of NAFLD has not been studied. **Objective:** To study the fetuin-A levels in patients with NDD and its correlation with NAFLD. **Methods:** A total of 60 newly diagnosed type 2 diabetes (NDD) were studied. Diagnosis of NAFLD was made on the basis of transient elastography. Serum fetuin-A and serum fasting insulin were measured along with other investigations. **Results:** Percentage of patients with NAFLD in NDD was 53.33%. Fetuin-A levels were significantly higher in NDD with NAFLD compared to those without NAFLD. There was no association of fetuin-A with age, both systolic and diastolic blood pressure, FBS, HbA1c, fasting insulin, HOMA-IR, QUICKI and markers of advanced fibrosis. Fetuin-A levels beyond 1166.5 mcg/ml could predict the development of NAFLD with OR of 4.33 (95%CI:1.364–13.77) which remained significant after adjustment for various confounding factors. **Conclusion:** Fetuin-A is a reliable marker of NAFLD in NDD and is positively associated with IR. The observation in this study suggests that high serum fetuin-A levels in patients with NAFLD do not merely reflect the effects of insulin resistance, but also a more extensive distortion of liver architecture.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS AND COMORBIDITIES

Glycemic Control & Morbidity in Diabetics With COPD Exacerbation. A Retrospective Study.

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Background: Diabetes and chronic obstructive pulmonary disease (COPD) are widely prevalent and comorbidity with these diseases is quite common. However, there is limited data on the interrelation between glycemic control and COPD exacerbations in diabetic patients.
Objective: To study the association between pre-admission glycemic control and COPD clinical outcomes including mortality, risk of hospital readmission and the need for mechanical ventilation.
Methods: A retrospective population-based cohort study. We screened for patients with both diabetes and COPD exacerbation aged 35 years and above. Pre-admission glycemic control was defined by the last HBA1C level prior to hospitalization. Patients with HBA1C>8% were defined as uncontrolled. We evaluated the difference between controlled and uncontrolled groups in the rates of mortality, readmission and the need for mechanical ventilation. We examined demographic and clinical parameters that might reflect COPD severity including: COPD medication use, blood hemoglobin, platelets, LDH and CRP levels.
Results: 513 hospitalizations with diabetes and COPD were screened. 222 hospitalization were excluded either due to unestablished diagnosis of COPD or due to lack of HBA1C test in the preceding year. Of the remaining 291, 208 admissions were with controlled diabetes whereas 83 were uncontrolled. Although not statistically significant, the rate of re-hospitalization was higher in the uncontrolled group (OR 1.99, CI 0.99–4.0, p-value 0.051). There was no statistically significant difference in mortality (OR 1.6, CI 0.73–3.5, p-value 0.243). The use of oxygen and the need for noninvasive mechanical ventilation were significantly higher in the uncontrolled group (67.5% *vs.* 52.4%, p-value 0.019, 33.7% versus 18.8%, p-value 0.006, respectively). There was no significant difference in possible confounders tested between the groups.
Conclusion: Uncontrolled diabetes may adversely affect patients with COPD exacerbation. Larger studies are needed to conclusively determine the impact of glycemic control on COPD morbidity and mortality.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS AND COMORBIDITIES

Hyperglycemia Regulated Circulating MicroRNAs and Their Effects on Renal Function Decline in Type 2 Diabetes

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Background: It has been reported that microRNAs (miRNAs) play an important role in the pathogenesis of diabetic complications. We aimed to search for circulating miRNA that were associated with hyperglycemia in type 2 diabetes and examine their effects on renal function decline.
Methods: Using the next-generation sequencing-based HTG EdgeSeq miRNA platform, a total of 2,083 miRNAswere measured in baseline plasma specimens obtained from73 subjects with type 2 diabetes (T2D) and normal renal function (discovery panel) and 136 subjects with T2D and impaired renal function (replication panel). Subjects in both panels were followed for 6–12 years to determine eGFR decline. **Results:** We identified 11 candidate miRNAsthat were strongly associated with elevated levels of glycated hemoglobin (HbA1c) in both screening and replication panels. Using bioinformatics analyses, we found that the candidate miRNAs targeted proteins of 6 pathways (the Ras signaling pathway, Signaling pathways regulating pluripotency of stem cells, the MAPK pathway, Glutamatergic synapse, the Rap 1 signaling pathway, and the AMPK signaling pathway). Importantly, 4 of these 11 miRNAs were significantly associated with risk of renal function decline.
Conclusion: There were few previous reports about the association between circulating miRNAs, hyperglycemia, and diabetic kidney disease in T2D. The present study comprehensively examined and identified hyperglycemia-regulated miRNAs in human samples. Our finding are novel in that circulatingmiRNAsregulated by hyperglycemia are associated with risk of eGFR decline in T2D.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS AND COMORBIDITIES

Identification of ANXA2 as a Potential Susceptibility Gene for Diabetic Retinopathy in a Genome-Wide Association Analysis in Chinese Patients With Type 2 Diabetes Mellitus

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Background: Diabetic retinopathy (DR) is the most frequent microvascular complication of type 2 diabetes mellitus (T2DM). Variation in allele frequencies between different ethnic groups may influence the detectability of the risk variants in different populations. It is therefore important to conduct ethnic-specific association analysis to discover novel loci. The major objective of this study was to conduct a 2-stage genome-wide association study (GWAS) to identify novel susceptibility single nucleotide polymorphisms (SNPs) for sight-threatening DR in Chinese patients with T2DM.

Methods and Materials: The discovery stage consisted of 681 STDR cases and 758 non-STDR controls of Southern Chinese ancestry. The Illumina Infinium Asian Screening Array (ASA) was used for genotyping of the subjects. Imputation was performed using the TOPMed Imputation Server. SNPs with minor allele frequency (MAF) <0.01 and INFO score <0.3 were excluded. Single variant association analysis was performed in SNPTEST using the multiple logistic regression model with adjustment for age, gender, duration of diabetes, hypertension, hemoglobin A1c (HbA1c), and the first five principal components. The replication cohort was comprised of an independent sample set of 278 STDR cases and 834 non-STDR controls. Meta-analysis of the association results of the discovery and replication stages was conducted using the "GWAMA" software. The inverse variance fixed-effect method was used to meta-analyze the summary statistics of the two stages.

Results: In the discovery stage, the strongest association was detected at an intronic variant of *ANXA2* ($P=1.87\times10^{-7}$; OR[95%CI]:1.59[1.31–1.96]). Ninety-three SNPs showing suggestive associations ($P<5\times10^{-5}$) with STDR in the discovery stage were selected for replication. In the meta-analysis of the two stages, the *ANXA2* SNP again showed the strongest association with STDR ($P=2.18\times10^{-6}$; OR[95%CI]: 1.45[1.24–1.70]). *ANXA2* encodes the annexin A2 which has been shown to play an important role in promoting angiogenesis. An intronic SNP of *DOC2B*, a tumor suppressor gene that exhibits functions in cell proliferation and migration, also demonstrated a marginal association with STDR ($P=5.17\times10^{-6}$; OR[95%CI]: 1.41[1.22–1.63]). Two intergenic variants located at the *RPL31P11-FCRLA* ($P=7.25\times10^{-6}$; OR[95%CI]: 1.54[1.27–1.85]) and *COL6A1-COL6A2* ($P=9.60\times10^{-6}$; OR[95%CI]: 0.73[0.63–0.84]) loci also showed suggestive associations with STDR.

Conclusion: Several novel STDR-associated genetic variants were identified in this genome-wide association study. Our findings have shed new lights on the genetic basis of STDR in Chinese patients with T2DM. Further validation in independent cohorts to validate our findings are warranted.

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DIABETES COMPLICATIONS AND COMORBIDITIES

Immune Checkpoint Inhibitor Mediated Insulin Dependent Diabetes: Observations at a Cancer Center

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Immune checkpoint inhibitors (ICIs) have rapidly changed the landscape of oncologic care and are now often used in the front line setting for many types of cancers. These agents attempt to harness the immune system to target cancer cells (ICIs) by releasing inhibition of T cell response against tumor cells. With increasing use of ICIs, a new spectrum of immune-related adverse events (irAEs) has emerged including a number of endocrinopathies. A distinct form of ICI-mediated insulin dependent diabetes (ICI-DM) has become increasingly recognized. To better characterize this disease entity and longer-term consequences, we performed a retrospective review of medical records of patients diagnosed with ICI-DM between April 2014 and July 2020 at the MD Anderson Cancer Center. This cohort of 68 patients represent the largest single institution cohort described to date. Baseline characteristics of our cohort are consistent with what has been reported in other case series and meta-analyses with median age at presentation 61 years old (range 32–83 years old), slight male predominance (59% vs 41%), and strong association with anti-programmed cell death protein 1 (anti-PD-1) therapy (59%). Melanoma was the most commonly represented underlying malignancy (29%). The majority of patients (66%) presented with diabetic ketoacidosis. At presentation, median HbA1c was 7.8 % (n < 5.7%) and median C-peptide was 0.2 ng/ml (range <0.1–3.4). Pancreatic autoantibodies were present in 49% of patients. Median insulin dose was 0.54 units per kg per day[T1] (range 0.25 to 1.07 units per kg) at first follow up suggesting these patients may have varying levels of insulin sensitivity[T2]. On most recent follow up at a median[T3] of 40 weeks (range 8 to 261 weeks), median HbA1c was 7.9% and median insulin requirement remained 0.54 units per kg (range 0.14 to 1.2 units per kg). 22% of patients were on insulin pump therapy[T4]. ICI-DM is an irreversible immune-related adverse endocrinopathy characterized by frequent presentation with fulminant hyperglycemia and DKA, persistent beta cell dysfunction necessitating long term insulin therapy and mixed evidence of beta-cell autoimmunity. Median insulin requirement was