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INTRODUCTION

In this study we investigated mortality in children with monogenic diabetes (neonatal DM (NDM) and MODY).

METHOD

Within the Ukrainian Pediatric Diabetes Register (UPDR) the number of children 0-17 y.o. in 2019 with:

*DM1 was 9860 (1 in 769),
DM2 - 36 (1 in 210,547),
NDM - 65 (1 in 115,000),
MODY - 40 cases (1 in 114,844).*

We used targeted next generation sequencing (tNGS) of all known NDM genes in any child diagnosed in the first 9 months of life and all known MODY genes in those who was diagnosed after 9 months of life.

RESULTS

Among 106 children with monogenic diabetes 9 patients died to date (8.5%). Eight of them (88.8%) had NDM.

We found 3 patients with autoimmune monogenic diabetes mellitus (ADM) with mutations in *AIRE*, *FOXP3* and *LRBA*, two of whom had NDM (hemizygous *FOXP3* p.R347H and homozygous *LRBA* p.Glu946Ter). 2 children with ADM/NDM died before age 1 year, and the patient with *AIRE* p.Cys311fs/p.Arg257Ter died at 15 years. He was admitted to ECU with hypoparathyroidism and died due to severe dyselectrolythemia (Ca 1,2 mmol/l), ischemic stroke and myocardial infarction. The patients with *FOXP3* and *LRBA* died due to respiratory insufficiency and intestinal gangrene respectively. In both NDM cases results of genetic testing were obtained after death.

The patient with a homozygous *IPF1* c.1A>G mutation, was diagnosed with NDM at the age of 6 days and died at 6 months due to cytolysis syndrome, cholestatic hepatitis, sepsis and systemic multiple organ failure.

The patient with *INSR* p.Tyr94*/p.Arg1020* was diagnosed with NDM at the age of 1 month and died at age 4 months and 13 days due to systemic multiple organ failure.

Two NDM patients with *EIF2AK3* (p.D164fs/p.E421fs and homozygous p.G1010V) died at an early age. The patient with *EIF2AK3* p.D164fs/p.E421fs was diagnosed with diabetes at the age of 13 weeks and died at 3 months due to cerebral edema. The patient with *EIF2AK3* p.G1010V had multiple inpatient admissions due to cytolysis syndrome and died at age 2y 2 months due to systemic multiple organ failure.

Two siblings with NDM and *ABCC8* p.I49F died at the age 5 and 9 y.o., where 5 y.o. girl died because of pneumonia (had also severe rickets and curvature of the chest) and her 9 y.o. brother died within 1 day after admission to the ECU because of hypertermia, cytolysis syndrome and systemic multiple organ failure.

CONCLUSIONS

Whilst ADM, *EIF2AK3* and *INSR* are described as a well known cause of death in patients with monogenic diabetes, the cause of death in patients with *IPF1* and *ABCC8* has not yet been widely described.

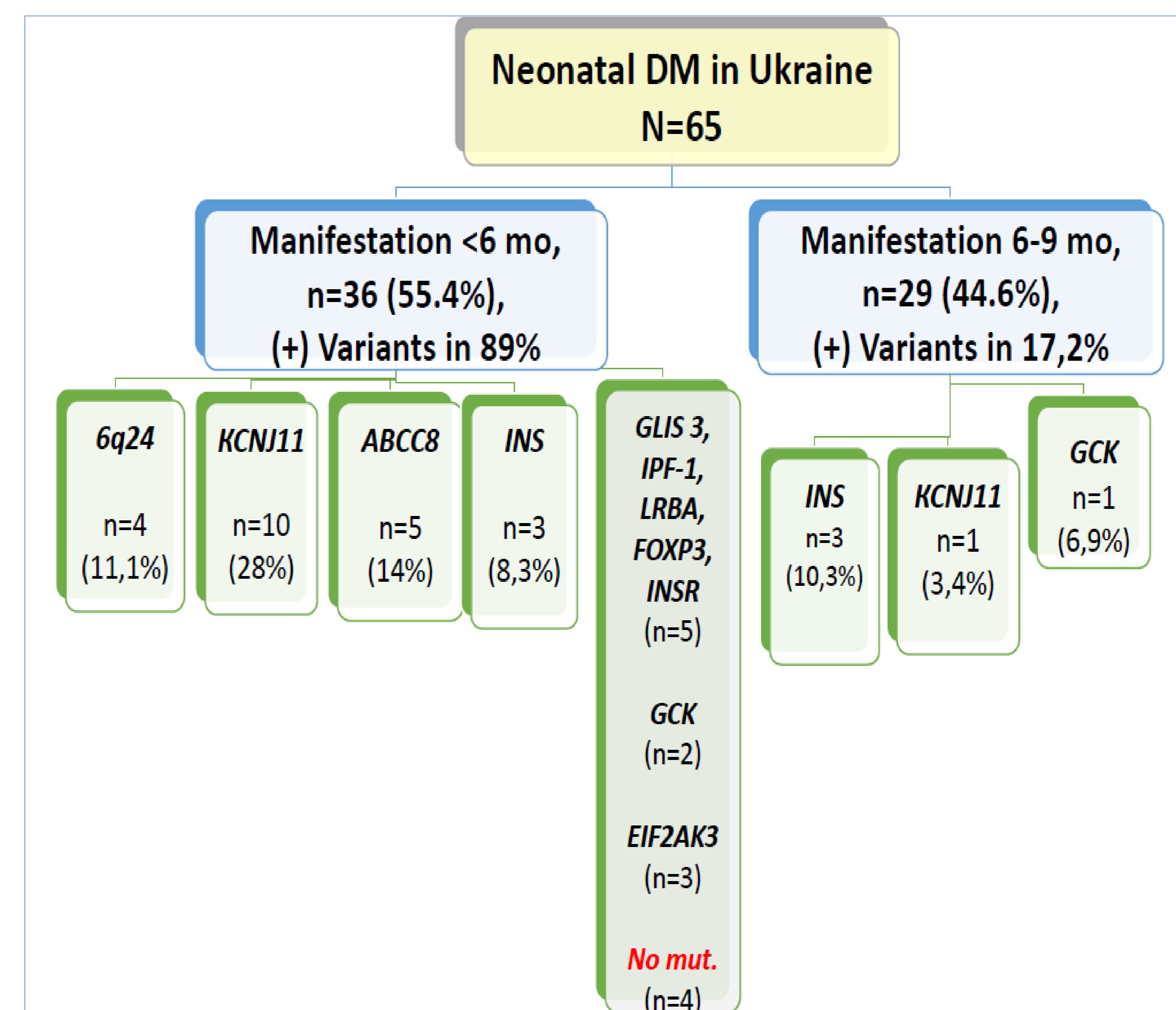


Fig.1. Distribution of children with NDM according to the Register

REFERENCES

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