

(GDM) were included in the analysis. Patients were started on insulin therapy (faster acting insulin aspart  $\pm$  basal insulin) once medical nutrition therapy for 2 weeks failed to achieve control, that is., fasting plasma glucose  $\geq 90$  mg/dL and/or 1.0 h postprandial plasma glucose  $\geq 130$  mg/dL. Basal insulin dose was titrated to achieve a fasting of 90-100 and the Faster aspart was titrated to achieve a post-meal of 120 and not exceeding 130. Patients were followed once every 4 weeks until the 28<sup>th</sup> week, then once every 2 weeks until 32<sup>nd</sup> week, then once every week until delivery, and the final visit was on  $30 \pm 7$  days after delivery of the child. **Results:** Out of 37 full term deliveries, only two had macrosomia. No congenital defects were noted in the anomaly scan and at births. There were no episodes of neonatal hypoglycemia reported. Only one episode of post-meal symptomatic maternal hypoglycemia was reported. Mean number of FiASP injections per day was  $2.88 \pm 0.39$ . Mean daily dose of FiASP used was  $22.7 \pm 6$  international units. A total of 89% of the patients received faster aspart thrice daily and remaining received it twice daily. **Conclusions:** Faster acting insulin aspart was found safe in pregnancy, however, more studies with double-blind, standard controlled studies are required to confirm the findings of this study.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINE CASE REPORTS II

#### *Long-Term Developmental Impact of Withholding Parenteral Nutrition in Pediatric-ICU:*

#### *A 4-Year Follow-Up of the PEPaNIC Randomized Controlled Trial*

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#### MON-LB012

**Aim:** Between 2012-2015, the PEPaNIC randomized controlled trial, which included 1440 critically ill infants and children, showed that withholding parenteral nutrition during the first week in the pediatric intensive care unit (PICU) (late-PN), as compared with initiating supplemental PN early (early-PN), improved PICU outcomes (1) and improved neurocognitive development assessed 2 years later (2). The latter was explained by avoiding early-PN induced adversely altered DNA-methylation of 37 CpG sites (3). As a large number of patients were younger than 1 year of age at randomization and given that assessment of most neurocognitive domains is only possible from 4 years of age onwards, we performed a 4-year follow-up to determine the impact of late-PN versus early-PN on physical, neurocognitive, and emotional/behavioral development. This pre-planned, 4-year follow-up study of the 1440 PEPaNIC patients and of 369 matched healthy children was blinded for treatment allocation (ClinicalTrials.gov-NCT01536275). **Methods:** Studied clinical outcomes included anthropometrics, health status, parent/

caregiver-reported executive functions, and emotional/behavioral problems, and clinical tests for intelligence, visual-motor integration, alertness, motor coordination and memory. Univariable and multivariable linear and logistic regression analyses adjusted for risk factors assessed the impact of late-PN versus early-PN on the outcomes and investigated a potential mediation role of the adversely altered DNA-methylation of 37 CpG sites previously shown to be evoked by late-PN as compared with early-PN (3). **Results:** Overall, at 4 years follow-up, patients (356 late-PN patients, 328 early-PN patients) could be tested neurocognitively. They revealed worse anthropometric, health status, neurocognitive and emotional/behavioral developmental outcomes than the healthy control children. Outcomes of late-PN patients were never worse than those of early-PN patients. In contrast, late-PN patients had fewer internalizing ( $P=0.042$ ) and externalizing problems ( $P=0.046$ ), and fewer total emotional/behavioral problems ( $P=0.007$ ) than early-PN patients, which were normalized by late-PN. Avoiding the early-PN induced adversely altered DNA-methylation status of the 37 CpG sites statistically explained its impact on the behavioral outcomes. **Conclusion:** Four years after randomization to late-PN or early-PN in the PICU, late-PN did not show harm, and was found to protect against emotional/behavioral problems, with altered DNA-methylation as a potential biological mediator hereof. These data further support de-implementation of PN-use early during critical illness in infants and children. (1) Fivez et al. N Eng J Med 2016 (2) Verstraete et al. Lancet Respir Med 2019 (3) Guiza et al. Lancet Respir Med 2020 (in press)

## Reproductive Endocrinology

### REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

#### *Assessment of Endothelial Dysfunction by Flow Mediated Dilation in Postmenopausal Women*

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#### MON-LB7

Menopause is defined by the World Health Organization as the permanent cessation of menses as a result of the loss of ovarian follicular function or surgical removal of ovary. Menopausal health demands priority in Indian scenario due to increase in life expectancy and growing population of menopausal women. It is well known that cardiovascular risk is higher in postmenopausal women than in premenopausal women, but it is unclear how much of the elevated risk is related to aging, menopause itself or presence of other confounding factors. Endothelial dysfunction is one of the most important predictors for determining early atherosclerotic risks as it precedes overt vascular disease by years and may itself be a potentially modifiable risk factor. Although no gold standard for the measurement of endothelial function exists, the measurement of flow mediated dilation (FMD) in the brachial artery, assessed with Doppler ultrasonography, is the most

studied method and seems most promising for clinical application. **Objective** - To compare effect of menopause on endothelial dysfunction by brachial artery flow mediated dilation (BAFMD) in postmenopausal women versus menstruating non-diabetic, non-obese females of same age group. **Methodology**: We conducted a case control study in Departments of Obstetrics & Gynaecology and Cardiology, PGIMER, Chandigarh. Subjects were menopausal women between 45- 55 years of age. Controls included the women of same age group who had not attained menopause. To detect a statistical significant difference of approximately 4-8% between cases and controls, 50 women were recruited in both groups with a power of 90% and confidence interval of 95%. The study was approved by the ethics committee of the institute. Effect of menopause on BAFMD, NMD (nitro-glycerine mediated dilation), FRS (Framingham Risk score) and individual components of FRS was studied. **Results**: A statistically significant negative correlation was found between BAFMD and FRS, BAFMD and age and BAFMD and duration of menopause. On studying the effects of FRS, individual components of FRS and duration of menopause on smooth muscle function, statistically significant negative correlation was found between NMD and FRS and NMD and Age. **Conclusion**: It was concluded that the menopausal status does not affect endothelial function in women who are at low risk of cardiovascular disease but it affects the vascular smooth muscle function. We also found significant correlation between FMD and NMD ( $p = 0.00$ ) signifying that both endothelial dysfunction and vascular smooth muscle dysfunction are inter-related. On evaluating the strength of correlation of FMD with FRS, different parameters of FRS and duration of menopause, FMD was found to have a statistically significant negative correlation with all these parameters.

## Thyroid

### THYROID NEOPLASIA AND CANCER

#### *Do Ultrasound Patterns and Clinical Parameters Modify the Probability of Thyroid Cancer Predicted by Molecular Testing in Thyroid Nodules With Indeterminate Cytology?*

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### MON-LB79

**Background**: Molecular testing (MT) is commonly used to refine cancer probability in thyroid nodules with indeterminate cytology. Whether or not ultrasound (US) patterns and clinical parameters can further modify the risk of cancer in nodules predicted to be positive or negative by molecular testing remains unknown. **Aim**: To test if clinical parameters, including age, gender, nodule size (by US), Bethesda category (III, IV, V), US pattern (American Thyroid Association [ATA] system vs American College of Radiology TIRADS), radiation exposure, and family history of thyroid cancer (TC) can modify the probability of TC or NIFTP predicted by MT in thyroid nodules with indeterminate cytology. **Methods**: We studied 257 thyroid nodules from 10 study centers with fine-needle aspiration (FNA) yielding indeterminate cytology and informative MT results using the ThyroSeq v3 genomic classifier (TSv3). Univariate and multivariate logistic regression were used for data analysis. **Results**: In this group of thyroid nodules, out of all parameters studied using univariate regression, patient gender, age, and Bethesda category were significantly associated with TC/NIFTP probability ( $P < 0.05$  for each). The ATA US patterns showed a positive trend ( $P = 0.1211$ ), whereas TIRADS was not predictive ( $P = 0.3135$ ). A multivariate regression model incorporating the four most informative covariates (gender, age, Bethesda category, and ATA US patterns) (model #1) yielded a C index = 0.653;  $R^2 = 0.108$ . Male gender and Bethesda category V significantly increased risk, and age demonstrated a nonlinear risk profile. When TSv3 was added to model #1, the C index increased to 0.888;  $R^2 = 0.572$ . However, age ( $P = 0.341$ ), Bethesda category ( $P = 0.272$ ), and the ATA US patterns ( $P = 0.264$ ) had limited predictive ability in comparison with TSv3, which dominated the predictive performance ( $P < 0.001$ ). Gender was the only parameter showing tendency for significance beyond MT ( $P = 0.095$ ). The most parsimonious model incorporated gender and TSv3 (C index = 0.889;  $R^2 = 0.588$ ). **Conclusions**: While often useful in selecting thyroid nodules for FNA, neither the ATA US nor the TIRADS scoring systems were informative in further predicting TC/NIFTP in thyroid nodules with indeterminate FNA cytology. Although age and Bethesda category were associated with TC/NIFTP probability on univariate analysis, they had limited incremental value above the high predictive ability of TSv3. Gender was the only parameter with potential contribution to predicting TC/NIFTP in addition to MT.

## Diabetes Mellitus and Glucose Metabolism

### CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

#### *FGF-21 Is A Reliable Marker Of Insulin Resistance Before The Occurrence Of Glucose Intolerance*

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