Hypoglycemia in Infancy and Childhood

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Abstract: Medical records of infants and children evaluated for hypoglycemia, in the period January 1989 and December 2014, were retrospectively reviewed. Data included age, sex, maternal history, dietary history and drug intake, concomitant illness, clinical presentation, and results of relevant laboratory and radiological investigations. Glycogen storage disease, metabolic disorders, and hormonal disorders were excluded as recommended. Fifty-two patients were born in or referred to King Khalid University Hospital were evaluated. Wide spectrum of causes was noted with persistent hyperinsulinemic hypoglycemia of infancy (PHHI) in infants, while ketotic hypoglycemia was the commonest beyond infancy. The frequency and aetiological pattern of hypoglycemia is variable with persistent hyperinsulinemic hypoglycaemia of infancy (PHHI) was the commonest encountered in 10 (19.2%) infants, and while ketotic hypoglycaemia was the most common cause of hypoglycemia in children beyond infancy found in 9 (17.3%) patients.

Keywords: Hypoglycemia, infancy, childhood, pattern, Saudi Arabia.

INTRODUCTION

Dysfunctional carbohydrate metabolism is one of the most common endocrine disorders of infancy and childhood. Hypoglycemia has various causes, which can lead, if untreated, to serious neurological damage. Intra-uterine growth retardation (IUGR) and having a mother with diabetes (IDM) were among the common causes in the neonatal period. However, ketotichypoglycemia is the commonest form of hypoglycemia in children beyond infancy. Persistent hyperinsulinemic hypoglycaemia of infancy (PHHI), though an uncommon disorder, was considered as one of the major causes in our community. Hypoglycemia which can be severe enough to cause coma, is an important clinical feature of childhood isolated adrenocorticotrophic deficiency [1-6].

This communication is an attempt to report on the pattern of hypoglycaemia in infancy and childhood in a cohort of patients born or referred to King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia and evaluated by the principal author (NJ) over twenty-five years period (January 1989 - December 2014), at a major teaching hospital of Central Province, Saudi Arabia.

MATERIALS AND METHODS

During the period under review (January 1989 and December 2014), a total of 52 patients were born in or referred to King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia for the evaluation of possible hypoglycaemia. Hypoglycemia was defined as a blood sugar of ≤ 3.3 mmol/L, or with clinical symptoms and signs of hypoglycaemia. Intrauterine growth retardation (IUGR) was based on birth weight and infants of diabetic mothers (IDM) on history. The diagnosis of persistent hyperinsulinemic hypoglycaemia of infancy (PHHI) was based on persistently low blood sugar, negative urinary ketone bodies and reducing substances, positive glucagon stimulations test results and high insulin to glucose ratio. Glycogen storage diseases, metabolic disorders, and hormonal deficiency were diagnosed as recommended [1, 7].

Data were retrospectively obtained from the medical records and included age, gestational age, maternal history including drug intake, dietary history and frequency. Concomitant illness, birth weight, clinical presentation, and the relevant laboratory and radiological investigations.

RESULTS

Fifty-two patients aged from newborn to 12 years were evaluated for hypoglycaemia. Ketotichypoglycaemia was the most common cause, beyond the infancy period, found in 9 (17.3%) patients, aged 18 months to six years. While in infancy the most common aetiology was persistent hyperinsulinemic hypoglycaemia of infancy (PHHI) presented in 10 (19.2%) patients. see Table. As not all patients with intrauterine growth retardation (IUGR), and hypoglycaemia in infants of diabetic mothers (IDM) were referred to endocrine service, this might create a bias in this study only 5 (9.6%) patients with IUGR and IDM in six (11.5%). A three-month-old male child presented with hypoglycaemia, was found to have
micropenia, central hypothyroidism and, adrenal insufficiency. He was diagnosed with panhypopituitarism. Two patients were diagnosed to have isolated adrenocorticotropic hormone (ACTH) deficiency, a 3 month-old and 11 years and 6 month-old boys, primary adrenal insufficiency in three, while isolated neonatal growth hormone deficiency in one patient.

Sepsis was also known to cause hypoglycaemia presented in six (11.5%) patients. The bacteriologic findings were significantly variable with pneumococcal infection being commonest. Unfortunately, we could not identify an etiological cause in four patients. However, in one patient the diagnosis of ketotichypoglycaemia was entertained at a later time.

### Table 1: Aetiological cause in 52 patients with hypoglycaemia.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketotic hypoglycemia</td>
<td>9</td>
<td>17.30</td>
</tr>
<tr>
<td>Persistent hyperinsulinemic hypoglycaemia</td>
<td>10</td>
<td>19.2</td>
</tr>
<tr>
<td>of infancy (PHHI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants of Diabetic Mother (IDM)</td>
<td>6</td>
<td>11.5</td>
</tr>
<tr>
<td>Intrauterine growth retardation (IUGR)</td>
<td>5</td>
<td>9.6</td>
</tr>
<tr>
<td>Isolated adrenocorticotropic deficiency</td>
<td>2</td>
<td>3.8</td>
</tr>
<tr>
<td>Isolated neonatal growth hormone deficiency</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>Pan Hypopituitarism</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>Primary cortisol deficiency</td>
<td>3</td>
<td>5.0</td>
</tr>
<tr>
<td>Idiopathic hypoglycaemia</td>
<td>4</td>
<td>7.7</td>
</tr>
<tr>
<td>Fructose 1,6 diphosphotase</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>Galactocemia</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>Sepsis</td>
<td>6</td>
<td>11.5</td>
</tr>
<tr>
<td>Hypoglycaemia (Diabetic patients)</td>
<td>3</td>
<td>5.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>52</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

DISCUSSION

Hypoglycaemia is one of the most frequent endocrine disorders encountered in infants and children. It can be caused by various conditions. The most common cause in childhood is insulin-treated type 1 diabetes. Many of the etiologies of hypoglycaemia may carry the same consequences, complicating the casual distinction. Infants and children with asymptomatic hypoglycaemia have been shown to have neurological dysfunctions at the time of hypoglycaemia, including impaired auditory and sensory evoked responses and impaired test performance. Long term consequences of hypoglycaemia include decreased head size, lowered IQ and specific regional brain abnormalities observed using magnetic resonance imaging (MRI) [2].

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Hypoglycaemia, which is potentially severe enough to cause coma, is an important clinical feature of childhood adrenocorticotropic hormone (ACTH) deficiency and was presented in all reported cases including our cases [4, 13]. In adrenal insufficiency related to adrenal insensitivity to ACTH, hypoglycaemia is also very frequent. This is in contrast to primary adrenal insufficiency where it is much less frequently reported. In a study of 165 children with primary adrenal insufficiency Artavia-Loria et al [15], have shown that hypoglycaemia occurred in 18%. So as Al Jurayyan in his study of primary adrenal insufficiency [16]. This reason for the discrepancy is unclear. Delayed and diminished secretion of adrenaline in response to hypoglycaemia, low alanine level and decreased rate of glycogenoeogenic have been shown to play a major role in the pathogenetic of hypoglycaemia. The lack of unrecognized pituitary factors such as β-endorphin has also been suggested [17]. Congenital isolated growth hormone deficiency and hypopituitarism are known causes, found in one each in our series [18, 19]. Sepsis was also known to cause hypoglycaemia. The bacteriological findings were variable with pneumococcal infections were the commonest.

In conclusion, the frequency and aetiological pattern of hypoglycaemia in this study is showing a wide pattern. Persistent hyperinsulinemia/hypoglycaemia of infancy (PHHI) was common in infancy period (19.2%), while ketotichypoglycaemia was the most common in childhood beyond infancy. In its typical presentation, a previously healthy, one to six years old, with normal growth and development who presents with the first episode of symptomatic hypoglycaemia following fasting, and appreciated degree of ketonuria.

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REFERENCES


