Congenital Hyperinsulinism: Management & Outcome in West of Scotland

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Introduction:

Hyperinsulinemic hypoglycaemia (HH) is the most frequent cause of persistent hypoglycaemia in neonates and infants[1].
The most severe forms of HH are inherited and referred to as Congenital Hyperinsulinism (CHI) [1]. Hypoglycaemia is the main feature of CHI and early diagnosis and immediate management are essential to reduce the high risk of neurological damage[2].
Diazoxide is the mainstay of medical treatment with surgery being an option in appropriate cases[3].

Objectives:

To describe management and outcome of patients with hyperinsulinemic hypoglycaemia within our region.

Methods:

Children diagnosed with HH were identified between 2009 and 2017 (figure1). Clinical course, genetic data, interventions and follow-up data were documented.

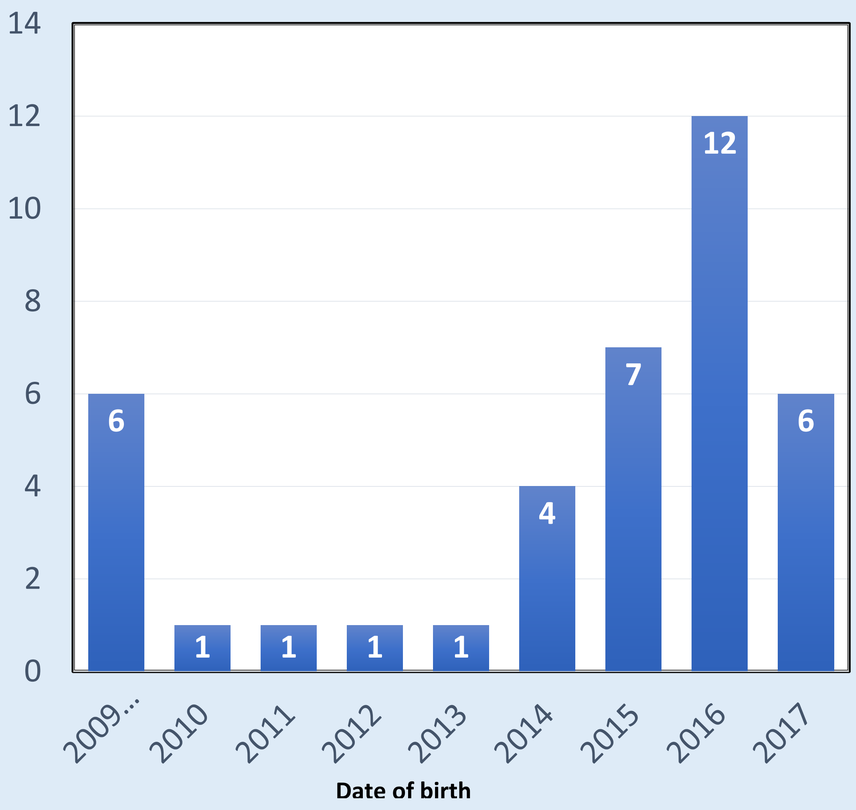

Figure 1 : Patient referred to HI clinic during study period

Results:

A total of 39 children (25 males) were identified, with increasing frequency of referrals during the study period (24/39 – during 2015-2017). Seven patients with secondary and syndromic HH were excluded. Most were born with an appropriate weight for gestational age (62.5%) and only (15.6%) were large for gestational age (Figure 2). Maximum glucose requirement ranged between 6.7-18.8 mg/kg/min (median 13.1). Median insulin level in critical samples was 11.9 mIU/L (range 1.3-110).
Diazoxide was started in all patients. Most patients responded, however; 7 did not and required octreotide/continuous feeding, with 6/7 requiring surgery.
Adverse effects to diazoxide therapy requiring discontinuation were observed in 4 patients, mainly pulmonary hypertension.
Genetic mutations were detected in 12/32 (37.5%) (Table 1).
Hyperinsulinism resolved in conservatively treated patients within 12 months in 11/32 (34.3%) compared to 14/32 (43.7%) requiring more than 12 months of medication with 11/14 having no identifiable mutation (Figure 3).
A total of 7 (21.8%) patients underwent pancreatectomy (3-subtotal/near-total, 4-focal). Patients with subtotal/near total pancreatectomy still required diazoxide/octreotide post-surgery, with 2/3 developing diabetes.

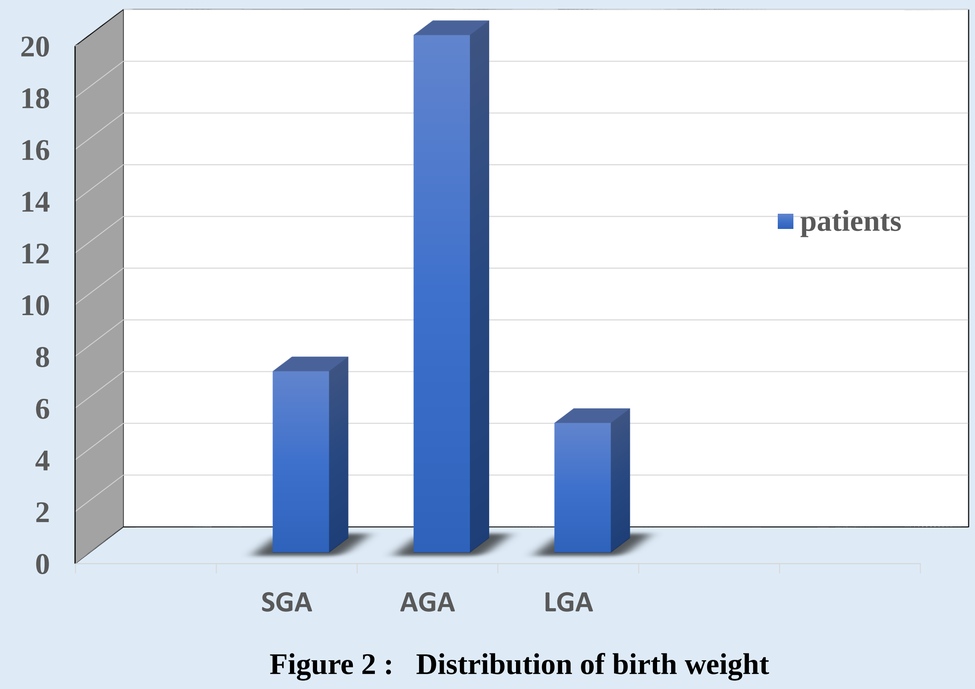

Figure 2 : Distribution of birth weight

#	Birth Weight (gram)	Insulin level mIU/l	GIR (mg/kg/m)	Gene	PET-scan	Surgery	Outcome
1	3728	41.3	18	ABCC8	Focal	Focal	Off medication
2	3800	41	18.8	KCNJ11	-	Near-total pancreatectomy	Diabetes Mellitus
3	3762	-	10.4	KCNJ11	-	-	Octreotide
4	3700	-	13	GLUD1	-	Sub-total pancreatectomy	Off medication
5	2530	-	12.4	KCNJ11	Diffuse	-	Off medication
6	3275	19	18	KCNJ11	Diffuse	-	Off medication
7	3734	12	13	ABCC8	Focal	Focal	Off medication
8	2900	11.9	17	ABCC8	Focal	Focal	Off medication
9	3380	13.2	13	KCNJ11	Diffuse	-	Off medication
10	3600	-	8	GLUD1	-	-	Diazoxide
11	3080	5.6	12	GLUD1	-	-	Diazoxide
12	2580	1.6	14	ABCC8	Focal	Near-total pancreatectomy	Diabetes Mellitus

Table 1: Characteristics and outcomes of patients with genetic mutations

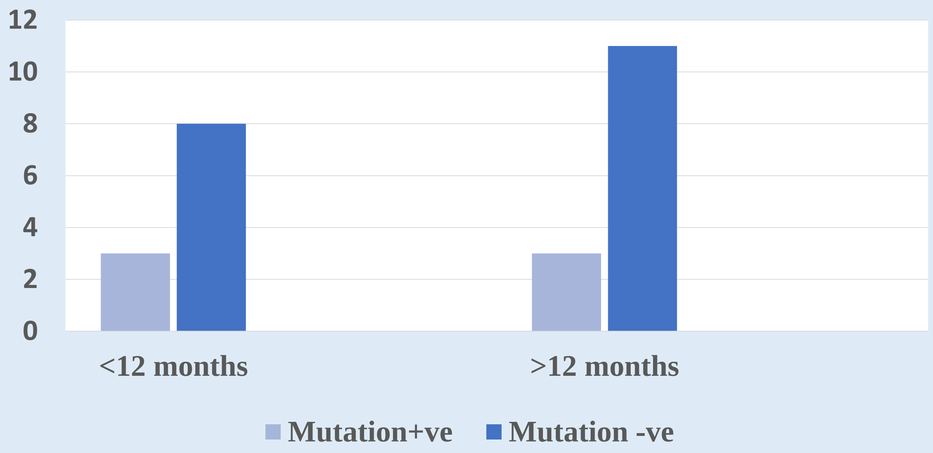

Figure 3 : Need for Medical treatment

Conclusion:

Although macrosomia and SGA are risk factors, most babies in our cohort were of normal birth weight. Initial glucose requirement and insulin level at diagnosis do not influence disease outcome. Genetic mutation does not exclude medical remission; long-term conservative treatment of CHI is feasible as surgery doesn't guarantee complete remission but carries risk of future pancreatic dysfunction. The need for ongoing treatment in the absence of gene mutations suggests that there may be other novel genetic mechanisms involved in regulating insulin secretion. Early management of hypoglycaemia remains critical to prevent long term neurological deficits.

References:

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