The Genetic Causes and Phenotypic Characteristics of Egyptian Patients with Neonatal Diabetes Mellitus

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Introduction

Neonatal Diabetes Mellitus (NDM) is a rare form of monogenic diabetes that typically presents during the first 6 months of life. Its prevalence is about 1:100,000 live births[1]; however it may rise up to 1:29,000 in highly consanguineous populations[2]. Mutations in 21 different genes are reported as well as methylation defects at the 6q24 locus; with the most common cause being potassium channel subunit gene (*KCNJ11/ABCC8*) mutations[3].

Causative mutations among consanguineous populations seem to differ. Studies on NDM in these populations are still limited.

Aim

To identify the genetic causes among a group of Egyptian patients with NDM and to describe their clinical phenotypes.

Materials and Methods

A cohort of 16 patients from different areas of Egypt from 2012-2016

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Diabetic neonates <6 months, attending the Diabetic Endocrine and Metabolic Pediatric Unit (DEMPU) of Cairo University Children's Hospital

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Parental consent and ethical approval obtained
Data collection, physical examination and sampling

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Sequence Analysis for
ABCC8, KNCJ11,INS and *EIF2AK3* genes

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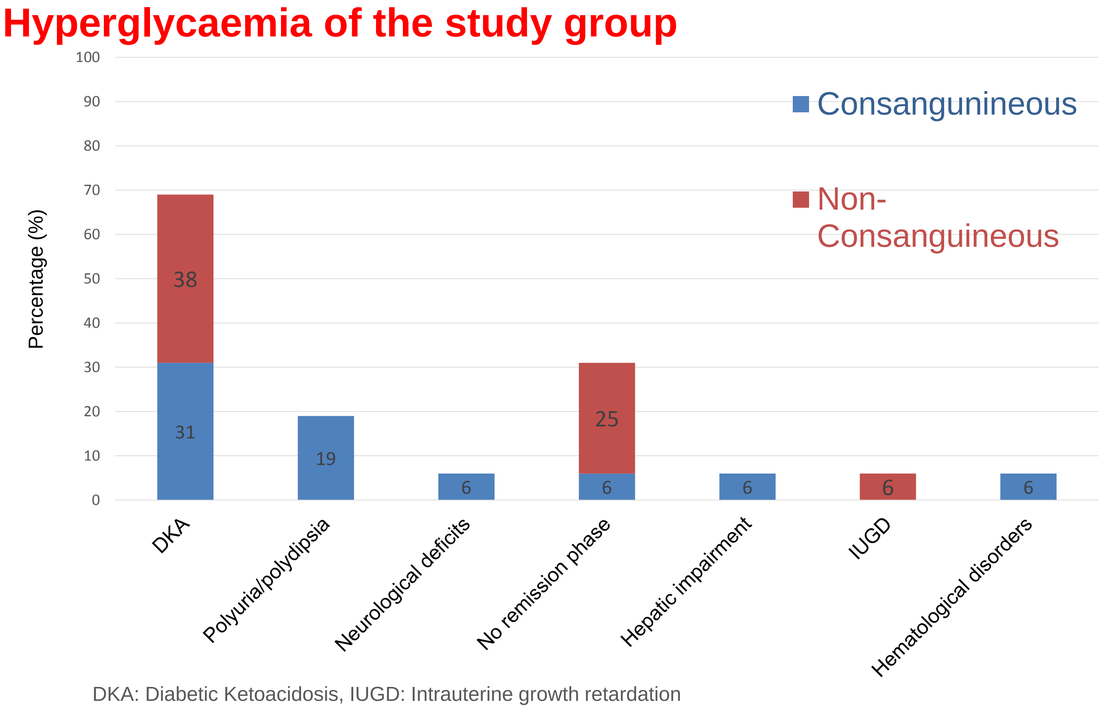
Targeted sequencing
According to the presenting phenotype

Results

Patients demographic data

Male/Female, (n)	Mean Age of Onset (months)	Mean Gestational Age (weeks)	Mean Birth Weight (g)	Mean Plasma Glucose Level at Onset (mg/dl)	Mean HbA1C Level (%)	Mean Insulin Dose at onset (U/kg/day)	Positive Family history of DM, n (%)	Consanguinity, n (%)
10/6	2.6	37	2500	529	8.2	0.7	9 (56%)	10(62.5%)

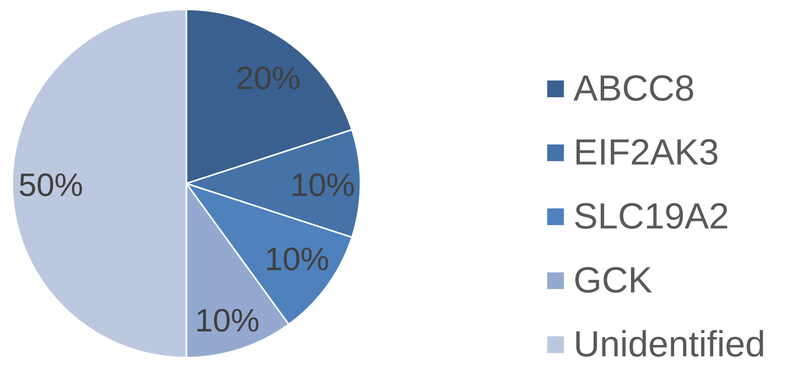
Clinical presentations associated with Neonatal Hyperglycaemia of the study group



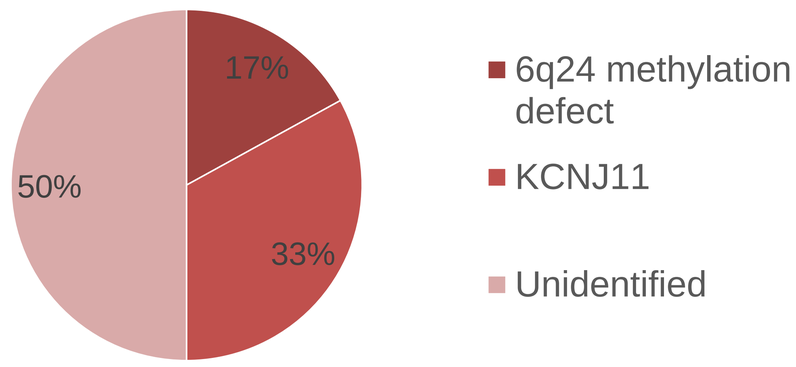
DKA: Diabetic Ketoacidosis, IUGD: Intrauterine growth retardation

Genetic causes of Neonatal Diabetes in the study group

Consanguineous group (10/16, 62.5%)



Non-consanguineous group (6/16, 37.5%)



Conclusion

- The genetic causes identified among the studied group were heterogeneous.
- Potassium channel subunit gene mutations were identified in 25% (4/16) of the total studied group, which is less than the reported percentage in European populations.
- A variable spectrum of clinical phenotypes were associated, however diabetic ketoacidosis was the most common presentation.
- Syndromic forms of NDM were more identified in the consanguineous group.

Acknowledgment

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Declaration of interest

None of the authors have any conflict of interest to declare

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