it had AUROCs of 0.73 and 0.74, sensitivities of 59.5 and 92.9, and specificities of 79.7 and 32.7. The Gholam score was developed in a sample of obese patients and uses aspartate aminotransferase (AST) and type 2 diabetes diagnosis. It had an AUROC of 0.82, a sensitivity of 0.76, and a specificity of 0.66. We performed multinomial logistic regression to compare each NASH population to the normal population (those with no or only mild HS). We identified 1236 subjects as having NASH by at least one method. 18% of these were identified by all 3 methods, while 20% were identified by 2 methods. All three methods identified significant risk factors for NASH ($p<0.05$) as being overweight or obese, having elevated AST or ALT levels, and having elevated C-peptide, serum glucose, or serum triglyceride levels. However, the HAIR and Gholam methods also identified being Mexican-American as a significant risk factor, with the NASH liver fat score did not. Being a former alcohol drinker and not meeting guidelines for physical activity were significant risk factors when using the NASH liver fat score. Further refinement of a noninvasive method for identifying NASH is required. Considerable care must be taken in interpreting risk factors, because the results differ depending which method is used. This could have implications in clinical practice as well, where patients and their risk factors may be mis-identified if formulas are used and not liver biopsy.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

Transient Neonatal Diabetes Mellitus Triggered by EIF2AK3 and PTF1A Mutation

Moon Bae Ahn, MD, Yoon Ji Lee, MD, Na Yeong Lee, MD, Seul Ki Kim, MD, Shin Hee Kim, MD, Won Kyoung Cho, MD, PhD, Kyoung Soon Cho, MD, Min Ho Jung, MD, PhD, Byung Kyu Suh, MD, PhD.
Catholic University of Korea, College of Medicine, Seoul, Korea, Republic of.

SAT-681

Background: Neonatal diabetes mellitus (NDM) occurs within the first 6 months of life. Advances in molecular genetics have identified various causatives genes. Mutations in *EIF2AK3* causes Wolcott-Rallison syndrome characterized by NDM, multiple epiphyseal dysphasia and growth retardation. *PTF1A* is associated with the development of pancreas and cerebellum. Both *EIF2AK3* and *PTF1A* mutations are causative genes for permanent NDM with spontaneous and autosomal recessive inheritance. We report a neonate with transient NDM with both *EIF2AK3* and *PTF1A* variants confirmed by Sanger sequencing where each parent found to be a heterozygous carrier of each mutation. **Case presentation:** A two-day old boy was transferred from a local hospital due to hyperglycemia (blood glucose of 385 mg/dL) and glycosuria. Serum c-peptide (0.06 ng/mL) and insulin (0.64 μU/mL) were low. The patient did not present sings of ketoacidosis and was screened negative for pancreatic autoantibodies. The patient did not have any family history of diabetes. Molecular genetic analysis was performed and continuous infusion of intravenous insulin with pre-prandial bolus was started. Oral sulfonylurea therapy was attempted to prevent adverse neurocognitive outcome however, it showed no response and unable to stabilize blood glucose level. Targeted panel sequencing identified two different novel variants: a heterozygous missense mutation (c.3272G>T) in exon 17 of *EIF2AK3* gene and heterozygous missense mutation (c.53C > T) in exon 1 of *PTF1A* gene; both of which have not been previously reported and were no likely pathogenic variants. The patient's father confirmed to be heterozygous carriers of the *EIF2AK3* mutation while mother being heterozygous carriers of the *PTF1A* mutation. Blood glucose level gradually began to stabilize with insulin therapy, and upon discharge the patient switched to continuous subcutaneous insulin infusion (pump) with continuous glucose monitoring. **Conclusions:** NDM caused by in combination of *EIF2AK3* and *PTF1A* gene mutation is a rare condition and could resemble the disease progress of transient form of NDM. Although hyperglycemia might not be an issue of lifelong period, early genetic screening and prompt insulin initiation with consistent glucose monitoring are able to prevent further diabetic complications. In addition, the result of genetic testing in our patient raises the possibility of NDM as polygenic form of diabetes.

Diabetes Mellitus and Glucose Metabolism

ISLETS, LIVERS, PLACENTA, AND VASCULATURE — THE MULTITISSUE IMPACT OF DIABETES

Circadian Regulation of Chromatin State Mediates Pancreatic Islet Incretin Response

Benjamin John Weidemann, BS[1], Mikoto Alfred Kobayashi, Diploma[2], Biliana Marcheva, PhD[1], Joseph T. Bass, MD,PHD[1].
[1]Northwestern University, Chicago, IL, USA, [2]Grinnell College, Roselle, IL, USA.

OR14-02

Circadian Regulation of Chromatin State Mediates Pancreatic Incretin Response

The circadian clock is programmed by an autoregulatory transcription feedback loop present in brain and peripheral tissues that coordinates metabolism with nutritional state and the sleep-wake cycle. Epidemiologic and genetic studies indicate circadian disruption as a risk factor in the development of diabetes. We have demonstrated that conditional ablation of the β cell clock in adult life leads to hypoinsulinemic diabetes, and through mRNA-sequencing in mouse and human islets we revealed clock control of gene networks involved in insulin secretion, nutrient sensing, and exocytosis. A remaining question is: How does the core molecular clock modulate time-of-day dependent chromatin state to regulate pancreatic islet response to glucose and insulin secretagogues? Here we report that loss of the pancreatic β cell molecular clock results in closed chromatin at cAMP-responsive gene regulatory elements and dysregulated cAMP-dependent coregulator recruitment following cAMP agonism, consistent with a role for the molecular clock in mediating cell response to environmental stimuli. Further, tandem analyses of ATAC- and ChIP-sequencing in synchronized islets revealed dynamic chromatin accessibility across the 24-hour cycle at genes regulating insulin secretion and at genomic regions