

# NEONATAL DIABETES MELLITUS: CLINICAL FEATURE AND OUTCOME

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## Introduction

- Neonatal diabetes mellitus (NDM) is a rare (1:300,000–400,000 newborns) but potentially devastating metabolic disorder characterized by hyperglycemia combined with low levels of insulin. Two main groups have been recognized on clinical grounds, transient NDM (TNDM) and permanent NDM (PNDM).
- TND is defined as diabetes that starts within the first weeks of life and recovers by 18 months. Patients are at increased risk of developing diabetes in later life. The disorder therefore has three phases: neonatal diabetes, apparent remission, relapse of diabetes.
- PNDM is mainly caused by activating mutations in the *KCNJ11* or *ABCC8* genes. Since 2006 many patients with PNDM due to *KCNJ11* and *ABCC8* mutations have been completely transferred from insulin to sulfonylurea

## Objectives:

To describe clinical features and laboratory manifestations of patient with NDM and evaluate outcome of management

## Methods:

- Case series study, clinical features, biochemical finding, mutation analysis and management outcome of 24 cases from 24 unrelated families were study.
- All exon of *KCNJ11*, *ABCC8* and *INS* genes were amplified from genomic DNA and directly sequenced. If the mutation of *KCNJ11*, *ABCC8* and *INS* has failed to detect, methylation – specific PCR will be done to detect the loss of methylated region on chromosome 6q24.
- Patients with *ABCC8/KCNJ11* will be transferd to sulfonylurea from insulin

## Results:

24 patients were diagnosed neonatal diabetes mellitus and were confirmed by molecular analysis.

### Demographics :

- Age of diagnosis was 67.3 76.7 days (median 44, 7-357 days)
- Gender: 13 males, 11 females
- Gestation age was 38.7 2.2 weeks
- BW: 2720.8 571.7 grams (2000 – 3900 g)

### Clinical Features and laboratory at diagnosis:

- Polydipsia, polyuria: 9/24
- Diabetic ketoacidosis: 17/24 cases
- Blood glucose levels on admission : 34.8 10.0 (mmol/l)
- HbA1C: 7.9 2.9 %
- pH: 7.13 0.18, HCO<sub>3</sub><sup>-</sup>: 9.2 8.7 mmol/l, BE -16.8 10.3 mmol/l (4 patients can't measure because of too low)

### Results of mutation analysis:

- *KCNJ11*: 6 cases
- *ABCC8*: 7 cases
- *INS*: 6 cases
- Chr6q24: 4 cases
- *IEF2AK3*: 1 case

### Management and outcome:

- Duration: 54.4 46.6 months (4 months – 14 years)
- 5 patients with TND
    - ✓ 4 cases have abnormal of 6q24, one case has *ABCC8* mutation
    - ✓ Stop insulin at 8.25 5.8 months of diagnosis
    - ✓ Normoglycemic (blood glucose: 5.0 and 5.9 mmol/l),
    - ✓ One patient has mild development delay and 4 patients have normal development
  - 19 patients with PNDM:
    - ✓ 13 /13 cases with *ABCC8* or *KCNJ11* successful transferring to Oral SU
    - ✓ 2/13 cases with DEND syndrome,
    - ✓ 11/13 cases have normal development
    - ✓ 6/19 cases require insulin

## Conclusions:

It is important to perform screening gene mutation for patients with diabetes before 12 months of age to control blood glucose and follow up the patients

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