# INTERNATIONAL SUMMIT ON DIABETES, ENDOCRINOLOGY, AND METABOLIC DISORDERS

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## Exploring the Severity and Early Onset of Familial Type 1 Diabetes in Romania: Genetic and Microbiota Insights

### Abstract:

#### Background

Type 1 Diabetes Mellitus (T1DM) is a chronic autoimmune disorder characterized by the destruction of insulin-producing beta cells. Familial T1DM (FT1DM) is associated with greater severity and earlier onset, particularly in cases with paternal inheritance. Research Question:To explore the association between specific HLA haplotypes, gut microbiota dysbiosis, and the severity of FT1DM in Romanian children.

#### Methods

Among 350 adult and pediatric T1DM patients evaluated, three Romanian families with FT1DM were studied between 2019 and 2021. Clinical, biological, and genetic assessments were performed, including high-resolution HLA typing and gut microbiota profiling through 16S rRNA sequencing. Data analysis focused on identifying genetic predispositions and dysbiotic patterns linked to disease onset and progression.

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**Results:**

Children with FT1DM displayed a severe onset, with a median age of 9 years and frequent diabetic ketoacidosis. Genetic analysis highlighted a strong presence of high-risk HLA haplotypes: DRB103:01-DQA105:01-DQB1\02:01 (DR3-DQ2) and DRB104:01/02/04/05/08-DQA103:01-DQB1\03:02/04 (DR4-DQ8) significantly associated with aggressive glycemic profiles. Notably, the protective allele DPB1*04:01 was exclusively found in sibling FT1DM cases. Gut microbiota analysis revealed marked dysbiosis, characterized by increased Enterobacteriaceae and Candida spp., alongside reduced populations of protective taxa such as Akkermansia muciniphila and Bifidobacterium spp.These microbial imbalances were correlated with heightened inflammation and disrupted gut barrier integrity.

**Conclusion:**

The first comprehensive evaluation of genetic and microbiota factors in Romanian FT1DM patients. The findings underscore the combined impact of specific HLA haplotypes and gut dysbiosis on the accelerated onset and severity of FT1DM. Early genetic screening and microbiota-targeted interventions may represent effective strategies for delaying disease progression and mitigating complications in high-risk pediatric populations.

**Keywords:** familial type 1 diabetes; pediatric diabetes; case series; microbiota

**Biography:**

Amalia Ioana Arhire, MD, PhD, is a specialist in Endocrinology, Diabetes, Nutrition, and Metabolic Diseases, and the visionary co-founder of Kilostop Junior, Romania's first pediatric nutrition and obesity clinic. She earned her PhD in Medicine in 2024 from "Carol Davila" University of Medicine and Pharmacy, with groundbreaking research on the genetic and microbiota determinants of familial Type 1 Diabetes. With over a decade of clinical expertise and a commitment to innovation in pediatric health, Dr. Arhire is dedicated to transforming children's lives through evidence-based interventions and personalized nutrition strategies, with over 20 articles and presentations in pediatric endocrinology and diabetes.

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