.18 U/L), and cytochrome 18 (CK18) M65 and M30 (890.3±166.4 vs 308.1±105.9 U/L and 241.8±56.1 U/L, respectively; Group 2 vs Group 1). Elevated Elevated CK18 M65/M30 ratio suggested a greater contribution of necrotic rather than apoptotic hepatocyte cell death in the liver injury observed in these individuals. Positive correlations were observed in Group 2 at T1 between both CK18 M65 and ALT (r = 0.473, p = 0.005) and CK18 M30 and ALT (r = 0.357, p = 0.041). CK18 M30 was positively correlated with average drinks per drinking day at T1 in males (r = 0.503, p = 0.007). Females showed greater elevations of liver injury markers compared to males (e.g., ALT 136.2±43.8 vs 90.19±6.9 U/L), although they had fewer drinks per day (10.5±1.9 vs 15±0.0) and shorter lifetime duration of heavy drinking (11.5±3.6 vs 18±2±9.1). Liver injury was associated with systemic inflammation, specifically, elevated plasma TNF- α levels. Compared to patients without liver injury, patients with mild ALD had greater endotoxemia (increased serum LPS levels), which decreased with abstinence and this decrease preceded the drop in CK18 M65 levels. A positive correlation between LPS and ALT levels was observed at T1 only in Group 2 males (r = 0.404, p = 0.037).

Conclusions: The study documented the association of mild alcohol-induced liver injury and endotoxemia, which improved with two weeks of abstinence, in a subset of alcohol-dependent individuals. Females demonstrated higher levels of biomarkers of liver injury compared to males, although they had lower daily alcohol intake and shorter lifetime duration of heavy drinking

Decrease of Urotensin-II Activity in Women with Restless Legs Syndrome


Background Restless legs syndrome (RLS) is a chronic sensorimotor disorder characterized by an irresistible urge to move the legs. The pathophysiological mechanism of RLS has not been completely elucidated. This study was undertaken to compare the levels of urotensin II, a vasoactive peptide, in patients with restless legs syndrome and healthy controls and to examine possible roles of urotensin in the development of restless legs syndrome.

Patients and Methods A total of 64 female patients and 53 age- and body mass index-matched healthy female controls were included. Patients with conditions known to influence the vascular tonus such as hypertension, diabetes, or vascular diseases were excluded. The diagnosis of RLS was based on the International RLS Working Group criteria and all patients met the four essential diagnostic criteria required to establish a diagnosis of RLS. International Restless Legs Syndrome Study Group (IRLSSG) which is an assessment tool directing questions on the typical symptoms of RLS using a 5-point scale (i.e. between 0 and 4). A total score of 0 to 10, 11 to 20, 21 to 30, and 31 to 40 is indicative of mild, moderate, severe, and very severe RLS, respectively. Also the severity of RLS was assessed using John Hopkins Restless Legs Severity Scale (severity score 1=mild 2=mild 3=mild 4=mild) The two groups were compared with respect to demographic data, routine blood tests, complete blood count parameters, and Urotensin II levels.

Results Average serum Urotensin II levels were significantly lower among restless legs syndrome patients than among controls (1.43±0.46 and 1.94±0.67, respectively). A significant negative correlation with increasing disease severity scores and Urotensin II levels was found (r=0.001, r = -0.301). Diastolic and systolic blood pressure values were normal in both groups with no significant differences (Table 1). On the other hand restless legs syndrome patients had significantly lower Hb, MCV, and MCH (p=0.014, p=0.015, p=0.04, respectively). No correlations between Urotensin II and CRP, ESR, glucose, HbA1c, vitamin B12, folic acid, albumin, total protein, and calcium were found.

Conclusion RLS is a disease of unknown etiology. Since a proposed mechanism for the development of RLS involves the alterations of the peripheral vascular tone, we decided to examine the association between RLS and urotensin, which is a neuropeptide with known effects on the vascular tone. Our results suggest that urotensin may have a role in the pathophysiology of RLS both through vascular mechanisms and also through interactions with the immune system.
A-129

Evaluation of the Stratus CS Acute Care Diagnostic System and ADVIA Centaur XP Immunoassay System for Cardiac Troponin I

C. Bethoney, Siemens Healthineers, Norwood, MA

Objective: The objective of this study was to demonstrate diagnostic equivalence between the troponin I (cTnI) method on the point-of-care Stratus CS Acute Care™ Diagnostic System and the laboratory-based ADVIA Centaur® Tnl-Ultra™ assay on the ADVIA Centaur XP Immunoassay System (both from Siemens Healthcare Diagnostics Inc.) in the determination of myocardial infarction (MI).

Relevance: Troponin is recognized as the preferred biomarker in detection of MI given its high clinical sensitivity and myocardial tissue specificity. The Third Universal Definition of MI, endorsed by national societies of cardiology and heart foundations, requires at least one cTnI value above the 99th percentile upper reference limit (URL) for detection of MI. The Stratus CS System and ADVIA Centaur XP systems display optimal precision at their 99th percentile URL with a CV≤10%, allowing reliable detection of changing cTnI values.

Methodology: A comparison study was performed on the Stratus CS and ADVIA Centaur XP systems using frozen plasma samples from 110 patients suspected of having MI at two time points per patient. Patients were categorized as positive or negative for MI based on the presence or absence of at least one elevated cTnI value for each platform relative to the URL. Final diagnosis according to the Third Universal Definition of MI was provided for each patient as the reference standard for comparison.

Validation: Contingency tables were generated comparing patient outcome as determined by each system to the reference standard. The 99th percentile URL for MI is 0.07ng/mL for the Stratus CS System and 0.04ng/mL for the ADVIA Centaur XP System. Comparative receiver operating characteristic (ROC) curves were generated for each time point.

Conclusion: Clinical concordance was demonstrated between the Stratus CS System and ADVIA Centaur XP Immunoassay System for troponin I.

Table 1. Diagnostic performance measures for cTnI on Stratus CS and ADVIA Centaur XP systems.

<table>
<thead>
<tr>
<th>Estimate</th>
<th>ADVIA Centaur XP System</th>
<th>Stratus CS System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, 95% confidence interval (%)</td>
<td>100.0 (92.9–100.0)</td>
<td>95.9 (86.3–98.9)</td>
</tr>
<tr>
<td>Specificity, 95% confidence interval (%)</td>
<td>100.0 (94.0–100.0)</td>
<td>100.0 (95.8–100.0)</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>100.0 (98–100)</td>
<td>100.0</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>96.7 (96.6–96.7)</td>
<td>98.0 (98.0–98.0)</td>
</tr>
</tbody>
</table>

**Draw 1 area under the curve, 95% confidence interval**: 0.947 (0.902–0.991)

**Draw 2 area under the curve, 95% confidence interval**: 1.00 (1.00–1.00)

**A-130**

The use of procalcitonin as a sepsis marker in a community hospital

N. De Oro, M. E. Gauthreaux, J. Scott, J. Lamoureux. West Kendall Baptist Hospital, Miami, FL

Background: Procalcitonin is a biomarker that shows good sensitivity and specificity in identifying septic patients. This study investigated the diagnostic accuracy of procalcitonin in a community hospital setting and how it compared to lactic acid. It also explored the impact on patient care pre and post implementation of procalcitonin in regards to direct costs and length of stay.

Methods: Two methods were used for this study. First, two comparative groups were analyzed using an exploratory descriptive case-control study with secondary analysis of retrospective data from a 19 month period when procalcitonin was implemented. Next, a retrospective quasi-experimental study was done using a control group of emergency department patients with a sepsis diagnosis. Data included 19 months prior to the implementation of procalcitonin.

Results: In objective 1, the sample consisted of 165 sepsis cases and there was a positive correlation between lactic acid and procalcitonin values (r=0.377, p < 0.001). From the 165 sepsis cases who had positive blood cultures, procalcitonin had a sensitivity of 89.7%. In objective 2, there post-procalcitonin samples were 165 cases and the pre-procalcitonin sample was composed of 69 cases. There was a significant decrease after the implementation of procalcitonin in cost of hospitalization compared to costs pre-implementation (Wilcoxon Z = 2.034, p = 0.042). Although this cost is highly correlated with length of stay, neither the hospital (Wilcoxon Z = 0.906, p = 0.959) or ICU length of stay (Wilcoxon Z = 0.037, p = 0.970), showed a difference with pre and post implementation.

Conclusion: Our findings indicate that procalcitonin values had a higher predictive usefulness than the lactic acid. A consideration for lactic acid was to lower the cutoff to 1.4 mmol/L, so its sensitivity is similar to that of procalcitonin but the specificity (45.7%) and positive predictive value (35.5%) were lowered. Based on information from objective 2, the decrease in costs could be associated with a variable outside of the length of stay, or the parametric test was not powerful enough to show a decrease in length of stay, or the decrease in costs is a spurious association. Although procalcitonin is a relatively new test, it demonstrates to be a better marker for early diagnosis of sepsis and positively impact the health care practices in a community hospital setting as indicated in objective 1. Although this test is not routinely utilized to its full potential, it offers an opportunity to reevaluate the sepsis protocols as an alternative use of procalcitonin versus lactic acid for early diagnosis.

**A-131**

Is There a Relationship Between Serum Fetuin A Levels and Hematological Parameters with Behcet Disease Activity

A. Erek Toprak¹, H. Bilen², A. Karadag³, N. Akdeniz⁴, R. Karadag⁵
¹Istanbul Medeniyet University, Istanbul, Turkey, ²Ataturk University, Erzurum, Turkey

Background: Behcet’s disease (BD) is a multisystemic inflammatory condition which has unclear etiology. Serum fetuin A concentrations were shown to be inversely related with serum C reactive protein (CRP) concentrations and cytokines which are participating in inflammation, thereby fetuin A categorized as a negative acute phase protein (APP). Also Neutrophil / lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) values are suggested as simple and inexpensive inflammation markers. Fetuin-A, a glycoprotein is composed by two cystatin like domains and a smaller part participating in inflammation, thereby fetuin A categorized as a negative acute phase protein. In objective 1, the sample consisted of 30 BD patients (21 active, 9 inactive) and 31 healthy controls. Fetuin A, CRP, erythrocyte sedimentation rate (ESR), neutrophil, lymphocyte and platelet test were analysed and NLR and PLR values were calculated in all subjects.

Results: BD patients in active phase had significantly lower serum Fetuin A concentrations than both of passive BD (p=0.009) and control (p=0.006) group. Mean serum levels of Fetuin A were 294.2±85.69 µg/ml in active BD patients and 374.8±118.02 µg/ml in passive BD patients and 359.6±63.46 µg/ml in control subjects. There was no significant difference between passive BD and control group fetuin A levels(p=1.000). P/L ratio was significantly lower in active (p<0.001) and passive (p<0.001) BD patients than control group.

Conclusion: Our findings suggest that serum Fetuin A levels are lower in patients with active BD. Fetuin A might be used in following the disease activity.

**A-132**

Serum fetuin A levels and Hematological Parameters in Chronic Kidney Disease and Hemodialysis Patients for Assessing Inflammation

A. Erek Toprak¹, F. Gerin¹, H. Erman¹, I. Duran¹, E. Atalay², F. Korlaelci³, U. Ozturk⁴, ¹Istanbul Medeniyet University, Istanbul, Turkey, ²Bingol Government Hospital, Bingol, Turkey, ³Kafkas University, Kars, Turkey, ⁴Derince Training and Research Hospital, Kocaeli, Turkey

Background: Chronic kidney disease (CKD), includes conditions that destroy the kidney and causes loss of its functions. Fetuin-A, also known as α-2 herman schemid glycoprotein belongs to the cystatin super family, a cluster of cysteine protease
Clinical Studies/Outcomes, R. Doroudian, P. Roworth, C. Aznar, R. Alikhani

Tuesday, August 1, 9:30 am – 5:00 pm

Results: There were significant difference in serum Fetuin A concentrations, NRL and MPV values among three groups (p<0.001, p=0.001, p=0.001). The correlation analyses revealed that Fetuin-A negatively correlated with urea, creatinine, PTH, ferritin, and CRP concentrations (r=-0.349, -0.367, -0.295, -0.399, -0.550, respectively). p<0.05

Conclusion: Fetuin A is lower than control group in CKD and hemodialysis patients, remarkable as a negative acute phase reactant. NRL and MPV values are higher in CKD group compared with control subjects. Determination of serum fetuin-A, NRL and MPV might present useful information to assess inflammation in chronic kidney disease and hemodialysis patients.

A-133

External validation of lab data-based mortality risk scores in patients undergoing coronary catheterization

Y. Dong1, M. Gerlinger1, M. James1, S. Wilton2, M. Knudtson3, C. Naugler3, L. de Koning1. 1Calgary Laboratory Services, Calgary, AB, Canada. 2University of Calgary, Calgary, AB, Canada

Background: Risk scores based on results from simple laboratory tests such as the basic metabolic panel are being used more often in the acute care setting as they provide fast, reliable and accurate predictions of serious outcomes such as death and readmission. However few studies have evaluated the performance of these risk scores in different geographic locations. Our objective was to test the prognostic power of a laboratory data-based mortality risk score developed in Calgary, Alberta, Canada (population 1.4 million) in Edmonton - the second largest city in Alberta (population 1.3 million).

Methods: Age, sex, CO2, chloride, sodium, MCH, MCV, platelet count, potassium, sodium, RBC, RDW, ferritin, CRP, INR, provincial healthcare number and test verification date were extracted from the laboratory information systems of Calgary Laboratory Services and Alberta Health Services (November 2009-December 2015) 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 merged only the last test taken up to 30 days prior to catheterization. Lab variables were divided into quintiles and programmed as four dummy variables to allow non-linear relationships. Using Calgary as a 'development' sample, logistic regression with a group LASSO penalty was used to select a panel of tests that yielded the highest c-index (measure of discrimination between deaths and survivors) and best calibration (difference of predicted vs actual death probabilities) slope p-value (non-significant = better calibration of model) for <60-day post-catheterization mortality and >= 60 day post catheterization mortality. Validation in Edmonton was done by multiplying scoring coefficients developed in Calgary by Edmonton patient values, and re-calculating c-indices, calibration slopes and slope p values. Model re-calibration was done by multiplying a scaling factor by Calgary coefficients if c-indices and calibration slopes did not match. Risk scores for each population were created by multiplying patient lab values by regression coefficients and adding the products together, after which discrimination and calibration were recalculated. Results: In the Calgary development sample, there were 141595 patients among which there were 216 deaths < 60 days, and 941 deaths >=60 days available for analysis. Final models contained age, sex, CO2, Sodium, Chloride, ferritin, CRP, INR, and RDW. The c-indices, calibration slopes and slope p-values for each score were: < 60 days: c=0.85, slope=0.1, slope p=0.75; >= 60 days: c=0.80, slope=0.99, slope p=0.73 - indicating good discrimination and model calibration for deaths < or >= 60 days after catheterization. In the Edmonton validation sample, there were 12394 patients among which there were 347 deaths < 60 days and 1073 deaths >= 60 days available for analysis. The c-indices, calibration slopes and calibration slope p-value for scores based on re-calibrated coefficients were: < 60 days: c=0.82, slope=1.05, slope p=0.07; >= 60 days: c=0.80, slope=1.02, slope p=0.05 - indicating similar discrimination but slightly worse calibration. Conclusion: Lab-based risk scores developed to predict mortality performed similarly in two large urban centres in Alberta, Canada. Our long-term plan is to implement these scores in coronary catheterization labs across Alberta.

A-134

Frequency of Mutations in the Galactose-1-Phosphate Uridyl Transferase Gene in California: Findings from an eight year study

M. R. Kartippour, R. Doroudian, P. Roworth, C. Aznar, R. Alikhani

Koupaei. Genetic Disease Laboratory Branch, Richmond, CA

Background: The deficiency of galactose-1-phosphate uridyl transferase (GALT) which converts galactose-1-phosphate to uridine diphosphate galactose results in an inherited metabolic disorder: classic galactosemia. Common mutations/variants of this enzyme are well-identified: IVS2-2A-G, S135L, T138M, Q188R, L195P, L218L, K255N, and N314D. The California newborn screening program uses newborn’s dried blood spots to screen for GALT deficiency. Follow-up testing for presumptive positive cases uses a whole-blood specimen to identify common mutations in the GALT gene. Prior studies have reported a high frequency of some mutations, such as Q188R, in select populations. Other mutations have been described as more common in certain race/ethnic groups, including the IVS2-2 mutation, which has been reported as being more prevalent in Hispanic populations. Data from eight years of newborn screening in California, our aim was to describe the frequency of the most common GALT mutations in the racially and ethnically diverse California Population.

Design: The Newborn Screening Program, administered by the California Department of Public Health, screens for GALT deficient newborns as part of routine newborn screening. Each year, approximately half a million newborns are tested for GALT deficiency using the API 300 Analyzer using dried blood spot specimens. Presumptive positive cases are followed up by DNA testing using a well-defined single nucleotide extension method to identify common GALT gene mutations. We studied the frequencies of 7 mutations and 2 variants in newborns tested between July 2008 and June 2016.

Results: Out of nearly 4 million babies screened in California during the 8-year period, 247 GALT-deficient newborns had follow-up mutation analysis. The Q188R (66.40%) mutation and the variant N314D (66.40%) had the highest frequency in one or two alleles. This was followed by IVS2-2G (7.69%), S135L (6.88%), K255N (2.43%), L195P (2.02%), Y209C (0.81%), and L218L (0.4%). The T138M mutation was not detected in any newborns. The frequency of homozygosity was 6.07% for the Q188R mutation, 4.45% for the N314D variant, and 1.21% for the S135L. We also found a higher prevalence of the IVS2-2 mutation, known to be more common in Hispanic populations.

Conclusion: To the best of our knowledge this is the largest study to describe the frequency of GALT mutations in a racially and ethnicity diverse population. This is also the first study to use single nucleotide extension to study the IVS2-2 mutation. In concordance with other studies, the Q188R was the mutation with a very high prevalence; and similar to other studies with extremely low frequency for T138M mutation, none of the specimens were detected with this mutation. The low percentage of L218L is due to the GALT deficient population being tested. L218L variant increases GALT and we didn’t expect high frequency of this variant in our GALT deficient population. Some of our findings were similar to studies from Texas, another state with a high Hispanic population. This includes a higher prevalence of the N314D and IVS2-2 mutations. The frequency of the IVS2-2 mutation was even higher than the Texas study and may reflect more births to newborns with Hispanic origin in California.

A-135

Prevalence and laboratory characterization of monoclonal gammopathy of undetermined significance by physical examination in Beijing

J. Han, Y. Liang, X. Liang, J. Li, X. Cao, T. Xu, J. Wu, C. Jin, W. Ji, Q. Di, J. Zhang, W. Su. Peking Union Medical College Hospital, Beijing, China

Background: Monoclonal gammopathy of undetermined significance (MGUS) is a benign condition present in monoclonal plasma cell proliferation in the people aged more than 50 years old. No studies have far evaluated a large population of apparently healthy adults in ethnically Chinese population. To gain further understanding about the prevalence and laboratory characters of MGUS in China mainland, the current study was designed as a general analysis that know the related lab features in people who underwent physical examinations in Beijing with MGUS.

Results: In the Beijing study and may reflect more births to newborns with Hispanic origin in California.
Methods
A total of 44443 adult patients from the physical examination center were retrospectively enrolled in the study. The age range of these subjects was from 18 to 96 years old and the mean age was 42.44±12.62 years. Capillary serum protein electrophoresis (SPE) was carried out as main screening test on the subjects. Serum samples were identified to be monoclonal bands or suspicious monoclonal protein (M protein) were subjected to agarose gel immunofixation electrophoresis (IFE) to identify. Serum free light chain (sFLC) and β2 microglobulin were quantified to the samples which IFE results were positive.

Results
A total of 295 patients were diagnosed as MGUS according to the definition and suggestion of clinicians. The overall prevalence of MGUS was 0.66%. The prevalence was significantly higher in males than that in females (0.78% vs. 0.52% respectively, P=0.001, P=0.001). MGUS prevalence also significantly increased with age and it was 1.05%, 1.79%, 4.17%, 4.53% respectively in subjects older than 50, 60, and 70 and 80 years old. Immunofixation electrophoresis analysis (IFE) showed that IgG kappa (39.32%), IgG lambda (32.88%) and IgA lambda (12.54%) were the predominant monoclonal immunoglobulin pattern in these MGUS subjects. Double-type and lambda light chain pattern were simultaneously found in MGUS patients. The monoclonal immunoglobulin concentration was from 0.02 g/dL to 1.92 g/dL in the MGUS patients. The median concentration was 2.80 g/dL and 95% confidence interval was 3.49 g/dL to 4.50 g/dL. The serum free light chain (sFLC) x:λ ratio range was from 0.00075mg/L to 34.077mg/L. There were respectively 32 (11.03%) and 33 (11.38%) serum samples which showed sFLC x:λ ratio lower or higher than the reference range. We found 12 (4.17%) samples in MGUS were higher than 3.5 mg/dL and 4 (1.39%) samples were higher than 5.5 mg/L with the concentration of serum β2-microglobulin.

Conclusions
The overall prevalence of MGUS in China mainland was 0.66%. The prevalence was gender and age dependent. Some main lab characters of MGUS patients were evaluated in Chinese population.

A-136
Diagnosis value of different detecting technologies in antinuclear antibody (ANA) in autoimmune diseases
Y. Huang, W. Wang, K. Chen. Sun Yat-sen University affiliated Zhongshan hospital, Zhongshan, China

Background: Autoimmune diseases refer to immune reaction between the body antibody and its own antigen, which results in tissue damage. Antinuclear antibodies (ANA) play an important role in the diagnosis, treatment monitoring and prognosis judgement of autoimmune disease. Antinuclear antibodies (ANA) is an important screening index of autoimmune disease. But detection methods of ANA are varied. So our study is to investigate the positive rate and the coincidence rate between different methods, and our further research is to investigate the inconsistent phenomenon and the solutions, in order to provide more valuable reference information for clinical diagnosis, treatment monitoring and prognosis judgement in autoimmune diseases. Methods: We collected 61 cases of patients with systemic lupus erythematosus (SLE), 181 cases of patients with autoimmune diseases but without SLE, 476 cases of patients without immune diseases, 710 cases of volunteers for control group. ANA was detected by ELISA-ANA or IIF - ANA screening and LIA-ANA for various specific autoantibodies detection at the same time, and pay attention to multi-index joint detection when we diagnose autoimmune diseases.

Conclusion: Different detecting technologies in ANA have differences between sensitivity and specificity. If you use only one kind of methods, it is likely to cause the positive ANA result omission and AID missed diagnosis. Therefore, clinical application, especially in patients with clinically suspected AID, we should carry out ELISA-ANA or IIF - ANA screening and LIA-ANA for various specific autoantibodies detection at the same time, and pay attention to multi-index joint detection when we diagnose autoimmune diseases.

A-137

Background: Urinalysis is a routinely ordered test to screen for urinary tract infections and renal abnormalities. During a recent open tender process, we evaluated the UX-2000, an automated test strip and particle analysis urinalysis instrument, to supersede our existing UF-1000 analyser. A comparison of the common urine sediments between the two instruments was used to evaluate the UX-2000.

Methods: Fresh mid-stream urine was collected from 113 patients in a multi-disciplinary acute care hospital and promptly sent to the laboratory for examination. These samples were analysed on both analysers concurrently, using an established workflow. The principle of analysis for both instruments is based on fluorescence flow cytometry. The parameters for the evaluation included: Red blood cells(RBCs), White blood cells(WBCs), Epithelial cells(ECs) and Bacteria. Trueness, imprecision, clinical sensitivity and clinical specificity were determined.

Results: Trueness studies against the UF-1000 yielded a relationship of y=0.85x+4.36, r=0.993, P<0.001. The analytical sensitivities were 98.1%, 95.6%, 94.6% and 97.9% while analytical specificities were 97.9%, 96.4%, 88.9% and 90.6% at their cutoffs of >13 cells/ul, >10 cells/ul, >7 cells/ul and >20 cells/ul for RBCs, WBCs, ECs and Bacteria respectively. The imprecision study performed using low level quality control material yielded a Coefficient of Variation of 5.4%, 7.9%, 2.6% and 9.4% for RBCs, WBCs, ECs and Bacteria respectively. Additionally, the imprecision study using high level quality control material yielded a Coefficient of Variation of 2.6%, 1.3%, 4.0% and 4.8% for RBCs, WBCs, ECs and Bacteria respectively. These values fall within the manufacturer’s recommendations of 10% for RBCs and WBCs, 30% for ECs and 20% for Bacteria.

Conclusion: Our study showed that the UX-2000 had an acceptable performance and is a suitable replacement for our current analyser, the UF-1000. We found good correlation between the two analysers for the automated quantification of RBCs, WBCs, ECs and Bacteria. In addition, the UX-2000 analyser’s built-in automated Dipstick analyser allows for lesser hands-on time which, which translates to increased productivity.

A-138
Development and evaluation of a serum biomarker panel in diagnosis of lung cancer
Q. Du1, H. Wang2, W. Zhang3, A. Beshiri1, A. Soh1, Y. Zheng4. 1Department of Pulmonary Medicine, Da lian Medical University 2nd Hospital, Da lian, China, 2Department of Pulmonary Medicine, Da lian Medical University 2nd Hospital, Da lian, China, 3Department of Mathematics & Statistics, University of Arkansas at Little Rock, AR, AK, 4Medical Scientific Affairs, Diagnostics Division,Abbott Laboratories, Chicago, IL, 5Medical Scientific Affairs, Diagnostics Division,Abbott Laboratories, Singapore, Singapore, 6Medical Scientific Affairs, Diagnostics Division,Abbott Laboratories, Shanghai, China

Background: Lung cancer is the most common cancer and leading cause of cancer-related deaths worldwide. With the progress of tumor stage, the prognosis was significantly worse. Thus, early diagnosis of lung cancer is important to improve patient survivals. Blood-based biomarkers are easily accessible measurements that define high-risk patients and enhance diagnostic capabilities. Although published data on individual
serum biomarkers for lung cancer have shown limited sensitivity and specificity, the combination of several biomarkers could improve the detection of early-stage lung cancer. Thus, the present study is to investigate the clinical diagnosis model for lung cancer diagnosis.

**Methods**

A total of 230 lung cancer patients (cancer group) and 80 subjects with benign lung tumors (control group), were recruited from Da’Lian Medical University 2nd Hospital in China. The study received ethical approval from the site.

**Results**

We examined the diagnostic value of CEA, SCC, CYFR211, ProGRP and HE4 individually or in combination for lung cancer using ROC curve analysis. The optimal cut-off value of each biomarker was obtained to yield the maximum Youden index. Compared with control, AUC of individual biomarker CEA, SCC, CY211, ProGRP and HE4 exhibited from 0.648 to 0.857. To increase the diagnostic value, these five biomarkers were combined and equation model was set up. The equation was P = 0.121*CEA + 0.568*SCC + 0.513*CY211 + 0.011*ProGRP + 0.036*HE - 3.972, with cut-off of 0.729. AUC in biomarker combination increased to 0.907 with sensitivity of 70.6% and specificity of 94.90%. According to sub-type analysis, biomarker panel combination showed better performance in SCC(Squamous carcinoma) and SCLC(Small cell lung cancer) compared with AD(Adenocarcinoma).

**Conclusions**

This study established a biomarker combination model for lung cancer diagnosis with significant clinical performance.
on patient management, by comparing physician responses to a questionnaire pre- and post-phi testing. The impact on decision to biopsy and proportion of negative biopsy results obtained was also evaluated.

Methods
An IRB approved observational study was conducted at four large urology group practices using a two-part questionnaire completed by the urologist. Patient recommendations were recorded before and after the phi score. A historical control group was queried from electronic medical records for eligible patients who did not receive a phi test. 502 men were prospectively, consecutively enrolled, and 575 additional men were included in the control arm, after exclusions. Subjects had PSA concentrations between 4-10 ng/mL, were ≥50 years of age, had a non-suspicious DRE, no prior suspicious or positive prostate biopsy, and were referred for biopsy based on elevated PSA. The PSA, free PSA, and [-2]proPSA concentrations were determined using the Beckman Coulter Access 2 Immunoassay Analyzer. phi was calculated as ([-2]proPSA/free PSA) x PSA½.

Results
The phi score impacted physician decisions in about 74% of cases (Figure 1), including performing biopsies when the phi score was elevated and identifying biopsies that may have been unnecessary or that could be delayed. In instances where the biopsy decision was unchanged, questionnaire responses showed phi helped confirm decisions and made discussions with patients easier.

<table>
<thead>
<tr>
<th>phi score group</th>
<th>Did phi score impact physician decision to Biopsy or Monitor patient?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-26.9 N (%)</td>
<td>Y es, phi score impacted physician’s decision</td>
</tr>
<tr>
<td>27.0-35.9 N (%)</td>
<td>No, phi score did not impact physician’s decision</td>
</tr>
<tr>
<td>36.0-54.9 N (%)</td>
<td>Total</td>
</tr>
<tr>
<td>55+ N (%)</td>
<td>Percent of Total</td>
</tr>
</tbody>
</table>

Conclusions
Results demonstrate that phi positively impacts patient care. The biopsy rate was significantly lower, and the percentage of GS ≥ 7 was significantly higher, post-phi testing versus controls, demonstrating a reduction in unnecessary biopsies and a selective shift toward identifying clinically significant PCa.

A-142
Serum Oxidative and Antioxidative Parameters in Obstructive Sleep Apne Syndrome Patients


Background: The purpose of this study was to evaluate markers of systemic oxidative stress and antioxidant capacity in subjects with severity of OSAS.

Methods: A total of 106 OSA patients were included in the study (18 controls, 14 with mild, 14 with moderate, and 60 with severe OSA). Patients were grouped according to apneahypopnea index (AHI) as mild, moderate and severe OSA. Patients with AHI<5 served as control group. Known risk factors for oxidative stress, such as age, sex, obesity, smoking, hyperlipidemia, and hypertension, were investigated as possible confounding factors. Plasma arylesterase, total oxidative stress (TOS), total antioxidant capacity (TAC), total thiol, catalase (CAT) levels were measured for all patients.

Results: The mean age was 52.49 ±12.9 years and 40.6 % (43/106) of the study population was female. Plasma arylesterase, TOS, TAC, total thiol, and CAT plasma values were not different between mild, moderate, severe OSA groups and controls (p > 0.05). Catalase levels were significantly lower in women patients with severe OSA compared to healthy women controls (p < 0.05). There was a negative correlation between AHI and serum total thiol levels (r = -0.289; p<0.05) in severe OSA groups.

Conclusion: The present prospective study provides evidence that OSA might be associated with decreased antioxidant burden possibly via catalase way.

A-143
Where we Stand on Omission of Biopsy for a Diagnosis of Celiac Disease

S. Jamshed, M. R. Al-Turkmani, L. V. Rao. University of Massachusetts Medical School, Department of Pathology, Worcester, MA

Background:
Duodenal biopsy has remained the gold standard for a Celiac disease (CD) diagnosis for decades. However, improved diagnostic accuracy of serological testing and potential risks associated with endoscopy in children has allowed omission of biopsy to become the standard of care in Europe under the 2012 ESPGHAN Guidelines. The diagnostic algorithm allows symptomatic children with screening tissue transglutaminase IgA (tTG-IgA) titer more than 10x upper limit of normal to undergo EMA and HLA testing. To date, this is the first widely accepted alternative to biopsy. Our aim is to retrospectively examine the performance of tTG-IgA at our institution to assess the feasibility of shifting towards a non-invasive diagnosis for CD in a specific pediatric population in the United States.

Methods:
Consecutive tTG-IgA serology was obtained on children aged 2 to 18 years from November 2015 to October 2016. Serology was performed using an immunoassay on QUANTA-Lite® tTG-IgA from INOVA Diagnostics and positive results reported when ≥4 U/ml. Patients with IgA deficiency and lab results/biopsy from outside institutions were excluded. Biopsy findings were graded according to Marsh-Oberhuber classification.

Results:
Total tTG-IgA serology performed yielded 2723 results. The distribution and characteristics of patients are summarized in Table 1. The sensitivity, specificity and PPV of tTG-IgA is 86.7%, 99.4% and 84.7%, respectively. According to 2012 ESPGHAN guidelines, duodenal biopsy may have been omitted in 38% of patients depending on EMA and HLA status.

Conclusion:
We report high sensitivity and specificity of tTG-IgA at our institution, and is comparable to the literature. These results strengthen the notion that this simple screening test, when paired with appropriate symptomatology, can reliably identify a select population in whom EMA and HLA may be warranted, and biopsy omitted. In order to initiate a non-invasive transition, more emphasis is necessary on helping clinicians better understand the performance of celiac serology testing.

Table 1.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tTG-IgA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>78</td>
<td>52 - Titer &gt;10x ULN (67%)</td>
</tr>
<tr>
<td>Negative</td>
<td>12</td>
<td>5 - Titer &gt;10x ULN (30%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

S41
**Clinical Studies/Outcomes**

**A-144**

**Comparison of Active B12 with Total B12 and Methylmalonic Acid in patients with cognitive impairment**

J. Boyd1, Z. Ismail1, A. Chin1, C. Naugler1, H. Sadrazadeh1. 1Calgary Laboratory Services, Calgary, AB, Canada, 2University of Calgary, Calgary, AB, Canada

**Background:** Patients with vitamin B12 deficiency are at risk for developing neurological abnormalities and methylmalonic academia. Although serum methylmalonic acid (MMA) can be used to confirm B12 deficiency, this test is not readily available in most laboratories. Instead, total B12 measurement are used as a surrogate, although it does not correlate well with MMA. Active B12 assays, which only measure B12 bound to transcobalamin, have been suggested to be a better marker of B12 deficiency than total B12. In this study, we evaluated the performance of active B12 compared to total B12, MMA and neurological evaluation.

**Methods:** This study was approved by our institutional ethics committee and patients were recruited at neurology clinics. Once consent was obtained, patients received neurological evaluation as per standard of care. Patients also had blood drawn for total B12, active B12 and MMA testing. Total B12 was measured using a Roche Cobas e601 platform. Active B12 was measured using Abbott Active B12 reagent on an Abbott Architect. MMA was measured by LC-MS/MS. Results: To date, 62 patients have been recruited into the study. These patients are a mixture of those with normal cognition, cognitive impairment and dementia. Preliminary results showed total B12 correlated well with active B12 (r=0.4254, 49.94; R2=0.6642). However, total B12 and MMA as well as Active B12 and MMA showed poor correlation. This relationship was maintained when only samples with MMA greater than 250 pmol/L were included. Data from neurological assessments of each patient is being collated and will be presented at the meeting.

**Conclusion:** Our preliminary results showed that B12 deficiency can be assessed by either active B12 or total B12. However, active B12 may not be a suitable surrogate for MMA analysis. Clinical information will be correlated with biochemical analysis and the results will be present completely in July.

**A-145**

**Genetic Risk Prediction for Developing Age-related Macular Degeneration and Disease Progression**

K. Gawlik, J. Lopez, S. Chang, R. Vairavan, F. Kureshy. AutoGenomics Inc., Carlsbad, CA

**Purpose:** Age-related macular degeneration (AMD) remains the leading cause of irreversible visual loss among the elderly in developed countries. The earlier asymptomatic form of AMD is characterized by the formation of confluent drusen in the macula, while advanced AMD includes geographic atrophy (GA) and choroidal neovascularization (CNV). It is likely that the management of patients with AMD will be influenced by assessment of genetic risk. The aim of this study was to develop a separate class prediction algorithm for AMD lifetime risk assessment and disease progression from intermediate AMD to either GA or CNV based on individual genetic profiles.

**Methods:** DNA samples were genotyped using the AutoGenomics INFINITI platform. AMD panel (for research use only) included ABCA1(rs1883025); APOE(rs429358, rs7412); ARMS2(rs10490924); C3(rs2230199); CCDC109B(rs17440077); CETFTR(rs3764261); CFTR(rs515669); FUT1(rs1048663, rs1061170, rs10737680, rs1329428, rs2274700, rs3766405, rs412852); CFTR(rs10033900); COLRA1(rs31059226); HTRA1(rs112006038); LIPC(rs493258, rs10468017); LPL(rs12678919); TIMP3(rs9621532) and VEGFA(rs3025000, rs943080). Class prediction model building and testing were performed using TreeNet software (Salford Systems, San Diego, CA). The binary logistic regression analysis with a 10-fold cross-validation method was applied in the algorithm development.

**Results:** We genotyped the selected 25 SNPs in 893 cases with advanced AMD (consisted of 206 GA and 687 CNV), 265 cases with intermediate AMD and 384 controls. Progression was defined as transition from intermediate to advanced AMD, either GA or CNV, in the worse eye during a follow up visit. We selected only patients with intermediate AMD who did not progress within 7 years to advanced stages and considered them as non-progressors. For model building we applied a ‘shaving’ technique, in which the predictors are ranked from top to bottom (the most important to the least important) at every step when the bottom predictor is removed and the model is rebuilt. This technique allowed us to choose three distinct models with the best performance and further evaluate. As a result, we developed three class prediction algorithms: 1) for AMD lifetime risk assessment in AMD patients versus controls based on 13 SNPs; 2) for progression to GA in GA progressors versus non-progressors based on 9 SNPs; 3) for progression to CNV in CNV progressors versus non-progressors based on 10 SNPs. The ROC of the model for AMD risk for the test set was 0.75 with 70% sensitivity and 68% specificity. The ROC of the model for progression to GA for the test set was 0.63 with 53% sensitivity and 72% specificity. The ROC of the model for progression to CNV for the test set was 0.55 with 55% sensitivity and 52% specificity.

**Conclusions:** Our results suggest that the INFINTI AMD panel can be successfully used for the AMD lifetime risk assessment as well as disease progression. In addition, risk of developing AMD and disease progression can be further improved when the panel is combined with environmental factors such as age, smoking and other variables. The proposed approach to AMD risk determination, separate for lifetime risk and disease progression, might provide a useful clinical tool and be potentially applied toward more personalized care.

**A-146**

**HE4 as a diagnostic and follow-up biomarker in non-small cell lung cancer**

U. Kumbasar1, Z. G. Dikmen1, Y. Yilmaz1, B. Ancın1, E. Dikmen1, R. Dogan1. 1Hacettepe University Medical Faculty Department of Thoracic Surgery, Ankara, Turkey, 2Hacettepe University Medical Faculty Department of Medical Biochemistry, Ankara, Turkey, 3Hacettepe University Medical Faculty Department of Thoracic Surgery, Ankara, Turkey

**Abstract**

**Background:** Early detection of non-small cell lung cancer (NSCLC) cases is crucial since nearly one third of them are unresectable during diagnosis and also the recurrence rates are high following treatment. Human epidymis protein 4 (HE4) is predominantly expressed in a variety of normal human tissues including epidymis, epithelial cells of proximal airways and the female genital tract. HE4 has emerged as one of the most promising diagnostic and prognostic biomarker in epithelial ovarian cancer. High levels of HE4 have also been detected in lung, breast and pancreas cancers. Thus, in this study we aimed to evaluate both the diagnostic performance and the post-resection progress of serum HE4 in patients with NSCLC.

**Methods**

Thirty-one patients who had benign lung disease (group 1) were compared with the same number of patients with resectable NSCLC (group 2). Blood samples were collected in serum separator tubes and were centrifuged at 1500g for 10 minutes (Rotanta 460). HE4 levels were measured by chemiluminescent microparticle immunoassay at ARCHITECT 2000SR immunassay analyzer (Abbott Diagnostics) at the time of diagnosis and following surgery - at post-operative 1st month. The cut-off limit for serum HE4 was considered 70 pmol/L.

**Results**

The serum HE4 in NSCLC group [median: 89.70 (58.10-397.00)] pmol/L was significantly higher than the benign group [median: 42.60 (28.10-198.90)] pmol/L, respectively (p<0.001). HE4 levels in NSCLC group significantly decreased from 89.70 (58.10-397.00) pmol/L to 71.50 (41.70-232.30) pmol/L following pulmonary resection (p<0.001). In advanced stages (stage III and IV) the decrease in serum HE4 levels [25.30 (10.50-164.70)] pmol/L was significant than the decrease in early stages (stage I-II, [14.60 (14.20-133.60)] pmol/L (p<0.025). According to ROC analysis, the area under the curve (AUC) of HE4 was 0.921 (95%CI, 0.843-0.998), (p<0.001). Both the sensitivity and specificity of HE4 as a biomarker was found 87.1%.

**Conclusion**

Our data demonstrated that HE4 is a potential biomarker for the diagnosis of NSCLC with high sensitivity and specificity. We believe that HE4 levels could also be used to monitor NSCLC recurrences and treatment response during follow-up.
Serum Growth Arrest Specific Protein 6 (Gas-6) Levels in Patients with Schizophrenia

F. Gerin1, A. Erek Toprak1, H. Erman1, S. Duruyen1, A. Bas2. 1Istanbul Medeniyet University, Istanbul, Turkey; 2Istanbul University Cerrahpasa Medical School, Istanbul, Turkey

Background: We have investigated serum growth arrest-specific protein 6 (Gas-6) levels from patients with schizophrenia divided into acute phase remission phases as well as control group.

Methods: This study was conducted in Psychiatry Department of Istanbul University Cerrahpasa Medical Faculty. The patients who were diagnosed with schizophrenia after regular psychiatric examination according to DSM-IV criteria (n=22) as well as control subjects were included in the study. Schizophrenia patients with acute phase and remission phase were evaluated by Positive and Negative Syndrome Scale (PANSS) and Clinical global Impression Scale (CGI-S). The serum GAS-6 levels of schizophrenia patients during acute phase and remission phase were compared with the serum GAS-6 levels of healthy controls. Serum GAS-6 levels were measured by commercial ELISA development kit (R&D).

Results: No difference was found in serum GAS-6 levels among the three groups; schizophrenia with acute phase, schizophrenia with remission phase, and controls. There were no correlations between serum GAS-6 levels and PANSS and CGI scores.

Conclusion: To reach a definitive data and better interpretation about the relationship between GAS-6 and schizophrenia, future studies with larger groups of patients with schizophrenia subdivided by drug naïve and treated with antipsychotics/other treatment modalities and controls are needed.

Risk assessment of opioid addiction with a multi-variant genetic panel involved in the dopamine pathway

S. Chang1, R. Hudspeth1, R. Vairavan1, F. Tennant2. 1AutoGenomics Inc, Carlsbad, CA, 2Heract Intractable Pain Clinic, West Covina, CA

Background: More than 116 million people worldwide are struggling with chronic pain and most require prescription drugs. In the US, opioid prescription misuse and heroin use has accounted for the majority of accidental overdose deaths in 2014. Genetic factors play a key role in opioid prescription addiction, but are generally not evaluated in clinical practice. Currently, there is no objective way for practitioners to identify pain patients in medical management who are at risk to abuse or become addicted to prescribed medication or to identify those pain patients who will require high dosages or an unusual regimen of medication. The purpose of this study is to assess a risk of developing prescription opioid addiction with a multi-variant addiction panel involved in the mesolimbic dopamine system.

Methods: We genotyped samples for 16 single nucleotide polymorphisms (SNPs) involved in the brain reward pathways from 70 patients diagnosed with prescription opioid/heroin addiction and 68 normal control patients with a multiplexed film-based microarray technology. The addiction panel targets 16 mutations: 5-HTTR2A (rs7997012), 5-HTTLPR (rs2553131), COMT (rs4680), DRD2 (rs1800497), DRD1 (rs4552), DRD4 (rs3578653), DAT1 (rs6347), DBH (rs1611115), MTHFR (rs1801133), OPRK1 (rs1051660), GABRA1 (rs211014), OPRM1 (rs7999717), MUOR (rs979757), GAL (rs948584), DOR (rs2236861) and ATP-BCT (rs1045642).

Serum Gas 6 and Omentin Levels and relationship with Flow mediated dilatation, Aortic distensibility, Left ventricle mass index and disease severity in Patients with Psoriasis


Background: Growth arrest-specific gene 6 (GAS6) encodes a vitamin K-dependent protein secreted by endothelial cells, vascular smooth muscle cells, and adipocytes that regulates inflammation, insulin resistance, angiogenesis, and atherosclerotic plaque formation. The level of GAS6 expression is associated with plaque stability and stroke. Changing in aortic distensibility (AoD) may reflect the features of the atherosclerotic process. Omentin, a novel adipokine secreted by the stromal vascular cells of adipose tissue, is considered associated with vascular, metabolic, and various chronic inflammatory diseases. Psoriasis is an autoimmune, inflammatory and chronic disease. This study aimed to determine the association between serum Gas6 and omentin levels with BMI, insulin resistance, flow mediated dilatation, Aortic distensibility and Left ventricle mass index in Patients with Psoriasis.

Methods: The study was conducted on 30 healthy subjects (mean age: 41 ± 10 years) who were free of coronary risk factors and 52 patients with psoriasis(mean age: 41 ± 10 years). Body mass index were calculated. Circulating glucose, cholesterol, insulin, HbA1C, CRP, Gas6 and omentin levels analysed and insulin resistance were determined. Gas6 and omentin were analysed with ELISA method with commercially available kits (Biovendor, Czech Republic). Transhoracic echocardiography was used to measure the Beta index, aortic distensibility (AoD), left ventricular mass index. Flow mediated dilatation was measured with high resolution B mode ultrasound machine (Toshiba, apio XU) with a 7.5 MHz linear transducer.

Results: Patients and control group were similar about age, body mass index, waist circumference and sex distribution. Insulin resistance (HOMA-IR) was high significantly in psoriasis patients. Levels of serum Gas6 levels were significantly higher (p<0.001) in patients group whereas omentin were significantly lower (p<0.001). Aort distensibility and beta index were low in patients group (p=0.01 and p=0.02 respectively). Also serum Gas6 levels were positive and significantly correlated with HOMA-IR (p=0.026, r=0.283) and left ventricle mass index (p=0.01, r=0.689). In addition, serum omentin levels were positive and significantly correlated with waist circumference (p=0.01, r=0.600). Disease severity/PSI psoriasis area and severity index) was not correlated with any parameter in the study.

Conclusion: Circulating Gas6 and omentin levels and aort distensibility and beta index are significantly different in two groups. Serum Gas 6 levels are strongly correlated with insulin resistance status and left ventricle function status. Gas 6 may play a role assessing insulin resistance and left ventricle function status in patients with psoriasis.

Performance Evaluation of the VITROS® Nephrocheck® Test*

G. Osbourn, S. Jackson, S. Clark, J. Parsells, S. Phonetosophswat. Ortho Clinical Diagnostics, Rochester, NY

Acute kidney injury (AKI) is a complex disorder with a high mortality due to comorbidities and management challenges, especially in the critically ill patient. The VITROS® NephroCHECK Test quantitatively measures Tissue Inhibitor of Metalloproteinase 2 (TIMP-2) and Insulin-like Growth Factor Binding Protein 7 (IGFBP-7) to generate an AKI risk index (AKIRISK® Score). Patients with an AKIRISK® Score less than 0.30 are at low risk of developing moderate to severe AKI within 12 hours of assessment while those with values ≥ 0.30 are at increased risk. We have evaluated the performance of the VITROS NephroCHECK Test on the VITROS 3600 Immunodiagnostic System and the VITROS 5600 Integrated System. The test is linear across the range of 0.4 to 29.7 ng/mL for TIMP-2; and 5.6 to 463.0 ng/mL for IGFBP-7 resulting in an AKIRISK® Score range of 0.002 to 13.8. Limits of Blank were determined to be 0.164 ng/mL and 0.456 ng/mL for TIMP-2 and IGFBP-7, respectively. Limits of Quantitation were determined to be 0.392 ng/mL for TIMP-2 and 1.393 ng/mL for IGFBP-7 respectively, resulting in an AKIRISK Score of 0.002. A 20-day precision study with pooled patient samples at mean AKIRISK Scores of 0.10, 0.32, 0.38, 2.24, 3.46, 6.72, and 8.16 resulted in within-laboratory percent coefficients of variation (%CV) of 10.9%, 10.6%, 12.3%, 11.3%, 8.7%, 6.9% and 6.9% respectively on the VITROS 3600 Immunodiagnostic System. Similar results were obtained from the VITROS 5600 Integrated System. Potential endogenous interfering substances likely to be present in urine including acetocetate, acetone, ammonia, albumin, creatinine, hemoglobin, myoglobin, urea and uric acid were tested and shown not to interfere in the assay. The accuracy of the test was evaluated with 145 patient specimens spanning the assay measuring range.
Alkaline phosphatase reference interval in children and adolescents in Brazil

P. Araujo¹, E. Mello Ribeiro², L. Vieira Neto³, M. Miguens Castelar Pinheiro⁴, Y. Schrank⁵, D. Valente Gomes⁶, M. Freire⁷, R. Fontes⁸, DASA, RJ, Brazil, Rio de Janeiro, Brazil, ¹UFU, RJ, Brazil, Rio de Janeiro, Brazil

Background: The interpretation of laboratory tests requires reference intervals (RI) that may vary between different populations. For the diagnosis of hypophosphatasia, disease presenting with low serum alkaline phosphatase (ALP), lower limits of RI must be well determined. Since the ALP methodology in practice in our clinical laboratory does not provide lower reference levels for children and adolescents, our aim was to validate lower limits through CALIPER findings, adjusted to the Brazilian population.

Methods: Serum specimens of 1950 children, from 1 to 18 years old, reporting ALP measurement, between April 2015 and March 2016, were retrospectively assessed. The same subgroups proposed by CALIPER study and the Clinical and Laboratory Standards Institute (CLSI) guideline have been used to validate obtained results. ALP was measured by the Roche/Hitachi platform Cobas. Inclusion criteria were patients with normal results for liver function, bone metabolism, kidney function, and blood counts. Exclusion criteria were hospitalization, low weight, use of drugs that could interfere in the ALP measurement, and patients in which ALP dosing was requested more than 3 times. The percentage of girls and boys excluded were 13.9% and 12.8%, respectively, therefore 1690 patients were selected. Data normal distribution was analyzed with Kolmogorov-Smirnov test. Outlying observations were calculated using Dixon test. RI was defined as 2.5-97.5%. The RI obtained in this study was analyzed with Kolmogorov-Smirnov test. Outlying observations were calculated using Dixon test. RI was defined as 2.5-97.5%. The RI obtained in this study was analyzed with Kolmogorov-Smirnov test. Outlying observations were calculated using Dixon test. RI was defined as 2.5-97.5%.

Results: The obtained RIs results and 90% confidence interval (CI) of ALP are shown in Table 1.

Conclusion: According to CLSI, the results of this study have been enabled for use as ALP RI when compared to CALIPER study, for the Brazilian children and adolescents' population.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Gen- der group</th>
<th>Total number of patients (n)</th>
<th>Patients excluded (n/%)</th>
<th>ALP RI (U/L)</th>
<th>ALP CI</th>
<th>Outsiders (n/%)</th>
<th>CALIPER RI (U/L)</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-9</td>
<td>Both</td>
<td>322</td>
<td>32/11.3</td>
<td>149-301</td>
<td>134-319</td>
<td>24/7.45</td>
<td>135-320</td>
<td>+10.0-6.0</td>
</tr>
<tr>
<td>10-12</td>
<td>Both</td>
<td>232</td>
<td>24/11.5</td>
<td>127-326</td>
<td>122-401</td>
<td>19/8.1</td>
<td>122-400</td>
<td>+4.0-18.5</td>
</tr>
<tr>
<td>13-14</td>
<td>Boys</td>
<td>197</td>
<td>12/6.0</td>
<td>129-437</td>
<td>101-454</td>
<td>18/9.1</td>
<td>109-449</td>
<td>+18.3-12.7</td>
</tr>
<tr>
<td>15-16</td>
<td>Girls</td>
<td>248</td>
<td>33/13.3</td>
<td>52-120</td>
<td>45-122</td>
<td>24/9.6</td>
<td>46-110</td>
<td>-11.5+90.1</td>
</tr>
<tr>
<td>15-16</td>
<td>Boys</td>
<td>250</td>
<td>39/15.6</td>
<td>78-268</td>
<td>62-334</td>
<td>9/3.6</td>
<td>77-317</td>
<td>+1.3-15.4</td>
</tr>
<tr>
<td>17-18</td>
<td>Girls</td>
<td>252</td>
<td>43/17</td>
<td>45-97</td>
<td>40-99</td>
<td>25/9.9</td>
<td>41-82</td>
<td>+9.7+18.2</td>
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<tr>
<td>17-18</td>
<td>Boys</td>
<td>250</td>
<td>43/17.2</td>
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<td>38-141</td>
<td>16/6.4</td>
<td>50-142</td>
<td>-9.1-9.1</td>
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</tbody>
</table>

Legend: ALP: alkaline phosphatase; Patients selected: Total number of patients minus patients excluded; ALP RI: Reference interval for ALP determined in this study; CI: 90% confidence interval; Outsiders: number of subjects tested in the present study that fell out 10% above or below the original reported limits; RI: reference interval; * Percent difference to plus (+) or minus (-) the results obtained in this study compared to CALIPER study. The first percentage refers to the inferior reference value difference and the second value refers to superior reference value difference; CALIPER: Canadian Laboratory Initiative in Pediatric Reference Intervals.