PP-D-19

MUTATION SPECTRUM OF MONOGENIC DIABETES IN SINGAPORE

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Su Fen Ang,[1] Li Xian Goh,[1] Lovynn Wan Ting Chan,[1] Winston Yin Chian Kon,[2] Rashida Vasanwala,[3] Wann Jia Loh,[4] Su Chi Lim[1,5,6,7]

[1]*Khoo Teck Puat Hospital, Singapore*
[2]*Tan Tock Seng Hospital, Singapore*
[3]*KK Women's and Children's Hospital, Singapore*
[4]*Changi General Hospital, Singapore*
[5]*Diabetes Centre, Admiralty Medical Centre, Singapore*
[6]*Saw Swee Hock School of Public Health, Singapore*
[7]*Lee Kong Chian School of Medicine, Singapore*

OBJECTIVES

Monogenic diabetes, a rare condition known to affect about 5% of young-onset diabetes, is not routinely investigated in our local population with diabetes. The NHG-KTPH Monogenic Diabetes Registry was set up in 2017 to study the prevalence of monogenic diabetes in Singapore as well as determine the underlying mutations responsible for this condition to facilitate the application of precision medicine to this group of individuals.

METHODOLOGY

Young-onset (≤35 years) individuals with atypical diabetes were enrolled into our monogenic diabetes study and subjected to genetic testing using 16-gene next-generation sequencing, mt.3243A>G TaqMan genotyping and multiplex-ligation dependent probe amplification (for HNF1A, HNF4A, GCK, HNF1B). Variants identified were annotated according to guidelines from American College of Medical Genetics and Genomics (ACMG). Likely pathogenic/pathogenic variants were validated using bi-directional Sanger sequencing.

RESULTS

Among 340 probands sequenced, 43 (12.6%) had a likely pathogenic/pathogenic variant in one of these 8 genes: HNF1A (27.9%), HNF4A (25.6%), GCK (16.3%), mt.3243A>G (16.3%), HNF1B (4.7%), ABCC8 (4.7%), PAX4 (2.3%) and NEUROD1 (2.3%). Most (95.3%) of the variants occurred in genes which are clinically actionable. Mutation-positive cases are mostly female (67.4% vs 49.8%, p=0.031), have lower BMI (median 24.9 vs 22.4 kg/m^2, p<0.001), lower waist circumference (74.0 vs 82.0 cm, p<0.001), higher HDL (1.41 vs 1.26 mM, p=0.003), lower triglycerides (0.95 vs 1.39 mM, p=0.005), lower C-peptide (506.2 vs 819.8 pM, p=0.013), lower hsCRP (0.70 vs 1.40 mg/L, p=0.007) and lower uric acid (5.45 vs 6.41 mg/dL, p=0.007) than mutation-negative cases.

CONCLUSION

Monogenic diabetes is non-trivial in our local population of young-onset atypical diabetes. The combination of clinical parameters and biomarkers can be explored to improve selection of individuals for genetic testing. This facilitates early and accurate genetic diagnosis of monogenic diabetes that can better inform clinical management.

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REGIONAL DISPARITIES IN THE PREVALENCE OF DIAGNOSED DIABETES IN RURAL VS. URBAN UNITED STATES, 2004–2019

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Sagar Dugani,[1] Brian Lahr,[1] Hui Xie,[2] Michelle Mielke,[3] Kent Bailey,[1] Adrian Vella[1]

[1]*Mayo Clinic, Rochester, United States*
[2]*Centers for Disease Control and Prevention, Atlanta, United States*
[3]*Wake Forest University, Winston-Salem, United States*

OBJECTIVES

United States (US) rural, compared to nonrural populations have less access to diabetes care. It is unknown if rurality also contributes to disparities in the prevalence of diabetes. The study objective was to evaluate the trend in US prevalence of diabetes from 2004–2019 by county-rurality and region.

METHODOLOGY

We used US Centers for Disease Control and Prevention (CDC) data on prevalence of diagnosed diabetes in adults aged ≥20 years, available for 97.6% of US counties (3147/3226) from 2004–2019. Trends in annual age-adjusted prevalent diabetes rate per 100 adults (AAPR) were assessed by weighted least squares regression. Year was fitted with a spline function, and AAPR change was tested by a model-based comparison of 2019 vs. 2004.

RESULTS

The overall AAPR increased from 6.5 (per 100) in 2004 to 8.4 in 2011 and 8.8 in 2019. The 2019 vs. 2004 percentage-increase (95% confidence interval) was present at all rurality levels: 33% (27%–40%) for noncore counties (most rural), 38% (37%–38%) for large fringe metro counties (second most urban), and 35% (35%–35%) for large central metro counties (most urban) (all, p<.001). Stratified by region, the AAPR percentage-increase was lowest in the Northeast (30% [28%–33%]; p<.001) and highest in the South (40% [39%–41%]; p<.001).

CONCLUSION

The US prevalence of diabetes increased from 2004 to 2019 across all county-rurality levels. This study revealed a worsening trend in the South vs. other regions, which may highlight areas for interventions to reduce diabetes incidence.