

Tuesday, July 31, 2018

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

Clinical Studies/Outcomes

A-114

Determination of bioenergetic defects in mitochondrial disease patients using extracellular flux analysisB. K. Chacko, G. Benavides, A. Hurst, D. Leon, E. Ubogu, R. Hardy, V. Darley-USmar. *University of Alabama at Birmingham, Birmingham, AL*

Background: Mitochondria control cellular homeostasis through maintaining proper bioenergetic programs. Defects in mitochondrial function arising from mutations in mitochondrial or nuclear genome, (mitochondrial diseases), can be presented with a wide spectrum of neurological, muscular and cardiac symptoms. The multi-system involvement and the heterogeneous features of these defects mimic neurological and systemic diseases that make diagnosis often challenging. The influence of genetic, environmental, lifestyle factors and age on mitochondrial activity further complicate the diagnosis. Use of invasive muscle biopsies provide only limited information and genomic analysis will not assess mitochondrial function. In this study we report the development and validation of a panel of minimally invasive mitochondrial assays that can assist diagnosis of mitochondrial diseases. **Methods:** This test utilizes the concept that circulating leukocytes and platelets can act as sensors or biomarkers of bioenergetic dysfunction that occurs in mitochondrial diseases. Monocytes, lymphocytes and platelets were isolated from healthy subjects and mitochondrial diseases patients using a protocol involving density gradient centrifugation and magnetic bead-based purification (MACS technology). Using the extracellular flux analyzer the oxygen consumption rates of mitochondria in intact monocytes and platelets are measured employing two different protocols (1) the mitochondrial stress test and (2) mitochondrial respiratory complex activities. The mitochondrial stress test will determine the bioenergetic parameters in intact cells (basal, ATP-linked, proton-leak, maximal, reserve capacity and non-mitochondrial respiration) which will be used to calculate the health of the mitochondria termed as the bioenergetic health index (BHI). For mitochondrial complex activity the plasma membrane is selectively permeabilized without altering the mitochondrial membrane and the maximal activity of mitochondrial respiratory enzyme complexes (Complex I, Complex II and Complex IV) are determined in the presence of specific metabolic substrates. **Results:** The results show that there is significant loss of specific mitochondrial complexes (Complex I, Complex II or Complex IV) exist in mitochondrial disease patients. The cellular bioenergetic parameters were also showed significant decrease in mitochondrial disease patients. The bioenergetic and mitochondrial profiles demonstrate a high degree of heterogeneity in specific defects among mitochondrial disease patients. **Conclusion:** This suggests that the mitochondrial assays have the potential to determine bioenergetic defects in mitochondrial diseases.

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Traumatic Brain Injury: Combining GFAP and UCH1-L1 Serum Biomarkers Predicts Head CT OutcomesR. H. Christenson¹, L. Ferland², N. B. Quigley³. ¹*University of Maryland School of Medicine, Baltimore, MD*, ²*ResearchDx, Orange County, CA*, ³*Geneuity Clinical Research Services, Maryville, TN*

Background: Traumatic Brain Injury (TBI) is caused by external force to the brain resulting in impaired cognitive and/or physical function. TBI causes ~3 million emergency department visits, hospitalizations, or deaths annually in USA. The standard of care for suspected TBI is neurological assessment followed by neuroimaging of the head by Computerized Tomography (CT), and exposure to substantial ionizing radiation. A blood test for TBI may reduce need for CT and would be very useful in military, sports, and traumatic injury applications. A test, coined Brain Trauma Indicator™ (BTI; Banyan Biomarkers), measures two brain-specific proteins, ubiquitin C-terminal hydrolase-L1 (UCH-L1) and glial fibrillary acidic protein (GFAP), which are rapidly released into the bloodstream in TBI. We characterized the measurement and clinical performance of UCH-L1 and GFAP testing by BTI in suspected TBI patients. **Methods:** Testing was performed at 3 sites. UCH-L1 and GFAP were assayed by chemiluminescent ELISA using the BTI. Lower and upper limits of quantitation were 80pg/mL and 2560pg/mL for UCH-L1, and 10pg/mL and 320pg/mL for GFAP. Cut-

offs are used for interpretation. Cutoffs (%CV) for UCH-L1 and GFAP were 327pg/mL (6.2%) and 22pg/mL (4.9%), respectively. If either or both biomarker(s) were above-cutoff, the result was Positive; if both results were below-cutoff, the result was Negative. Samples with Invalid or No Result measurements were re-tested so results for all subjects were reported. The BTI test was examined as a rule-out, so cutoffs were set to maximize sensitivity and Negative Predictive Value (NPV). The Figure shows Clinical Performance compared to CT. **Conclusions:** The BTI test's sensitivity was 97.5% in suspected TBI subjects; of the negative BTI results, very few were false negatives (NPV=99.6%). The high sensitivity and NPV support the clinical utility in an Emergency Department setting of the BTI to rule out the need for CT in subjects with suspected TBI.

Performance Characteristics, 6.2% Prevalence of CT ^a positive		
Sensitivity	97.5%	95% CI ^b : 92.9-99.5%
NPV^c	99.6%	95% CI: 98.7-99.9%
LR^d Negative	0.069	95% CL ^e : 0.170
Specificity	36.5%	95% CI: 34.2-38.7%
PPV^f	9.2%	95% CI: 7.6-10.9%
LR Positive	1.534	95% CL: 1.468

^aCT = computed tomography scan; ^bCI = confidence interval; ^cNegative Predictive Value; ^dLikelihood Ratio; ^eCL=confidence limit; ^fPositive Predictive Value

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Reference intervals for liver specific clinical chemistry parameters in apparently healthy nepalese adult population.R. V. MAHATO¹, M. Lamsal², K. Ichihara³. ¹*Tribhuvan University, Institute of Medicine, Kathmandu, Nepal*, ²*BP Koirala Institute of Health Science, Dharan, Nepal*, ³*Yamaguchi University Graduate School of Medicine, Ube, Japan*

Background: The reference interval (RI) is important for the screening, diagnosis, treatment, and monitoring of common disorders like liver diseases. During the last decades, the number of routine clinical chemistry tests has increased dramatically in Nepal. However, there are no valid RIs for any biochemical parameter in Nepal. RIs currently in use are those supplied by reagent manufacturers which are not derived from local population. Therefore, we conducted this study of establishing RIs of 25 major biochemistry parameters for Nepalese population, as a part of the IFCC global multicenter study on RVs. In this report, results of 7 parameters belonging to liver function tests are described. **Methods:** A total 617 apparently healthy individuals were recruited nationwide from five different regions of the country. Blood samples were collected and sera were separated and stored at -80°C. All the samples were measured collectively by auto-analyzer AU480 (Beckman-Coulter). Test results were standardized by measuring the value-assigned panel of sera which was provided by IFCC committee on Reference Intervals and Decision Limits (C-RIDL). With application of the latent abnormal values exclusion (LAVE) method, reference intervals (RIs) were derived by both parametric and non-parametric method by use of Reference Master software provided by C-RIDL. **Results:** The reference intervals (lower limit-upper limit) derived for [MF] males[M] and females [F], were total protein MF (67-82),M:(67-81),F:(66-82) gm/L albumin MF:(41-52),M:(43-53),F:(40-51)gm/L; Total Bilirubin (TBil) MF:(2.7-21.9),M:(2.6-23.5),F:(2.2-19.6) micromol/L; ALT MF(3-44)U/L, M:(4-57),F:(3-35)U/L;AST MF:(7-37), M:(8-41),F:(5-31) U/L;ALP MF:(131-339),M:(138-416), F:(113-355) U/L, γGT MF:(10-81),M:(11-107), F:(9-36) U/L. Furthermore, gender-wise evaluation showed prominent increase in ALP and γGT in females after 45 years of age. While albumin in males showed linear reduction with age. These variations may be attributed to smoking and alcoholic habits of male than females of this region. RI of total protein is shifted to the higher side and TBil and ALT are shifted to the lower side in Nepalese compared to those of other countries. **Conclusion:** : This is the first study to establish clinical reference intervals for healthy adult Nepalese population. Some of our RIs which were standardized based on the serum panel differ from those of other countries, indicating the importance of deriving country specific RIs.

A-117**High sensitivity C-reactive protein and lipid profile in Hypertension**

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Background:

Hypertension (HTN), a major public health problem worldwide has the prevalence of 33.8% in young adults in Nepal. Various studies have shown the co-existence of prevalence of HTN and dyslipidemia showing the adverse impact on the vascular endothelium resulting into enhanced atherosclerosis leading to cardiovascular diseases. High sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation and a strong predictor of future cardiovascular events is an acute phase reactant protein belonging to pentraxin family. Its level rises markedly after an acute inflammatory stimulus. hs-CRP levels <1 mg/L were considered low-risk, 1 to 3 mg/L as average risk, and >3 mg/L as high-risk for CVD. An early detection of the risk for cardiovascular diseases (CVDs) is essential to prevent the future cardiovascular events. Hence, the objective of this study is to determine the relationship between blood pressure, hs-CRP and lipid profile in hypertensive as well as in normotensive participants and to detect the risk for CVDs.

Methods:

Forty seven newly diagnosed cases of hypertension and fifty age and sex matched healthy controls with prior informed consent were enrolled. The patients were clinically diagnosed as hypertensive according to the recommendation by Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). Patients with chronic inflammatory diseases such as rheumatoid arthritis (RA), autoimmune diseases, tuberculosis and any previous history of diabetes/ stroke etc. were excluded from the study. The anthropometric measurements were done to calculate Body Mass Index (BMI), hs-CRP was measured by ELISA method and lipid parameters were estimated by spectro-photometric method in fasting blood sample. Non-HDL-C was calculated by subtracting high density lipoprotein cholesterol (HDL-C) from total cholesterol (TC). Data were analyzed by student 't' test, correlation was determined by Pearson correlation coefficient and P value was considered significant when P<0.05.

Results:

The result showed statistically significant increase in BMI (24.60 ± 3.72 Vs 22.55 ± 2.59), TC (178.27±37.14 Vs 146.28±26.31), LDL-C (108.46 ± 38.33 Vs 82.42 ± 20.41), Non-HDL-C (136.74± 35.58 Vs 104.12± 26.02), and hs-CRP (3.21 ± 3.03 Vs 1.35 ± 1.27) in hypertension as compared to controls (P< 0.05). However, the increase in TG and the decrease in HDL-C were statistically not significant. Furthermore, hs-CRP and Non-HDL-C had positive correlation with BMI, Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) and was statistically significant (P< 0.05).

Conclusions:

Hypertensive subjects have significantly higher values of hs-CRP, non-HDL-C and BMI than that in controls. Even more, the levels of hs-CRP and Non-HDL-C are also correlated significantly with systolic as well as diastolic blood pressure. Hence, hs-CRP and non-HDL-C can be used as a marker for the risk for CVDs.

A-118**Microalbuminuria in Chronic Obstructive Pulmonary Disease**

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Background

Chronic Obstructive Pulmonary Disease is a global disease which results due to the irreversible airflow limitation and its epidemiology is in increasing trend. Up to date COPD is the second most common noninfectious disease and fourth leading cause of mortality in the world, causing approx. 2.75 million deaths annually and global mortality is predicted to be more than double by 2020. Microalbuminuria (MAB) is believed to reflect a state of generalized endothelial dysfunction, and therefore it is an emerging therapeutic target for primary prevention strategies in COPD patients and to rule out their cardiovascular risk. Thus, this is the first study done in Nepal to rule out the relation between microalbuminuria in COPD patients.

Objectives

To determine urine microalbumin in COPD patients and asymptomatic smokers.

Methods

This is case control study involving two hundred and forty nine patients diagnosed with COPD, and ninety eight asymptomatic controls (smokers) who were matched according to age and sex. They were selected from outpatient department (OPD) and In patients Department (IPD) of Respiratory and Critical care

unit in Tribhuvan University Teaching Hospital (TUTH). Urine microalbumin, Arterial Blood Gas Analysis and Pulmonary Function Test were assessed in both groups. For comparison, COPD patients were divided into four different subgroups based on the duration of COPD. SPSS ver. 21.0 was used to analyze the data. Mean comparison was done by t-test. Group comparison was done by Chi-square test. Pearson's correlation was used to establish the correlation.

Results

Majority of patients with microalbuminuria (MAB) in this study were in the GOLD stage of I and II and rarely of stage III but stage IV was absent. Patients with COPD had significantly higher levels of microalbuminuria than control subject ; higher UACR ; lower FEV1 ; lower FVC and lower FEV1/FVC ratio with p<0.001, higher PCO2 (p=0.010) and lower PH (p=0.028) respectively. Out of two hundred and forty eight COPD patients, two hundred ten were with MAB and higher UACR (P<0.001), thirty eight patients were without MAB. COPD patients with MAB were more hypoxic and more hypercapnic compared to COPD patients without MAB but was statistically non-significant with p value of 0.172 and 0.313 respectively. To evaluate the impact of duration of occurrence of COPD, analysis was done by grouping the cases into four different continuous intervals according to duration of COPD (less than 5 years, 5 to 10 years, 10 to 15 years and more than 15 years). There were total of 248 cases among which 42 cases were below 5 years of duration having MAB (81.976±37.4175), 53 were in 5 to 10 years of duration having MAB (104.257±47.9539) , 77 were in 10 to 15 years of duration having MAB (104.955±40.44) and finally 77 were above 15 years having MAB (146.442±46.83) .

Conclusion

Microalbuminuria is found increased in patients with COPD compared to healthy smokers. Its level is also increased as the disease progresses in terms of duration. Microalbuminuria can be a clinically relevant tool identifying COPD patients with poor prognosis and their monitoring.

A-119**Effects of the levels of vitamin D in serum and seminal plasma on sperm motility and morphology**

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Background: Male factor infertility is responsible for about 25% of infertility causes. Sperm motility and morphology are the most important parameters in assessment of sperm functions. Although the mechanism of vitamin D (vit D) effect on male fertility has not been fully elucidated, possible mechanisms are being investigated in various studies. In these studies vit D receptors are detected on membrane of sperm and it is observed that vit D could increase the sperm motility by increasing the levels of intracellular calcium via vit D receptors. In this prospective study, it was aimed to investigate the possible effects of vit D levels in serum and preseminal fluid on male fertility by assessing the sperm parameters.

Methods: Samples of serum, sperm and preseminal fluid were collected from 100 men who applied to Hacettepe University Department of Obstetrics and Gynecology with infertility complains between September 2016 and October 2016. Sperm samples were assessed manually by the single-blind method according to WHO criteria in terms of sperm parameters. The levels of vit D in serum and seminal plasma were compared in terms of sperm parameters.

Results: There was not statistically significant difference between not only the levels of vit (p=0.463), but also the levels of intracellular calcium in serum and seminal plasma (p=0.878). Moreover, both total sperm motility (r=0.241) and progressive sperm motility (r=0.217) were found to be significantly correlated with the levels of seminal plasma calcium.

Conclusion: Any studies related to the comparison of the vit D levels and intracellular calcium in aforementioned fluids have not been found according to the current literature. As observed from our results, there was a significant positive correlation between the number of forward moving sperms, percentage of sperm in normal morphology and the levels of vit D. However, this research should be supported by studies that include more patients and compare the same parameters of healthy individuals.

A-120**Genotype-based epigenetic factors in identical twins discordant for positive TgAb**

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Background: Epigenetic factors associated with the development of autoimmune diseases are unclear. Monozygotic twin pairs discordant for positive anti-thyroglobulin autoantibodies (TgAb) are useful to examine the epigenetic factors because of their identical genetic background. To clarify the discordant epigenetic differences affecting the development of TgAb.

Subjects: We selected subjects from 257 Japanese monozygotic twins, recruited from the registry established by the Center for Twin Research at Osaka University. TgAb positive concordant (PC) pairs were 5.7% (4 pairs) and 9.6% (18 pairs) of male and female pairs, respectively. TgAb discordant (DC) pairs were 11.4% (8 pairs) and 8.0% (15 pairs) of male and female pairs, respectively. TgAb negative concordant (NC) pairs were 78.6% (55 pairs) of male pairs and 74.3% (139 pairs) of female pairs. To perform stricter grouping, in this study, we set the cut-off value for positive TgAb to 50.0 IU/mL (TgAb Negative: <28.0IU/mL, TgAb Positive: >=50.0IU/mL. TgAb Borderline: =>28.0IU/mL and <50.0IU/mL). Nineteen discordant (6 male and 13 female pairs) and 185 concordant pairs (48 male and 137 female pairs) for TgAb positivity were finally examined.

Methods: We evaluated DNA methylation levels of genomic DNA using the Infinium HumanMethylation450 BeadChip Kit (Illumina). We also genotyped gene polymorphisms using the Omni5-4 BeadChip Kit (Illumina) to clarify genetic background specific for discordant twins.

Results: We did not find any CpG sites with significant within-pair differences of methylation levels in TgAb DC pairs after correction for multiple comparisons. However, 155 polymorphisms specific for TgAb DC pairs were significantly different in genotype frequencies from those of concordant pairs, and none of them was located on the HLA region of chromosome 6. In TgAb DC pairs with some specific genotypes of these polymorphisms, we observed four CpG sites exhibiting significant within-pair differences in each DC pair, even after correction for multiple comparisons.

Conclusions: We found that the genetic background specific for TgAb DC twins who are susceptible to epigenetic changes are different from that specific for TgAb PC twins, and clarified the genotype-based epigenetic differences in TgAb-DC monozygotic twins.

A-121**Performance Evaluation of the VERSANT HCV Genotype 2.0 Assay (LiPA) Using Manual and Automated PCR Setup Workflow on the VERSANT kPCR Sample Prep Instrument**

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Background: The high degree of genetic diversity of the Hepatitis C Virus (HCV) poses a major challenge to its treatment. Determination of HCV genotype is needed to optimize HCV treatment type, dose, and duration to improve patient treatment outcome. The VERSANT® HCV Genotype 2.0 Assay (LiPA)* is a line-probe assay that identifies HCV genotypes 1-6 and subtypes a and b of genotype 1 in human serum or plasma specimens using reverse hybridization technology. The assay has a Limit of Detection (LoD) of 400 IU/mL in plasma and 650 IU/mL in serum. Previously, we have shown that the VERSANT HCV Genotype 2.0 Assay LiPA, using manual PCR setup, provides accurate determination of HCV genotypes 2, 3, 4, 5, 6, and subtypes 1a and 1b for optimal patient therapy (Abstract #B-089, AACC 2017). Automated PCR setup on the VERSANT kPCR Sample Prep instrument (SP) is now available for this assay and is evaluated here.

Methods: The current LiPA extraction workflow requires the operator to manually pipette the PCR master mix and extracted samples into the amplification plate after sample extraction on the VERSANT kPCR Sample Prep instrument SP. The new PCR setup software automates this process. Performance of VERSANT HCV Genotype 2.0 Assay (LiPA) using manual PCR plate setup vs. automated PCR plate setup was evaluated. Two unique HCV subtype 1a donor sera, initially genotyped using an NS5B sequencing method, were used to prepare replicate samples at three different viral concentration levels: 600 IU/mL ($1.5 \times \text{LoD}$), 1×10^4 IU/mL, and 6×10^5 IU/mL. The study design included a total of 368 HCV subtype 1a panel members for each method. The genotyping rate (GR) and genotyping accuracy (GA) were calculated to compare the manual and automated PCR setup methods.

Results: All runs in the study were valid, and all 368 samples tested for each method

produced interpretable results. The GR was 100% for all viral concentration levels with both automated and manual PCR plate setup, and all valid interpretable samples from each plate setup method were accurately genotyped (100% GA). The lower limit of the confidence interval (Wilson Score Method) was 95.99% for samples with $n = 92$ (6×10^5 and 10^4 IU/mL) and 97.95% for samples with $n = 184$ (600 IU/mL).

Conclusion: The present study demonstrates no difference in genotyping rate and accuracy between manual and automated PCR setup on the VERSANT kPCR Sample Prep instrument. The VERSANT HCV Genotype 2.0 Assay (LiPA) continually provides accurate identification of HCV genotypes as shown by GR and GA rates of 100%, while providing high throughput and automated workflow. *The VERSANT HCV Genotype 2.0 Assay (LiPA) (Reagents: Genotype 2.0 Kit, Amplification 2.0 Kit, and Control 2.0 Kit) is CE-marked in Europe and FDA-approved in the U.S. HOOD05162002791113

A-122**Evaluation of VACUETTE® BCA Fast Separator Blood Collection Tube for Routine Chemistry Assays**

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Background: Clotting time is an important factor in the work flow of blood collection tubes for routine chemistry testing from serum. To optimize laboratory workflow, reduced turnaround times are expected to provide precise test results. The key target of VACUETTE BCA Fast tubes consists in the faster processing time from blood collection to result availability. The faster clotting time in the VACUETTE BCA Fast tube provides a clotted sample by the time the sample reaches the laboratory and allows for immediate testing. Tubes containing a gel separator offer the option of replicate measurements up to 48h at refrigerator temperature.

Methods: This study was conducted in order to demonstrate the performance of VACUETTE BCA Fast tubes for routine chemistry analysis up to 48h in comparison to VACUETTE Serum Separator tubes. Venous blood was drawn from 50 healthy donors into two tubes. Tubes without thrombin were centrifuged after 30 min clotting time, and the tubes with thrombin were centrifuged after 5 min clotting time. All samples were centrifuged for 10 min at 1800g. Initial values of routine chemistry assays were determined on an AU680 and DxI800 from Beckman Coulter (Beckman Coulter, precision within-run <3%, total <3%). All samples were stored in an upright position at 4-8°C for replicate testing after 24h and 48h. Comparison analysis was performed at all time points. Clinical evaluation was based on CLIA (Allowable Total Error Table by Data Innovations).

Results: Equivalency for VACUETTE BCA Fast tubes to VACUETTE Serum Separator tubes was shown for routine chemistry assays on Beckman Coulter for healthy donors. Provided a completely clotted sample and clear serum specimens, no significant deviations were found for initial values as well as at 48h for 37 biochemical assays tested in both tubes according to CLIA tolerances. In agreement to literature, slight systematical deviations in the thrombin tubes were found for some assays such as sodium, potassium, chloride, and glucose due to the faster coagulation process. Stability over 48h was shown for all assays except troponin I (6h).

Conclusion: The thrombin tube gave comparable test results to current serum separator tubes for most common biochemical assays in clinical laboratories. The blood collection tube containing thrombin provides rapid turnaround times in the laboratory by shortening the clotting time, providing accurate testing results and being suitable for emergency testing, however, those tubes are not recommended for patients on heparin therapy, thrombin inhibitor therapy or with deficiency in the clotting factors.

A-123**Evaluation of IgG Index as a Biomarker for Multiple Sclerosis: Experience from a Tertiary Care Center in Saudi Arabia**

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Background: The diagnosis of multiple sclerosis (MS) is based on neurologic history, clinical findings on examination and exclusion of other disorders. The single most consistent laboratory abnormality in patients with MS exclusive of magnetic resonance imaging is increased oligoclonal immunoglobulin in cerebrospinal fluid (CSF). The presence of oligoclonal bands (OCB) in CSF but not in the serum is a strong indication of intrathecal antibody synthesis and is found in nearly all patients with MS. Furthermore, CSF IgG index is used as a measure of IgG production within the CNS; however, its biomarker potential for MS is not firmly established.

Aim: To determine the correlation between OCB and IgG index and assess the specificity of IgG index for the diagnosis of MS.

Methods: This study was conducted on 209 patients (92 males and 117 females) with suspected CNS immune mediated disorders (CIMD) or multiple sclerosis (MS). Sera and CSF samples were analyzed for IgG and albumin for computing IgG index. (Siemens BN II) Isoelectric focusing-immunoblotting was used for the detection of OCB. (H Sebia Hydrasys 2 System) Presence of three or more bands in CSF but their absence in serum indicated a positive pattern. Data were analyzed by one-way analysis of variance followed by Dunnett's test for comparing means and Spearman's test for correlations. **Results:** The positive OCB were observed in the CSF of 76 (36%) patients. The OCB were missing in the CSF of 113 patients while 20 patients showed matching OCB (both in CSF and sera). IGG index was significantly higher in OCB positive patients (1.35 ± 0.17) as compared to OCB negative (0.64 ± 0.07) or OCB matching patients (0.51 ± 0.02) (ANOVA $F=11.17$, $P<0.001$). There was a significant correlation between OCB and IgG index ($R^2 = 0.464$, $P<0.001$). Using a previously reported IgG index cut-point of 0.85, only few predictions were false-positive (2.25%) whereas the false-negativity was extremely high (50%). **Conclusions:** IgG index lacks the specificity for the diagnosis of MS due to extremely high false-negative predictions. Utilizing radiological examination in addition to OCB are required for more authentic validation of IgG index.

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Clinical performance of Dynamiker® Cryptococcal Antigen Lateral Flow Assay compared to IMMY® CrAg LFA in diagnosis of Cryptococcus

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Background

Cryptococcus is one of the major invasive fungal disease and early diagnosis plays an important role in treatment. Detection of cryptococcal antigen in blood and cerebrospinal fluid (CSF) is critical mycological evidence in diagnosis of Cryptococcus. In this study we evaluate the clinical performance of newly developed Cryptococcal Antigen Lateral Flow Assay(LFA) by comparing with IMMY® CrAg LFA.

Material and Method

Total of 82 CSF samples and 94 serum samples from patients who were at risk of Cryptococcus were retrospectively collected. Serum or CSF Cryptococcal Antigen levels were determined by using Dynamiker® Cryptococcal Antigen LFA and IMMY® CrAg LFA at the same time. An additional test was performed if initial test result was positive.

Results

Twenty-six of 82 CSF samples were determined as positive by Dynamiker® LFA while 25 samples were positive in IMMY® CrAg LFA. There were 37 positive serum samples determined by Dynamiker® LFA compared with 35 positive samples from IMMY® CrAg LFA. All IMMY® CrAg LFA positive samples were also Dynamiker® LFA positive in this study. The Kappa value for CSF samples and serum samples were 0.972 and 0.955, respectively.

Conclusion

The clinical performance of Dynamiker® Cryptococcal Antigen LFA is highly consistent with that of IMMY® CrAg LFA

CSF sample	IMMY LFA			
	Positive	Negative	Total	
DNK LFA	Positive	25	1	26
	Negative	0	56	56
	Total	25	57	82
Serum sample	IMMY LFA			
	Positive	Negative	Total	
DNK LFA	Positive	35	2	37
	Negative	0	57	57
	Total	35	59	94

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Evaluation of biochemical biomarkers in the CSF and with genotyping for the risk of Alzheimer's disease in patients with some neurological impairment.

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Background: The increase in life expectancy and the increasing rate of elderly people leads to a population projection for 2050 of 115400000 elderly with Alzheimer's disease (AD) in the world. The literature shows that the pathological process of AD begins at least 10-20 years before the onset of the first symptoms of dementia. Therefore, the prediction and treatment of asymptomatic individuals, in whom degeneration is not yet severe, is crucial. Several studies with AD have been carried out by genotyping for apoprotein E (ApoE) and its alleles (E2, E3 and E4) as well as the main biochemical markers in the cerebrospinal fluid (CSF) that relate to this disease as: total tau protein (t-tau), Beta Amyloid-42 (Aβ-42), which is identified early, before the onset of the first symptoms of AD. Thus, measurement of Aβ-42 in CSF may facilitate the diagnosis of incipient AD in patients with mild cognitive impairment. Recent studies have evaluated the diagnostic utility of the Aβ-42 / Aβ-40 ratio, although Aβ-40 is slightly increased or unchanged in the CSF of patients with AD. The t-tau is the major component of neurofibrillary tangles which is another key neuropathological feature of AD. It is known that these parameters also change in many conditions and neurological diseases and can also lead to dementias reaching to AD. In this study, the authors studied two groups of patients with neurological impairment of diabetic etiologies: infectious and non-infectious (other causes), evaluating biochemical parameters and genotyping for AD risk. **METHODS:** 44 patients who had been prescribed CSF for some diagnosis or monitoring hypothesis were invited to participate in this study and signed the TCLE. We divided the clinical groups into two: patients with suspected neurological involvement due to infectious causes (n = 26) and patients with noninfectious involvement. The following parameters were determined: (Aβ-42 and Aβ-40) and (t-tau) by the Elisa / Euroimmun Medizinische Labordiagnostika AG methodology. Apo E genotyping was determined by salivary collection by PCR method, using primers specific for the detection of E2, E3 and E4 alleles of ApoE gene polymorphism. **Results:** The results showed that, using ANOVA, that the Apo E genotype and the t-tau variation did not present a significant difference (p = 0.10) for all groups. Aβ-42 presented a difference between the E3 / E3 group, which showed higher levels than the E3 / E4 group (p = 0.006). Likewise, the Aβ-42 / Aβ-40 ratio presented a significant difference between the E3 / E3 group compared to the E3 / E4 group. Regarding clinical indication, the E3 / E4 group with infectious neurological involvement had a higher Aβ-42 / Aβ-40 ratio than the non-infectious E3 / E4 group. Patients with E2 / E3 from the infectious group showed a lower ratio than the E2 / E3 group from the non-infectious group. **Conclusion:** in conclusion of the findings, the noninfectious E2 / E3 group presented a lower risk for AD when compared to the infectious group. The E3 / E3 infectious group presented a higher risk than both E3 / E4 groups.

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Evaluation of C-reactive protein and white blood cell count as an early infection marker after the surgical operation of hip fracture

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Background: C-reactive protein (CRP) is a known inflammatory and infection marker. We examined the serial serum levels of CRP and white blood cell (WBC) count after the operation of hip fracture to evaluate the usefulness of CRP and WBC count as an early infection marker after the surgical operation of hip fracture. **Methods:** Postoperative CRP level and WBC count in 279 patients with hip fracture from January 2013 to December 2016 were retrospectively examined. The patients had the serial test results of both markers for more than 7 days after the operation. Mean and SD of both markers were obtained according to the day after operation. **Results:** Two hundred seventy-three of 279 (97.8%) had no infection after the surgical operation and the other 6 (2.2%) had infection. Postoperative mean WBC count of the patients without infection was follows: 10.8 K/uL just after the operation, 9.24 K/uL at first day, and 8.81 K/uL at second day. Postoperative mean WBC count of the patients with infection was 14.8 K/uL, 14.4 K/uL, and 15.3 K/uL, respectively. There was a statistical difference in WBC count between both

patient groups. Postoperative mean CRP of the patients without infection was follows: 5.65 mg/dL just after the operation, 8.36 mg/dL at first day, 11.0 mg/dL at second day, 9.15mg/dL at third day, 7.04 mg/dL at fourth day, 4.59 mg/dL at fifth day, 4.22 mg/dL at sixth day, and 3.44 mg/dL at seventh day. The CRP level reached the maximum value on the second day in the patient without infection. Postoperative mean CRP of the patients with infection was follows: 10.29 mg/dL just after the operation, 16.22 mg/dL at first day, 8.71 mg/dL at second day, and 16.43 mg/dL at third day. There was a statistical difference in CRP between both patient groups. Conclusion: CRP and WBC count could be an early infection marker after the surgical operation in the patients with femoral fracture.

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Effects of δ -Tocotrienol on Glycemic Control and Inflammatory Biomarkers in the Diabetic Patients

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Background: Diabetes mellitus is a complex, long standing health problem especially in Asian countries. Inflammation, increased oxidative stress and impaired insulin action are the main factors for development of multiple diabetes associated micro and macro vascular complications. Being potent anti-oxidative and anti-inflammatory agent, tocotrienol is continuously re-evaluated for a long time in different chronic diseases. Due to the diverse results and limited number of studies in the diabetic patients, there is need of further clinical trials in order to determine the impact of purified delta tocotrienol in type 2 diabetes mellitus patients. **Objective:** To find out the effect of delta tocotrienol (250mg) supplementation along with recommended diabetic medications on fasting glucose, glycated Hb, total cholesterol, triglycerides and hs C-reactive protein (hs-CRP) in patients of type 2 diabetes mellitus. **Method:** In this randomized control trial, 54 subjects age ≥ 30 years with serum fasting glucose and HbA1c levels ≥ 7 mmol/L and HbA1C $\geq 6.5\%$ were included. Persons having history of acute illness, liver, renal, thyroid disorders or malignancy and history of taking anti-inflammatory drugs, vitamin E were excluded from study. Patients were randomized into two groups, 27 patients in group A and 27 in group B by a simple random draw. Subjects in the group A were given capsules containing 90% pure δ -tocotrienol 125mg twice daily and group B was provided placebo twice daily for three months. Total 5 ml blood was collected for analysis of biochemical markers at the start of study and after three months. To compare the baseline and 3 month values in both groups paired student t-test was used. Statistical significance was set at $p < 0.05$. **Results:** Pre vs post levels of diabetic associated biomarkers including fasting glucose, HbA1c, total cholesterol, triglyceride and hs-CRP in tocotrienol group were 14.10 \pm 3.15 vs 11.65 \pm 2.71 mmol/L, 10.07 \pm 2.0 vs 8.98 \pm 1.70 %, 5.01 \pm 1.21 vs 4.47 \pm 1.33 mmol/L, 2.61 \pm 2.42 vs 2.40 \pm 1.25 mmol/L and 4.76 \pm 4.41 vs 2.95 \pm 2.73 mg/L were significantly decreased ($P < 0.05$) respectively. In Placebo group, pre vs post levels of these variables were 14.56 \pm 3.24 vs 14.12 \pm 3.01 mmol/L, 10.77 \pm 2.11 vs 10.45 \pm 1.83 %, 4.59 \pm 1.50 vs 4.53 \pm 1.31 mmol/L, 2.28 \pm 1.54 vs 2.22 \pm 1.15 mmol/L, 4.99 \pm 4.43 vs 4.78 \pm 3.65 mg/L ($p = NS$) respectively. **Conclusion:** The consumption of delta tocotrienol supplementation in addition to antidiabetic drugs at early phases of the disease can be helpful in the prevention of long term complications by improving glycemic control and reducing inflammatory process in the diabetic patients. Delta-Tocotrienol demonstrated significant reduction in serum lipid parameters which are associated with cardiovascular diseases in the diabetic patients.

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CoQ10 and Total antioxidant capacity in early breast cancer

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Background: Oxidative stress in the body, whether resulting from endogenous or exogenous factors, has been associated with the development of breast cancer. We aimed to assess Coenzyme Q10 (CoQ10) and Total Antioxidant Capacity (TAC) as indicators of antioxidant state in women with early breast cancer. **Method:** Serum samples were collected from 80 recently diagnosed non-intervened female breast cancer patients and 20 healthy control female volunteers. TAC was measured spectrophotometrically. CoQ10 was measured using HPLC technique using HPLC ClinRep™ kit from Recipe, Germany (Code: 31000) using a C18 column and an isocratic mobile phase. **Results:** A statistically significant increase in TAC levels was found in breast

cancer patients (1.80 \pm 0.35 mMol/L) when compared to the control group (1.62 \pm 0.29 mMol/L). Women having TAC levels above 1.5 mMol/L were 2.2 times more at risk of developing breast cancer than those with values below 1.5 mMol/L with odds ratio 2.211 (1.012-65.526) with a 95% confidence interval and p value of 0.049. Multiple linear regression analysis performed nullified the effect of BMI (body mass index) and found TAC to be an independent predictor of breast cancer. The adjusted odds ratio has also found TAC to be statistically significant. It was found to be 5.944 (1.203-29.371) with a p value of 0.029 at a 95% confidence interval. CoQ10 levels were significantly higher in the breast cancer group (1337.67 (630.36-3333.51) μ g/L) when compared to the control group (1195.30 (647.58-1775.01) μ g/L). A CoQ10 level above 1600 μ g/L was found to have an odds ratio of 7.878 (0.976-63.260) with a 95% confidence interval which possessed a risk for breast cancer development yet this risk was found to be of borderline significance ($p = 0.053$). **Conclusion:** significantly higher TAC and slightly higher CoQ10 levels in the breast cancer group were found compared to the control group. It is still unclear whether the increased host antioxidant defenses offer a selective growth advantage to tumor cells over their surrounding normal cells or serve as a protective measure by the body in an attempt to correct the assault triggered by the ROS. We suggest a potential role for antioxidants & CoQ10 in the development and progression of breast cancer. However larger sample size is recommended. Circulating CoQ10 may not be indicative of intracellular CoQ10 yet may be a response to chronic inflammation, heightened systemic or tissue-specific oxidation.

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A not so unusual complication? A case of urinary calculus formation caused by sulfamethoxazole-trimethoprim therapy

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Background: Sulfamethoxazole-trimethoprim (TMP-SMX) is a commonly employed antibiotic used for mild-to-moderate bacterial infections and as prophylaxis against opportunistic infections. Genitourinary side-effects such as crystalluria and urolithiasis have been reported, but infrequently. Furthermore, medication package inserts for common commercial preparations available in North America do not list urinary calculi formation as a potential adverse reaction or side-effect. Therefore, this potential complication may remain largely unrecognized by laboratories and clinicians. We describe a case of a bladder (vesical) calculus comprised of the TMP-SMX metabolite, N4-acetylsulfamethoxazole, as well as the validation of this metabolite in a basic urinary calculi spectral library. **Methods:** The urinary calculus was received by a regional reference laboratory for composition analysis by Fourier-transform infrared (FT-IR) spectroscopy. Observations were made regarding physical characteristics (size, colour, shape, and consistency). The specimen was ground, mixed with potassium bromide and analyzed by a Nicolet iS10 FT-IR spectrometer with OMNIC Spectra software. Spectral scans were compared to a basic urinary calculi spectral library as well as a pure chemical spectra library. **Results:** The calculus was retrieved from the bladder of a 66-year old male recovering from radical prostatectomy with no prior history of urinary calculi. Post-prostatectomy, the patient required prolonged catheterization during which he experienced difficulties with a blocked catheter. During that time period, he received Septra DS for two weeks. When assessed for catheter removal, a calculus was observed at the bladder neck, next to the catheter. This stone was mechanically broken and submitted for laboratory analysis. The stone was tan in colour, 4x3x1 mm in size with irregular shape, and a hard consistency. Initial analysis by FT-IR spectroscopy against a basic urinary calculi library provided no spectral match. However, comparison to a pure chemical spectra library provided a >95% probability match to N4-acetylsulfamethoxazole. To verify the composition match, a portion of the stone was sent for confirmation testing by a second reference laboratory, which confirmed the sulfa-drug metabolite. After stone removal, the patient was kept off Septra DS and has had no evidence of stone re-occurrence. **Conclusion:** Precipitation of sulfonamides may occur more frequently than previously recognized. A prior case of N4-acetylsulfamethoxazole urinary calculi formation noted that stone formation coincided with an obstructing calcium oxalate stone producing oliguria and acute azotemia (J. Urol. 1977; 117:397). We report an additional case of TMP-SMX-mediated stone formation, concurring with a clinical history of oliguria. Since sulfa-drug metabolites may not be included in basic urinary calculi spectral libraries, laboratories providing urinary calculi analysis should ensure that their system detects and classifies such stones. Clinicians should be aware that sulfa-drug metabolite stones may form with TMP-SMX treatment, particularly in patients with reduced urinary flow. Medication package inserts for TMP-SMX should be updated to include urolithiasis as a potential side-effect.

A-130**Prevalence and related factors to dyslipidemias in university students**

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Background: The dyslipidemias are a set of pathologies characterized by alteration of one and/or more parameters of the lipid profile; dyslipidemia is the biochemical manifestation of genetic variations or secondary to lifestyle factors; it also constitutes an important modifiable risk factor due to its direct relationship with the coronary disease. The objective of the study was to determine the prevalence and factors related to dyslipidemias in university students. **Methods:** Descriptive, cross-sectional, prospective study that was carried out during November 2012, in the study, 220 students were included through a non-probabilistic convenience sampling. Lipid profile measurements were made by enzymatic method and precipitation for cholesterol fractions, as well as anthropometric measurements; in addition, data such as age, sex, and personal and family history were recorded. The identification of dyslipidemias was based on the results of the lipid profile according to what was established by the NCEP - ATP III. A database was created in Excel 2010; continuous data were expressed descriptive statistic and frequency/percentages were qualitative variables. Multiple analysis a generalized linear model was used, family binomial link log to identify factors related to dyslipidemia. The software STATA version 13 was used. **Results:** A total of 220 students who participated in the study were evaluated, 167 (75.91%) were female, the average age was 21.19 years. The 80 (54.30%) and 38 (22.75%) of women presented central obesity and overweight respectively. The prevalence of dyslipidemia was 134 (60.91%). HDL was found to be reduced in 117 (53.18%) and 8 (3.64%) had alterations in all parameters of the lipid profile. No relationship was found between dyslipidemia and body mass index, family and personal history. In the multiple analysis, the prevalence of having dyslipidemia was associated with central obesity (PR 1.62; IC95% 1.30 - 2.0, $p < 0.05$) and the male sex (PR 0.61; IC95% 0.44 - 0.86, $p < 0.05$), after adjusting for family and personal background. **Conclusion:** It is concluded that there is a high prevalence of dyslipidemia (60.91%), with low HDL levels being one of the most frequent parameters; furthermore the main factors related to dyslipidemia were central obesity and the university students' sex.

A-131**The Hepcidin in the non-alcoholic fatty liver disease**

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Background: Hepcidin is a peptide mainly produced by hepatocytes and, through a connection with ferroportin, it regulates iron absorption in the duodenum and its release of stock cells. The non-alcoholic fatty liver disease (NAFLD) is associated with resistance to insulin action, metabolic syndrome and hyperferritinemia. The mechanism of increased iron absorption in NAFLD is incompletely understood but is likely caused by decreased hepcidin production in the diseased liver. **Objective:** This study evaluates hepcidin levels in patients with NAFLD and its relationship with iron overload and severity of liver disease. **Methods:** Patients with diagnosis of NAFLD after hepatic biopsy and clinical cirrhosis were included in this study. We exclude alcohol consumption above 20g / day, drugs that cause liver damage and infectious or autoimmune hepatitis. Hepcidin was measured by immunoassay DRG 25 Bioactive ELISA-Etimax, normal values: 0.91-33.55ng/mL and Ferritin for ICMA (Beckman Coulter). The correlations between hepcidin, ferritin and histopathological findings after hepatic biopsy were calculated by correlation coefficient (pearson). Patients were divided as to severity of liver disease in hepatic steatosis and cirrhosis (Metavir-Fibrosis F = 4). A total of 48 patients performed magnetic resonance (MR) for quantification of the iron hepatic deposit. **Results:** Eighty-six patients were studied, the majority of females (72%), with a mean age of 56 years \pm 10, BMI 33 \pm 6 kg / m², CA 110 \pm 12 cm). Of these, 64% had Diabetes, 81% hypertension and 97% metabolic syndrome. Of the 73 biopsy patients 31% had mild steatosis, 48% moderate and 21% severe. And Of this total of 73 patients 66% had Steatohepatitis and 21% had cirrhosis; Ferritin was elevated in 28% (21% with increase of 1 to 2 times the normal and 7% with an increase of more than twice the normal value. Only 8% had iron overload in MR, all cases with mild overload. We found a negative correlation between hepcidin and ferritin ($r = 0.356$ $p = 0.002$) and also between hepcidin and liver disease severity, with lower levels of hepcidin in patients with hepatic cirrhosis (46 \pm 22 vs. 29 \pm 20; $p = 0.005$).

Conclusion: Patients with advanced DHFBD (cirrhosis) have lower levels of hepcidin; however, despite their correlation with serum ferritin, There was no correlation between Hepcidin and a significant iron overload in the liver observed in MR.

A-132**A comparative study to assess serum sFlt-1 to PIGF ratio in pregnant women with and without Preeclampsia**

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Background

Preeclampsia is a disorder of widespread vascular endothelial malfunction that occurs after 20 weeks of gestation. Abnormalities in the development of placental vasculature early in pregnancy may result in relative placental underperfusion, which then leads to release of antiangiogenic factors into the maternal circulation that alter maternal systemic endothelial function and cause hypertension and other manifestations. Imbalance in, placental soluble Fms like tyrosine kinase -1 (sFlt-1) which is antiangiogenic factor; and placental growth factor(PlGF) which is involved in angiogenesis during placenta and fetus development, is proved to have role in endothelial damage in Preeclampsia. At a time when most public health facilities are lacking standardized testing tools for pre-eclampsia and eclampsia, there is need of an innovate and improved tool for screening of preeclampsia, which is the leading cause of maternal mortality in Nepal. This study was designed to compare sFLT1: PLGF ratio in pregnant women with and without Preeclampsia attending Tribhuvan University Teaching Hospital (TUTH). Similarly, correlation of sFlt1: PIGF ratio with diastolic blood pressure and severity of proteinuria in women with preeclampsia was also done.

Method

A case control study was done in Gynecology and Obstetrics department of TUTH involving forty-four subjects with preeclampsia and forty-four age and gestational weeks matched, normal pregnancy as controls. Cases were divided into mild and severe group of preeclampsia according to the criteria defined by the American College of Obstetricians and Gynecologists. Blood pressure, urinary protein, serum sFlt-1, serum PlGF and sFlt-1: PIGF ratio were compared in both case and control. Concentration of sFlt-1 and PlGF were measured with commercially available ELISA kits. SPSS ver. 17.0 was used to analyze the data. Tests were performed with T test, Mann-Whitney test, and Spearman's rank correlation test. Normally distributed variables were expressed in terms of mean \pm SD. A p-value < 0.05 was considered statistically significant.

Results

There was no significant difference in age and period of gestation in both study groups. Mean concentration of sFlt-1 in preeclampsia was higher (2575.50 \pm 775.03 pg/mL) compared with normal pregnancy (453.75 \pm 156.24 pg/mL). Mean concentration of PlGF was lower in preeclampsia (86.31 \pm 26.9 pg/mL) compared with normal pregnancy (155.41 \pm 63.89 pg/mL). Ratio of sFlt-1 and PlGF concentration was significantly higher in preeclampsia (P value 0.000) than in normal pregnancy. Similarly, the diastolic blood pressure significantly correlated with the sFlt-1: PIGF ratio in preeclamptic group (p-value 0.000) whereas the severity of proteinuria did not significantly correlate with the ratio of sFlt-1: PIGF in preeclamptic women (p-value 0.773).

Conclusion

sFlt-1 level is increased and PlGF level is decreased in preeclampsia compared to the normal pregnant women. sFlt-1/PlGF ratio is significantly higher in women with preeclampsia than in normal control. This ratio can be a potential marker for diagnosis of preeclampsia.

A-133**Post-Partum Glucose Testing: Missed Opportunities for Assessing and Preventing Diabetes mellitus in women with Glucose Intolerance in Pregnancy**

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Background

Gestational diabetes mellitus (GDM) is a common medical problem in pregnancy and predict future Type 2 Diabetes Mellitus (T2DM). Expert guidelines encourage postpartum glucose testing at the 6 weeks post-natal visit to properly evaluate and manage women who were diagnosed with GDM during pregnancy. We followed up women diagnosed with GDM and overt DM to examine the post-natal care, prevalence of postpartum glucose testing and the factors associated with testing.

Methods

This was a retrospective study of 142 women who were identified as having GDM or Overt DM using the Modified WHO 2013 diagnostic criteria after a 75-g oral glucose tolerance test (OGTT) between April 2013 and April 2017 among preg-

nant women referred to the metabolic Clinic of the Clinical Chemistry Department of Jos University Teaching Hospital. Fifty eight women responded to followed up phone calls to determine their post-pregnancy status. Socio-demographic data and obstetric history were obtained from hospital and laboratory records.

Result

The Mean (SD) age of the women was 33.6(5.0) yrs; 34(58.6%) and 24 (41.4%) had GDM and overt DM respectively. Most of the women had tertiary education 47(81%); were less than 35 years of age 34(58.6%) and Grandmultiparous 39(67.2%). Median (IQR) Gestational Age at testing was 30 (23.5-32.0) weeks. Only twenty women (34.5%); 4(6.9%) by OGTT and 16 (27.6%) by random glucose were tested six weeks post delivery. Thirty seven (63.8%) and 19 (32.8%) had fasting and random glucose testing respectively while 8(13.8%) did not have any form of glucose testing after delivery. Most of the testing were done by Point of Care Testing (POCT) 42(72.4%); 10 (17.2%) were tested in a clinical laboratory. Only 28 (48.3%) had been counseled to repeat OGTT post-delivery while 19 (32.8%) were referred for further treatment. A diagnosis of overt DM was significantly associated with random glucose testing after 6 weeks visit (P= 0.019) and testing carried out in the laboratory P=0.043. The category of diagnosis (GDM or Overt DM) was not associated with repeat OGTT/random glucose, testing by POCT, counseling for repeat OGTT or referral for further treatment (P> 0.05).

Conclusion

This study highlights that OGTT or random glucose test at 6 weeks post delivery for women diagnosed with GDM or overt DM is very low. Poor counseling and referral for treatment suggest a gap in post-partum care given to women with glucose intolerance in Pregnancy and represents missed opportunities for assessing and preventing Diabetes mellitus and Cardiovascular Diseases in such women. In view of the increased risk of T2DM in women diagnosed with GDM, there is urgent need for local guidelines and coordinated multidisciplinary approach to follow-up testing for such women. Post-partum screening for DM and CVD risk assessment should be incorporated into existing integrated care programmes for mother and child at the 6-weeks post-partum visit. Laboratories should play more prominent role in post-partum glucose testing and closer collaborations between clinical laboratories and clinicians is crucial for slowing the progression to overt DM and attendant complications.

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Clinicopathological features and survival outcome according to KRAS, NRAS and BRAF mutation status in patients with colorectal cancer

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Background: Colorectal cancer (CRC) is a leading cause of cancer deaths worldwide. One of the fundamental processes driving the initiation and progression of CRC is the accumulation of a variety of genetic and epigenetic changes in colonic epithelial cells. In this retrospective observational study, frequencies and clinicopathological features of KRAS, NRAS, BRAF mutations were evaluated in patients with colorectal cancer. Among patients who treated, progression-free survival (PFS) and overall survival (OS) were appraised according to gene status. **Methods:** Between 2002 and 2017, a total of 246 patients with colorectal cancer who were treated and followed up in our oncology center were analyzed. KRAS, NRAS, BRAF mutations analysis was performed using quantitative PCR evaluation of the DNA from the tumor tissues. Progression-free survival (PFS) and overall survival (OS) were calculated for each of the patients and the relationship between survival and mutation status was evaluated. **Results:** One hundred and fifty four (62.6 %) were male and ninety two (37.4 %) were female, with a median age of 55 years (range 23-86). Based on tumor localization, 153 patients (62.2 %) were classified as colon cancer patients and 93 patients (37.8 %) were classified as rectal cancer patients. The majority of patients (86.2 %) had adenocarcinoma histology, while 24 cases (9.8 %) had mucinous adenocarcinoma. Among 246 patients, mutations in KRAS exon 2, exons 3 or 4, NRAS and BRAF were detected in 33.5 %, 1.6 %, 1.2 %, 4.0 % and 1.6 %, respectively KRAS mutations were detected in 103 of the patients (41.9 %). The median overall survival (OS) and progression-free survival (PFS) time were 39.9 and 7.5 months for the patients with KRAS mutations tumors. For the patients with all wild-type tumors, OS and PFS were 43.4 and 13.3 months. **Conclusion:** Our data suggest that mutations in KRAS are associated with inferior PFS and OS of CRC patients compared with patients with non-mutated tumors.

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Multicenter Evaluation of Ceftazidime/Avibactam MIC Results for Enterobacteriaceae and Pseudomonas aeruginosa Using MicroScan Dried Gram Negative MIC Panels

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Background: A multicenter study was performed to evaluate the accuracy of ceftazidime/avibactam on a MicroScan Dried Gram Negative MIC (MSDGN) Panel when compared to frozen CLSI broth microdilution reference panels. **Materials/Methods:** For efficacy, an evaluation was conducted at three sites by comparing MICs obtained using the MSDGN panel to MICs using a CLSI broth microdilution reference panel. A total of 618 *Enterobacteriaceae* and *Pseudomonas aeruginosa* clinical isolates were tested using turbidity and PromptTM methods of inoculation. For challenge, a set of 116 organisms was tested on MSDGN panels at one site. For reproducibility, a subset of 16 organisms was tested on MSDGN panels at each site. MSDGN panels were incubated at 35 ± 2°C and read on the WalkAway System, the autoSCAN-4 instrument, and read visually. Read times for the MSDGN panels were at 16-20 hours. Frozen reference panels, prepared according to CLSI methodology, were inoculated using the turbidity inoculation method. All frozen reference panels were incubated at 35 ± 2°C and read visually at 16-18 hours. FDA breakpoints (µg/ml) used for interpretation of MIC results were: *Enterobacteriaceae* and *Pseudomonas aeruginosa* ≤ 8/4 S and ≥ 16/4 R. **Results:** When compared to frozen reference panel results, essential and categorical agreements for all isolates tested in Efficacy and Challenge are as follows:

Read Method	Essential Agreement %		Categorical Agreement %		VMJ [*] %		MAJ [*] %	
	T	P	T	P	T	P	T	P
Visually	98.8 (725/734)	97.7 (717/734)	99.2 (728/734)	99.0 (727/734)	6.5 (2/31)	3.2 (1/31)	0.1 (1/703)	0.3 (2/703)
Walk Away	98.9 (726/734)	95.2 (699/734)	98.8 (725/734)	98.4 (722/734)	3.2 (1/31)	3.2 (1/31)	0.3 (2/703)	1.0 (7/703)
auto SCAN-4	98.8 (725/734)	97.3 (714/734)	99.2 (728/734)	98.9 (726/734)	6.5 (2/31)	6.5 (2/31)	0.0 (0/703)	0.0 (0/703)

T = Turbidity inoculation method, P = PromptTM inoculation method
* = calculated without 1 well dilution errors

Reproducibility among the three sites were greater than 95% for all read methods for both the turbidity and PromptTM inoculation methods. **Conclusion:** This multicenter study showed that ceftazidime/avibactam MIC results for *Enterobacteriaceae* and *Pseudomonas aeruginosa* obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels. * PROMPT is a registered trademark of 3M. © 2018 Beckman Coulter. All rights reserved. Beckman Coulter, the stylized logo and the Beckman Coulter product and service marks mentioned herein are trademarks or registered trademarks of Beckman Coulter, Inc. in the United States and other countries.

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Multicenter Evaluation of Ceftolozane/Tazobactam MIC Results for Enterobacteriaceae and Pseudomonas aeruginosa Using MicroScan Dried Gram Negative MIC Panels

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Background: A multicenter study was performed to evaluate the accuracy of ceftolozane/tazobactam on a MicroScan Dried Gram Negative MIC (MSDGN) Panel when compared to frozen CLSI broth microdilution reference panels. **Materials/Methods:** For efficacy, an evaluation was conducted at three sites comparing MICs obtained using the MSDGN to MICs using a CLSI broth microdilution reference panel. A total of 575 *Enterobacteriaceae* and *Pseudomonas aeruginosa* clinical isolates were tested using turbidity and PromptTM methods of inoculation. For challenge, a set of 118 organisms was tested on MSDGN panels at one site. For reproducibility, a subset of 16 organisms was tested on MSDGN panels at each site. For reproducibility, a subset of 16 organisms was tested on MSDGN panels at each site. For reproducibility, a subset of 16 organisms was tested on MSDGN panels at each site. For reproducibility, a subset of 16 organisms was tested on MSDGN panels at each site.

ibility, a set of 17 organisms was tested on MSDGN panels at three sites. MSDGN panels were incubated at 35 ± 2°C and read on the WalkAway System, the autoSCAN-4 instrument, and read visually at 16-20 hours. Frozen reference panels, prepared according to CLSI methodology, were inoculated using the turbidity inoculation method. Frozen reference panels were incubated at 35 ± 2°C and read visually at 16-18 hours. FDA breakpoints (µg/ml) used for interpretation of MIC results were: *Enterobacteriaceae* ≤ 2/4 S, 4/4 I, and ≥ 8/4 R and *Pseudomonas aeruginosa* ≤ 4/4 S, 8/4 I, and ≥ 16/4 R. **Results:** When compared to frozen reference panel results, essential and categorical agreements for all isolates tested in Efficacy and Challenge are as follows:

Read Method	Essential Agreement %		Categorical Agreement %		VMJ %		MAJ %		MIN %	
	T	P	T	P	T	P	T	P	T	P
Visually	96.5 (669/693)	95.2 (660/693)	98.0 (679/693)	97.0 (672/693)	0.0 (0/63)	1.6 (1/63)	1.0 (6/623)	1.0 (6/623)	1.2 (8/693)	2.0 (14/693)
Walk Away	96.4 (668/693)	92.8 (643/693)	97.8 (678/693)	95.2 (660/693)	1.6 (1/63)	3.2 (2/63)	0.3 (2/623)	3.0 (19/623)	1.7 (12/693)	1.7 (12/693)
auto SCAN-4	95.5 (662/693)	94.9 (658/693)	98.1 (680/693)	97.1 (673/693)	1.6 (1/63)	3.2 (2/63)	0.5 (3/623)	1.1 (7/623)	1.3 (9/693)	1.6 (11/693)

T = Turbidity inoculation method, P = Prompt* inoculation method

Reproducibility among the three sites were greater than 95% for all read methods for both turbidity and Prompt* inoculation methods. **Conclusion:** This multicenter study showed ceftolozane/tazobactam MIC results for *Enterobacteriaceae* and *Pseudomonas aeruginosa* obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels. * PROMPT is a registered trademark of 3M. © 2018 Beckman Coulter. All rights reserved. Beckman Coulter, the stylized logo and the Beckman Coulter product and service marks mentioned herein are trademarks or registered trademarks of Beckman Coulter, Inc. in the United States and other countries.

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Prevalence of MGUS and risk factor evaluation for progression to malignancy in a mexican population

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Background: Monoclonal gammopathy of undetermined significance (MGUS) is characterized by the presence of a monoclonal protein in the serum of asymptomatic individuals who do not meet the diagnostic criteria for other plasma cell disorders. It is defined as having <30g/L of a serum monoclonal protein, clonal bone marrow plasma cells <10% and the absence of end-organ damage that can be attributed to the plasma cell disorder. MGUS is present in approximately 3% of individuals aged 50 or older and increases with age. Whilst most MGUS patients have a stable condition and remain asymptomatic, a small proportion will progress to MM or a related B-cell or lymphoid cancer. This equates to a 1%-per-year lifelong risk of malignant transformation. The actual prevalence in Mexican population is unknown. **Objective:** To determine the prevalence of MGUS in the Yucatan population in Mexico and risk stratify when possible. **Methods:** We studied Yucatan native patients older than 30 years old from January 2015 until June 2017. An SPE (Interlab) was performed to detect M protein. All positive SPEs (monoclonal bands) samples were tested by IFE (Interlab) and Free Light Chains (FLC, Freelite, The Binding Site) according to manufacturer's instructions and using the suggested reference range for FLC ratio (0.26-1.65). **Results:** We analyzed 2053 serum samples (1020 men and 1033 women) and detected 61 cases of MGUS among them. The general prevalence rate was 2.97% in our population. 64% of them had an IgG M protein, 15% had an IgA M protein, 13% has an IgM M protein and we found an 8% of MGUS with only FLC as M protein. Thirty seven patients were further analyzed for risk stratification and FLC ratio analysis showed that 57% of samples had an abnormal FLC ratio. When all risk factors were analyzed (level of M protein ≥ 15g/L, M protein IgA or IgM and abnormal FLC ratio) we found that 24% of MGUS patients had no risk factors, 46% had 1 risk factor, 27% showed 2 risk factors and 3% had the 3 risk factors. The most repetitive risk factor in our study population was an abnormal FLC ratio, in 21 patients. **Conclusion:** For the first time, we were able to analyze MGUS patients in a Yucatan population, where the prevalence was found to be 2.97% which is different from general Mexican population according to the literature (Agarwal *et al.* Clin Cancer Res 2013). In our cohort, most MGUS patients showed to have 2 MM risk factors and

57% of Yucatan MGUS patients have abnormal FLC ratios, which is notably higher than the 33% reported for the general population (Rajkumar *et al.* Blood 2008). Whilst the 1% average annual risk of MGUS developing into MM or a related condition is well documented, progression among individual MGUS patients is highly variable. Therefore, recognition of risk factors for progression is of clear benefit. This allows the identification of patients at highest risk, which will benefit most from close monitoring. We hope to improve the rates of early diagnosis with this kind of studies.

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Incidence Of Microbial Colonization And Relevance Of Salivary IgA Estimation In Patients Receiving Chemo-Radio-Therapy For Head And Neck Cancer

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Background: Head and neck cancers make up 4-5% of all cancers. Radiotherapy (RT), on its own or in combination with other treatments like chemotherapy (CT), is an important option in many of these cancers. Microbial colonization/infection of damaged mucosal surfaces by mostly Gram-negative organisms and yeast is a common complication, and this may be exacerbated by concomitant neutropenia. Saliva consists of various chemical components, of which IgA has antimicrobial activity and prevents growth, adherence and aggregation of micro-organisms like various viruses, bacteria and fungi. Aim of this study was to determine the incidence of microbial colonization in Head & Neck cancer patients, post-chemotherapy/radiotherapy and to determine the contribution of levels of salivary immunoglobulin (IgA) on oral health.

Methods: We examined 150 salivary samples and oral swabs in 50 cases of diagnosed and operated head & neck cancer patients. Swabs & salivary samples were collected before patients were started with either chemotherapy or radiotherapy after their operations to remove the tumour, followed by at 3rd and 6th weeks after chemo/radiotherapy was started. Swabs were processed for microbial culture on blood agar and MacConkey agar. Salivary samples were processed for estimation of IgA on Siemens Dimension analyser using dedicated reagents. Results of microbial culture were documented and compared along with salivary sample reports in pre-chemotherapy and post-chemotherapy groups. Reference range for salivary IgA was considered as 12.43-33.53 mg/dl.

Results: Of 50 pre-chemo/radiotherapy samples 25 samples showed no growth, 17 samples showed bacterial growth of which Klebsiella pneumoniae was commonest. In 100 post-chemo/radiotherapy samples 33 samples showed no growth and 54 samples showed bacterial growth. When pre and post-chemo/radiotherapy groups were compared for values of IgA, salivary samples showing presence of Klebsiella pneumoniae infection showed significantly increased levels of IgA in post-chemo/radiotherapy group (p=0.0492). In all 150 samples examined, samples with Klebsiella pneumoniae infection (p=0.0022) and all bacterial infection samples (p=0.0426) showed significantly high levels of IgA. When compared to all samples with no growth, IgA levels were significantly high in Klebsiella pneumoniae infection group (p=0.001) and all bacterial samples group (p=0.0005). There was significantly increased incidence of bacterial infection in post-chemo/radiotherapy group (p=0.0233) compared to pre-chemo/radiotherapy group.

Conclusion: Post-chemo/radiotherapy, there is significantly increased incidence of bacterial infection in head & neck cancer patients. Salivary IgA with its anti-microbial property can be a marker for detection of early infection.

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An ELISA serum assay using monoclonal antibodies against Amyloid beta aggregates

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Alzheimer's disease (AD) is most common dementia. In recent years, the number of AD patients is increasing, because of an aging population. Early diagnosis of AD is desirable for early medical treatment to suppress the progression of the disease. A diagnosis of probable AD is made after medical assessments, and the definitive diagnosis is possible by examining brain tissue after death. Pathological hallmarks of AD brains are the formations of senile plaque (SP) which are mainly extracellular deposition of amyloid β (Aβ). The distribution of SP is classified into three Braak stages (stages A, B and C). Aβ also deposits on the blood vessels of the central nervous

system that is known as cerebral amyloid angiopathy (CAA). Neurofibrillary tangles (NFTs) are intracellular accumulation of hyperphosphorylated tau protein (p-Tau), and its distribution is classified into six Braak NFT stages (I to VI). The reliable biochemical diagnosis is currently low A β_{42} levels or elevated levels of p-Tau in cerebrospinal fluid surrounding brain. Here, 392 serums, including those of 376 AD patients and 16 control subjects, of definitively diagnosed individuals through post-mortem examination of the brain were assayed by ELISA. The utilized monoclonal antibodies were 77-3 and 37-11, which react specifically with conformational epitopes on soluble aggregates of A β_{42} having diameters greater than 20 and 220 nm, respectively. Using 77-3, higher values were obtained in serum samples from patients with Braak senile plaque stage B (n=24) than from those of the stages 0 (n=25) and C (n=53). Using 37-11, significantly higher than control values were detected in serum samples from patients with moderate-to-very severe cerebral amyloid angiopathy (n=42), a cerebrovascular disorder caused mainly by accumulation of A β . No significant differences of the values were detected when patients were classified based on Consortium to Establish a Registry for AD scores or Braak NFT stages. A commercial antibody (82E1) detected little A β monomer in sera. These results suggest that ELISA using these antibodies is useful for quick method of diagnosing AD using non-invasive serum.

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Evaluation of the performance of Candida Mannan IgG antibody lateral flow assay for rapid diagnosis of invasive candidiasis

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Background

Despite the recent achievement in disease management, invasive candidiasis is still a life-threatening disease that affects millions of patients worldwide. The objective of this retrospective study was to evaluate the clinical performance of newly developed Candida Mannan IgG lateral flow assay (LFA) in diagnosis of invasive candidiasis.

Material and Methods

Serum samples from 42 adult patients were retrospectively collected in this study. Twenty-three patients had at least one positive candida culture from blood or sterile body fluids, while 19 patients had no clinical signs of candida infection were defined as control group. All patients enrolled in this study were non-neutropenic or immunocompromised. Serum Candida-specific IgG antibody levels were determined by using Candida Mannan IgG antibody LFA (Dynamiker Biotechnology Ltd, China). An additional test was performed if the initial test was positive to confirm the results.

Results

Eighteen of the 23 patients with invasive candidiasis had positive Candida Mannan IgG results, while 5 patients were Candida Mannan IgG positive in control groups. All positive results were confirmed by additional LFA tests. The sensitivity and specificity of Candida Mannan IgG LFA were 78.2% and 73.6%, respectively.

Conclusion

The sensitivity of Candida Mannan IgG LFA was reasonable good, and the specificity was moderate. Considering it only takes 20 minutes to perform the test, the Candida Mannan IgG LFA may provide a rapid diagnostic aid in diagnosis of invasive candidiasis. Table 1 Evaluation of clinical performance of Candida Manna IgG LFA

	Candida Culture			
	Positive	Negative	Total	
LFA(IgG)	Positive	18	5	23
	Negative	5	14	19
	Total	23	19	42

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Prognostic Value of Pretreatment Albumin to C-reactive Protein Ratio in Patients with Hepatocellular Carcinoma

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Background: Despite the recent advances in hepatocellular carcinoma (HCC) treatment, the prognosis of HCC patients remains substandard. Recent evidence revealed that systemic inflammatory response markers play a key role in the prog-

nosis evaluation. The aim of this study was to investigate the prognostic value of the pretreatment Albumin to C-reactive Protein Ratio (ACR) in HCC patients. **Methods:** We retrospectively collected 409 newly diagnosed HCC patients and investigated the correlations among the pretreatment ACR, baseline clinicopathologic features, and overall survival (OS). We applied the X-tile software to determine optimal cut-off points for ACR. A chi-squared test was performed to compare baseline clinicopathologic features in different subgroups, Cox regression and log-rank tests to assess the association of ACR with OS, and Kaplan-Meier curves to estimate OS. **Results:** Patients with a lower ACR significantly associated with advanced clinicopathologic parameters and poor OS, with optimal cut-off points of 5.4 (high ACR, n=236 versus low ACR, n=173). Multivariate analysis demonstrated that ACR was associated with OS (hazard ratio (HR): 0.544, 95% confidence interval (CI): 0.385-0.769, p=0.001) along with tumor size (<5cm/≥5cm), TNM stage (IandII/IIIandIV), Treatment exposure (Hepatic resection/others), and serum AFP level (<400ng/L/≥400ng/L). **Conclusion:** Pretreatment ACR is a convenient and useful parameter for HCC patients predicting OS. Lower ACR was correlated with large tumor size, advanced TNM stage and a high concentration of AFP. If validated, these results may prove to be useful in designing strategies to personalize management approaches among these patients.

A-142

Comparison of Presepsin (PSEP) and Procalcitonin (PCT) for Risk Stratification in the Setting of a Cardiovascular Intensive Care Unit

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Background

PSEP concentrations have been shown to increase as a result of systemic inflammation triggered by bacterial infections. Clinical severity of sepsis and mortality risk can be predicted already by a single determination of PSEP at first presentation to the emergency department.

Objective

The purpose of our study was to investigate whether PCT and PSEP can contribute to detection of sepsis and risk stratification of critical patients from cardiovascular conditions admitted at the intensive care unit (ICU).

Methods

71 patients admitted at the ICU were included in the study. The study examined 4 patient groups: 0: patients with transfemoral implantation of a prosthetic aortic valve (TAVI) without evidence of infection or sepsis who served as control group (n=17), 1: patients with sepsis (n=20), 2: patients after sudden cardiac death and resuscitation (n=22), 3: patients with severe pneumonia requiring assisted ventilation (n=12). PSEP and PCT were determined at the time of admission to the ICU by using PATHFAST Presepsin (LSI Medicine Corporation, Tokyo) and cobas PCT BRAHMS (Roche Diagnostics). C-reactive Protein (CRP) was measured using the cobas assay (Roche Diagnostics).

Results

The patients with sepsis revealed higher PSEP and PCT values compared to the other patient groups. Discrimination between controls and sepsis revealed RO-AUC values of 0.924 and 0.967, respectively. 23 patients died and 28 patients developed acute kidney injury receiving dialysis. Non-survivors (n=23) and patients with AKI/Dialysis (n=28) showed significantly elevated values. The results are summarized in the table. As CRP is commonly used as inflammatory marker in the ICU we added the CRP values for comparison.

Conclusion

PSEP showed the best diagnostic performance and discriminative power and may be used for risk stratification in general in the ICU setting. PATHFAST PSEP can be determined in whole blood within 17 min and is suitable as POC assay in the ICU.

Summary of results						
	AKI, (N=28) Median (IQR)	Non-AKI, (N=43) Median (IQR)	RO-AUC	Non-survivors, (N=23) Median (IQR)	Survivors, (N=48) Median (IQR)	RO-AUC
PESP, ng/L	2293 (1290-3511)	634 (393-861)	0.855	2462 (1188-3706)	710 (508-1238)	0.798
PCT, ng/ml	8.95 (3.42-26.4)	0.29(0.07-4.27)	0.797	8.77 (3.34-39.4)	0.68 (0.08-6.18)	0.734
CRP, mg/dl	136 (47-204)	44 (13-132)	0.680	134 (50-201)	52 (14-141)	0.650
SOFA score	11.0 (8.0-13.0)	8.0 (1.010.0)	0.718	11.0 (9.0-13.0)	7.0 (1.0-10.0)	0.781

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Implementation of an innovative plasma separation technology enabling improved laboratory efficiency

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Background: Laboratories have many challenges in order to obtain high quality blood samples, generate accurate results and meet turnaround time (TAT) targets. Poor sample quality impacts laboratory operations and quality of results, often requiring manual remediation. A published survey indicated that with a 3% incidence rate, fibrin strands are one of the most common issues. Although some laboratories have implemented significant improvements, including the use of automation and plasma-based samples, challenges still remain. While potentially reducing fibrin-related issues, a change from serum to plasma gel samples has also historically meant reduced analyte stability due to entrapment of cells in plasma above the gel barrier and the potential for instrument interference from the gel remains. The BD Vacutainer® Barricor™ Plasma Blood Collection Tube (BD Barricor) uses an inert mechanical (non-gel) separator technology, creating a high quality plasma sample for a wide range of chemistry applications, with serum-like stability of up to 7 days for many analytes. As a historic serum user with laboratory automation, we partnered with BD to measure the efficiency and economic impact of implementing BD Barricor on a number of laboratory key performance indicators (KPI). **Methods:** A non-randomized, non-interventional, prospective observational study comprised of a 6-month pre-phase, with BD Vacutainer® SST™ II Advance Blood Collection Tube (BD SSTII) and a 6-month post-phase, with BD Barricor, conducted in the department of clinical chemistry of the Erasmus Medical Centre (EMC, Rotterdam, The Netherlands). For each phase, KPI which included TAT, defined as receipt in lab to result reported on lab information system (LIS), percentage of achieved STAT TAT goal, sample remediation activities and instrument maintenance and downtime were measured using data from the LIS and time and motion observations. Descriptive statistics and p values were determined to allow comparison of the two phases of the study. Metrics from the EMC lab were used to estimate the opportunity created as a result of the implementation of the new tubes. **Results:** 220,418 pre-phase and 228,796 post-phase tubes were assessed. Implementation of BD Barricor in the post-phase resulted in a TAT reduction of 11.16% across all tubes processed in the laboratory (2.6% for STAT and 13.2% in routine and external samples). This translated to an increase from 78% to 80% tests meeting the current STAT goal of 90 minutes. Sample quality was improved in the post-phase, with the incidence of fibrin, clot or gel-related issues reduced from 3.2% to 0.16%. Data extrapolated over 6 months indicated that there was a 94.8% reduction in remediation activities (7,009 incidences to 365). **Conclusion:** By implementing BD Barricor, we have seen improvements in chemistry sample quality, associated with reduced laboratory TAT and an increase in STAT TAT goal achievement. The enhanced efficiency through shorter TAT and reduction in fibrin, clots and gel-related issues provides an opportunity for the redeployment of valuable resources to other tasks, providing an economic benefit to the lab.

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The Prevalence Of Hypoglycemia In Geriatric Patients With Chronic Kidney Disease

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Background: An estimated 1 in 10 American adults suffer from some degree of Chronic Kidney disease (CKD), along with millions of others at an increased risk of acquiring the disease. The prevalence of CKD increases with age; and it is estimated that more than 40% of adult over the age of 60 years have some degree of CKD. It has been reported that patients with CKD have an increased chance for hypoglycemia than those without CKD. **Methods:** 28,000 specimens were collected from patients residing in long-term care facilities, 11,470 were male and 16,530 were female. Glucose and serum creatinine were measured using Roche/Hitachi P Modular; a eGFR was calculated based on MDRD equation using serum creatinine, age, gender, and race. Patients' data were separated into 5 groups based upon eGFR; and was analyzed further based on gender and age. The prevalence of patients with glucose <50 and <65mg/dL was calculated. Statistical analysis was done using Analyse-it. **Results:** 58% of the patients had eGFR >60 mL/min/1.73 m² and the percentage starts declining with age, to reach 23.3% of the patients in the >90 year old group. The prevalence of Glucose <50 mg/dL and <65 mg/dL increased with the decrease in eGFR. Patients older than 81 year old had the highest prevalence of low glucose.

eGFR mL/min/1.73 m ²	Total specimens	Glucose <50 mg/dL	Glucose <65 mg/dL
<15	787	5.3%	16.5%
15-29	2483	2.9%	11.2%
30-44	3813	2.4%	9.4%
45-59	4459	2.0%	8.9%
<60	16460	1.0%	9.1%

Conclusion: Hypoglycemia is more common in patients with a decrease in kidney function, which could be due to very tight glycemic control, a decreased insulin degradation in peripheral tissue, and a prolonged the life of antidiabetic medication due to a decreased renal clearance. Hypoglycemia should be suspected in patients with CKD who present with mental or neurological changes. In addition, diabetic management in these patients should be addressed very cautiously, and one may require adjustments for his or her oral hypoglycemic medication and insulin dosage.

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Combined approach for validation of the pneumatic tube systems

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Background: pneumatic tube system (PTS) is a major transportation route for delivering specimens to the laboratory throughout medical centers. This system offers several advantages such as improving the turn-around times and reduced cost and labor; however, it can cause pre-analytical variations by affecting the quality of blood samples due to acceleration forces, transportation speed, or lack of cushioning inside the sample carriers. In this study, we aim to validate PTS in a recently built hospital in the Emory Healthcare System as well as assess the performance of existing PTSs. **Methods:** we first collected the blood samples from 60 individuals in duplicates and transferred them to the Emory Core Laboratories, one sample via the PTS and one on foot. Samples were tested for 41 analytes. Statistical analysis of differences in obtained test values was performed using a paired Student *t*-test. Moreover, previous studies have shown that the three-axis acceleration/g-forces, time and distance have an impact on cell hemolysis. We utilized smartphone accelerometers and data-logger apps to compare the g-forces for the phone transferred to the laboratory on foot and via PTS route. **Results:** our results indicate a statistically and clinically significant increase in aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) levels while transported via the PTS. We applied sponge-rubber inserts inside the carriers to prevent the hemolysis during the transport, which significantly decreased the discrepancy found in LDH and AST values in samples carried via the PTS. The results from our cell phone study also showed that the highest impact on the samples that were hand-delivered (5 g) was at least 2 times less than the highest impact seen for samples transferred with PTS (11 g). In addition, hand-delivered samples did not have abrupt changes in g-forces compared to samples transferred via PTS. **Conclusion:** using a combined approach of testing clinical samples as well as assessing g-forces provides hospitals with more detailed assessment of the existing or newly built PTS.

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1/3 hours rule in and rule out algorithm for NSTEMI Using a High-Sensitivity Cardiac Troponin I at Emergency Department in Chinese Population

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Background: Acute myocardial infarction (AMI) is a leading cause of morbidity and mortality worldwide. Use of high sensitivity cardiac troponin (hs-cTn) assay can improve the early diagnosis of AMI, especially non-ST-elevation myocardial infarction (NSTEMI). Current European Society of Cardiology (ESC) guidelines recommend 0-1-hour and 0-3-hour 'Rule-in' and 'rule-out' algorithms for NSTEMI by using hs-cTn. However, it lacks Chinese population data based on such diagnosis process. Thus, this study is to validate 1-hour and 3-hours diagnostic strategy using hs-cTnI (ARCHITECT) in Chinese patients with suspected NSTEMI. **Methods:** From January to December in 2017, 283 patients with suspected ACS presenting to the emergency department were included. Patients aged 18-75 years without STEMI, major operation within 4 weeks, severe renal insufficiency (Cr <30 ml/min), acute myocarditis or chronic heart failure. Serial measures of hs-TnI level were performed at 0 hour, 1 hour and 3 hours in patients with suspected AMI. The diagnosis of each enrolled patient will be made according to routine clinical approach and 1-hour and 3-hours clinical approach, respectively. The routine clinical diagnosis will be made by cardiologist panel according to third universal definition of myocardial infarction through reviewing all available medical records. The NSTEMI diagnosis depended on hs-cTnI(Architect) assessment will be made a senior cardiologist according to 1-hour and 3-hours clinical approach recommended by 2015 ESC guidelines for the management of NSTEMI. Finally, the positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity are evaluated by using 0-1-hour and 0-3 hours algorithm. Statistical analyses were undertaken using MedCalc software version 15.2.2 (MedCalc Software, Mariakerke, Belgium). **Results:** The age of the study population was 59.5 years (95%CI, 58.2-60.8); 91 patients(32.2%) were diagnosed with NSTEMI. The hs-cTnI concentrations of patients with NSTEMI at 0h, 1h and 3h were significantly higher than non-ACS, 3.925ng/mg, 1.065 ng/ml and 0.908 ng/ml respectively. The 0-1-hour hs-cTnI change was 0.613ng/ml (95% CI, 0.321-0.906), and 0-3-hour hs-cTnI change was 3.011 ng/ml (95% CI, 0.283 - 5.740). The PPV of 1-hour algorithm was 91.0% and 97.4% for the 3-hours algorithm. The NPV of the 1-hour algorithm was 91.3% and 90.4% for 3-hours algorithm. The sensitivity and specificity was 92.9% and 89.0% for 1-hour algorithm, 87.4% and 98.1% for 3-hour algorithm. When using a baseline hs-cTnI concentration of 0.029ng/ml in male, the PPV is 87.5%, the NPV is 95.5, sensitivity is 93.33%, the specificity is 91.30%. While the PPV in female is 85.7%, the NPV is 95.7%, sensitivity is 92.31%, the specificity is 91.84% using the baseline hs-cTnI concentration of 0.021ng/ml. **Conclusion:** The diagnosis of NSTEMI based on hs-TnI in Chinese patients is similar with previous studies in European and American population. The application of absolute hs-TnI changes after 1 hour and 3 hours may facilitate rapid rule-in and rule-out of patients at Chinese emergency department.

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Circulating Soluble Urokinase-Type Plasminogen Activator Receptor (suPAR) Levels Reflect Renal Function in Newly Diagnosed Patients with Multiple Myeloma Who Are Treated With Bortezomib-Based Therapy

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Background: Renal impairment is a common complication of multiple myeloma. suPAR is the circulating form of a glycosyl-phosphatidylinositol-anchored three domain membrane protein that is expressed on a variety of cells, including immunologically active cells, endothelial cells, and podocytes. suPAR has been implicated in the pathogenesis of kidney disease, specifically focal segmental glomerulosclerosis and diabetic nephropathy, through interference with podocyte migration and apoptosis. We aimed to investigate a possible link between suPAR plasma levels and renal function decline in newly diagnosed patients with symptomatic myeloma before and after frontline therapy with bortezomib-based regimens. **Methods:** We studied 47 newly-diagnosed MM patients (26M/20F, median age 69.5 years) before the administration

of any kind of therapy and after best response to bortezomib-based therapy. Thirty(64%) patients had IgG-myeloma, 7(15%) had IgA and 10(21%) had light-chain only myeloma; 13(28%) patients had ISS-1, 19(40%) ISS-2 and 15(31%) had ISS-3 disease. Twenty-seven(57%) patients had eGFR<60 ml/min/1.73m², 23(49%) had eGFR<50 ml/min/1.73m² and 10(21%) had eGFR<30 ml/min/1.73m²; no patient was on dialysis. suPAR concentration was measured in the serum of all patients and of 24 healthy individuals by means of an immunoenzymatic assay (ViroGates, Denmark) along with a series of other blood chemistry markers: of renal function (Cystatin-C) and injury (NGAL); inflammation hs-CRP and IL-6; as well as parameters of cardiac function such as hs-Troponin-T and NT-proBNP. eGFR values were calculated based on CKD-EPI/Cystatin-C equation. **Results:** We found that suPAR levels were elevated in MM patients at diagnosis compared to healthy individuals (4.1±2.2pg/mL (1.4-13.0pg/mL) vs. 1.8±0.3pg/mL (1.1-2.6pg/mL), p<0.001). Similarly, all other markers of cardio-renal dysfunction and inflammation were elevated in MM patients compared to controls (p<0.01 for all comparisons). suPAR levels strongly correlated with disease stage (ISS-1: 2.4±1.2pg/mL; ISS-2: 3.6±1.8pg/mL and ISS-3: 5.1±2.2pg/mL; p-ANOVA <0.001). After bortezomib-based frontline therapy (VCD=32, VTD=7, VMP=7, VD=1), 9(19%) patients achieved a complete response (CR), 11(23%) very good partial response (vgPR) and 19(40%) PR. Of 23 patients with eGFR<50 ml/min/1.73m², 18(78%) showed at least minor renal response to bortezomib-based frontline treatment, according to IMWG criteria. However, at patients' best response no significance changes of suPAR (4.4±2.7pg/mL) levels were observed (p=0.31). On the other hand, suPAR levels both at diagnosis and at best response strongly correlated with eGFR values (r=-0.700, p<0.001 and r=-0.890, p<0.001, respectively) and NGAL levels (r=0.657, p<0.001 and r=0.586, p<0.001, respectively). suPAR levels at diagnosis and at best response also correlated positively with log(IL-6) and log(hs-CRP) values (p<0.001) and markers of cardiac function hs-Troponin-T and NT-proBNP (p<0.001). **Conclusions:** We conclude that suPAR levels are associated with renal function in patients with multiple myeloma both at diagnosis and at best response to bortezomib-based frontline therapy. Although suPAR correlates with disease stage, confirming previous observations, responders to anti-myeloma therapy continued to have elevated circulating suPAR, possibly reflecting persistent kidney damage, despite their renal response. Furthermore, suPAR correlated with the degree of inflammation and heart dysfunction in these patients. Future studies are needed in order to explore whether changes in suPAR may reflect increased risk for renal failure and/or progression in patients with multiple myeloma.

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Association of oxidative stress and inflammation with the markers of non-invasive peripheral arterial disease in metabolic syndrome

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Background: Oxidative stress and chronic inflammation contribute to the initiation, progression and thrombotic complications of peripheral arterial diseases (PAD). Ankle brachial pressure index (ABPI) and toe brachial pressure index (TBPI) are commonly used non-invasive markers for assessing PAD. The present study aims to find out if novel cardiovascular risk factors: oxidative stress, chronic inflammation and thrombotic markers, are associated with these non-invasive PAD markers in metabolic syndrome. **Methods:** One hundred volunteers with and without diagnosed diabetes and hypertension were recruited. Brachial, ankle and toe blood pressure and anthropometric measurements were performed. Toe brachial pressure was measured from the great toe using SysToe that uses photoplethysmographs. Ankle pressure was measured from the dorsalis pedis by the hand held Doppler probe. Inflammatory markers- hsCRP, thrombotic marker- D-dimer and oxidative stress markers- erythrocyte reduced glutathione (GSH), erythrocyte superoxide dismutase (SOD), and f₂-isoprostanes were analysed from the blood or urine sample of the participants. Data was analysed by IBM SPSS statistics 20. **Results:** 36 out of 100 volunteers were classified under metabolic syndrome using the National Cholesterol Education Panel, Adult Treatment Panel III definition. Jonckheere trend analysis showed that there was a significant linear increase in the level of the TBPI across the quartiles of GSH (p trend < 0.0005) and SOD (p trend = 0.009) and a significant linear decrease across the quartile of D-dimer (p trend = 0.007), whereas, ABPI showed a significant linear decrease across the quartiles of GSH (p trend = 0.012) only. ABPI and TBPI did not show any significant patterns across the quartiles of hsCRP and f₂-isoprostanes. TBPI was significantly correlated with GSH, SOD, f₂-isoprostanes, D-dimer and hsCRP among volunteers with metabolic syndrome. **Conclusion:** The findings of the present study underscore the potential mechanism of oxidative stress-driven progression of peripheral atherosclerotic disease. Association of ABPI and TBPI with D-dimer in metabolic syndrome group also indicates that increased activation of fibrinolytic system in metabolic syndrome may be associated with the development of PAD.

A-149**Viability assessment of in vitro fertilized embryos using a novel biomarker candidate.**

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Objective

Infertility is a spreading phenomenon worldwide resulting in an increasing need for assisted reproduction and *in vitro* fertilization procedures. Since multiple embryo transfer increases the prevalence of multiple gestation, single embryo transfer gains ground. Therefore, finding the embryo with the best implantation potential is crucial. In retrospective experiments a previously identified possible biomarker - the alpha-1 fragment of human haptoglobin (HptA1) - was quantitatively measured in spent culture media of *in vitro* fertilized human embryos.

Relevance

Non-invasive viability assessment from the culture medium of *in vitro* fertilized embryos provides an additional approach to select embryos with the best implantation potential. The field is still developing by mass spectrometric and proteomic approaches. The final goal of the described research is to adapt a complex mass spectrometric assay to a lab-on-a-chip measurement.

Methodology

The study involved 122 patients, aged 26-43 years (mean: 34.4±4.7 years) with a BMI of 17.9-31.6 (mean: 23.2±2.9) representing single and double embryo transfers. HptA1 in spent embryo culture medium samples (n=201) were measured using liquid chromatography coupled mass spectrometry (LC-ESI TOF MS) in retrospective, blind experiments. Haptoglobin and also HptA1 is present in the culture medium and the concentration increases during *in vitro* embryonic development. Embryos were diagnosed as “non-viable” by the mass spectrometric assay if the amount of HptA1 was elevated with more than 20% compared to the blank control medium, otherwise embryos were assigned as “viable”. Samples were divided into two groups: in the control group (n=102) embryos of the patients were assessed using the traditional morphological examination, while in the double-assay group (n=101) embryos were assessed by both the morphological and the mass spectrometric assays. Live birth rates were compared between the two groups.

Validation

In the control group, the embryos were only assessed by the Istanbul Consensus Criteria System (“good” or “fair”). 28 cases of live birth were observed out of 102 transfers meaning a live birth rate of 27.4%. In the double-assay group (n=101) samples of embryos were assessed as “good” or “fair” by the morphological assay as well as assessed “viable” by the mass spectrometric assay. 47 cases of live birth were observed meaning a live birth rate of 46.5%. The difference in the concentration of HptA1 according to outcomes “live-birth” and “no-birth” was significant (p<0.001). The clinical sensitivity was 100%, while specificity 55%, area under ROC curve was 0.906.

Conclusions

The increased amount of HptA1 in culture media samples of *in vitro* fertilized embryos negatively correlates with implantation potential. By combining the traditional morphological evaluation with the mass spectrometric assay, an increment in live birth rate was found in retrospective experiments. The HptA1 assay might serve as an additional tool to increase success rate of *in vitro* fertilization.

A-150**Evaluation of the Modified Carbapenem Inactivation Method for Carbapenemase Activity Assay in Carbapenemase-producing Enterobacteriaceae**

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Background: Carbapenems are commonly used as primary option for treatment of multi-drug resistant *Enterobacteriaceae*, that are often considered last-line antibiotics. The emergence and dissemination of carbapenemase-producing *Enterobacteriaceae* (CPE) are significant clinical in public health concern. Therefore, correct detection of CPE is essential for determining appropriate antimicrobial therapy and infection control measures to avoid spread and potential outbreaks. Although several tests are described for the screening and detection of carbapenemases, there are limitations in each method for identification of CPE, such as requiring special reagent or equipment. Clinical and Laboratory Standards Institute (CLSI) guidelines (M100-S27) reported modified carbapenem inactivation method (mCIM) has been developed in 2017 as a phenotypic technique for detecting carbapenemase activity. In this study, we evaluated the carbapenemase activity with mCIM for routine assay in laboratory to detect CPEs from clinical specimens.

Methods: The clinical specimens were collected from August 2011 to Dec 2017 and tested for drug susceptibility to imipenem, meropenem, and ertapenem using disk diffusion method. The production of carbapenemase was detected by mCIM that contents of a 10 µg meropenem (MEM) disk was degraded through carbapenemase activity when the disk was incubated in a bacterial suspension of CPE. MEM degradation was assessed by subsequently incubating the disk on a lawn of a sensitive *Escherichia coli* indicator strain. Using specific primers were confirmed carbapenemase genes (KPC, NDM, IMP, VIM, and OXA-48) by multiplex polymerase chain reaction (PCR). The mCIM results were compared with multiplex PCR.

Results: A total of 320 CPE clinical specimens was isolated and analyzed from En Chu Kong hospital in Taiwan. Among those bacterial strains, the most common species were *Klebsiella pneumoniae* (n=194), followed by *Escherichia coli* (n=40), *Morganella morganii* (n=30), and other species (n=56). We found out there were fifteen strains of KPC gene, nine strains of IMP gene, two strains of VIM gene, two strains of NDM-1 gene, ten strains of OXA-48 gene detected in samples, and one strain simultaneously expressed KPC and OXA-48 genes. All multiplex PCR positive strains showed carbapenemase activity by mCIM, except two false-negative results for OXA-48 producers (bacteria strains) that were further confirmed by sequencing and BLAST alignment of National Center for Biotechnology Information of the United States National Library of Medicine. CLSI guidelines reported mCIM > 99% sensitivity and specificity for CPE detection. In this study, the sensitivity and specificity of mCIM were up to 95% and 100%, respectively.

Conclusion: Our research showed higher performance (sensitivity/specificity) in mCIM for CPE detection which the test procedures are simple without special reagents, equipments, or technique. Thus mCIM is suitable screen test of carbapenemase activity assay in microbiological laboratories.

A-151**Clinical evaluation of a rapid fully-automated multiplex biochip array for Stroke diagnosis**

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Background: Stroke is a cerebrovascular event, which impedes or reduces blood supply to the brain resulting in localized cell death. Haemorrhagic stroke (HS) describes the rupture of a cerebral artery resulting in intracranial bleeding, whilst an ischemic stroke (IS) describes thrombotic occlusion in a cerebral artery resulting in ischemia. Transient ischemic attack (TIA) - defines a transitory disruption of the blood flow to the brain, which prevails for less than 24 hours. The accurate and timely diagnosis of stroke subtype is critical for determining an effective treatment strategy, which ultimately impacts patient prognosis and survival. However, accurate diagnosis and classification of stroke subtype currently presents a significant clinical challenge, and represents an unmet clinical need. Recent advances in clinical research have identified biomarkers with the potential to assist clinicians in diagnosing and classifying stroke. Radox presents a multiplex biochip array hosting a panel of 6 biomarkers - D-dimer, Soluble Tumour Necrosis Factor Receptor 1 (sTNF-R1), Parkinson disease protein 7 (PARK 7), Glial Fibrillary Acidic Protein (GFAP), Interleukin 6 (IL-6) and Fatty Acid Binding Protein 3 (FABP3) - aimed at the rapid diagnosis and differentiation of stroke. The aim of this study is to demonstrate the utility of a multiplex biochip array, incorporating a collection of novel biomarkers, to rapidly diagnose and differentiate stroke subtypes. **Methods:** A cohort of 192 samples (EDTA plasma) including 76 acute stroke patients following hospital admission (53 confirmed IS; 10 HS; 13 TIA), 37 stroke mimics and 79 controls were tested using the Radox Stroke Array. The methodology utilizes simultaneous chemiluminescent sandwich immunoassays immobilized at discrete test regions on the biochip surface. The array was applied to the new, fully automated Evidence Evolution analyser, which can produce the first set of results within 36 minutes, and one set of results per minute thereafter, enabling efficient, automated sample analysis. **Results:** Elevated biomarker levels were observed in stroke samples compared to normal controls - D-dimer (AUC = 0.957; p < 0.001), FABP3 (AUC = 0.926; p < 0.001), IL-6 (AUC = 0.917; p < 0.001), sTNF-R1 (AUC = 0.855; p < 0.001) and PARK 7 (AUC = 0.826; p < 0.001). Furthermore, the Radox Stroke Array successfully differentiated stroke patients from stroke mimics (e.g. hypoglycaemia, hyponatraemia, seizures, migraines, brain tumour, subdural haematoma or brain tumour) - D-dimer (AUC = 0.839; p < 0.001), FABP3 (AUC = 0.821; p < 0.001), IL-6 (AUC = 0.75; p < 0.001), PARK 7 (AUC = 0.852; p < 0.001) and sTNF-R1 (AUC = 0.78; p < 0.001). Significantly, plasma GFAP levels were increased in HS patients compared to IS patients (AUC = 0.902; p < 0.001) indicating the potential

of this marker to distinguish between IS and HS. **Conclusion:** These findings demonstrate that the Radox Stroke Array can be utilized to reliably diagnose and differentiate stroke subtypes, in an efficient manner using the fully automated, Evidence Evolution analyser. This advancement is poised to become an invaluable adjunctive diagnostic tool in the diagnosis and treatment of stroke.