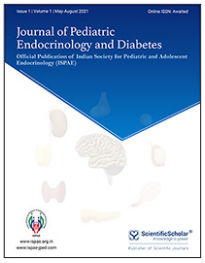
ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://ispae-jped.com/

Journal of Pediatric Endocrinology and Diabetes



Editorial Commentary

Evaluation of the etiology and outcome of hypoglycemia in young children – A challenging task

Senthil Senniappan[1], Anand Ramakrishnan[1]

[1]Department of Paediatric Endocrinology, Alder Hey Children's Hospital, Liverpool, United Kingdom.

***Corresponding author:**
Senthil Senniappan,
Department of Paediatric Endocrinology, Alder Hey Children's Hospital, Liverpool, United Kingdom.

senthilkss@yahoo.co.uk

Received: 27 February 2024
Accepted: 27 February 2024
Published: 05 April 2024

DOI
10.25259/JPED_7_2024

Quick Response Code:

Evaluating the etiology of hypoglycemia is challenging in both the neonatal and pediatric age groups. It is important to understand that the two groups have significant differences in etiologies. Although the screening investigations are similar to cover most etiologies, hyperinsulinism is much more common in the neonatal group.

The issue in evaluating neonatal hypoglycemia is related to the fact that different teams tend to use different cutoffs to define hypoglycemia, and the definition of neonatal hypoglycemia remains controversial. A survey conducted by the British Association of Perinatal Medicine (BAPM) found massive variation in cutoffs used in the UK, ranging from 2.0 to 4.0 mmoL/L (36–72 mg/dL).[1] Many patients with known risk factors are not evaluated unless they have refractory or persistent hypoglycemic episodes. An operational cutoff of 3.0 mmoL/L (54 mg/dL) to investigate and treat hypoglycemia has been recommended by the UK Congenital Hyperinsulinism of Infancy Consensus to balance the risks of under-treatment and over-evaluation.[2] There are also specific indications mentioned in the National Health System Greater Glasgow and Clyde (NHSGGC) guidelines used in Scotland for investigating neonatal hypoglycemia. These include refractory hypoglycemia (needing glucose infusion at a rate >8 mg/kg/min), persistent (3 or more episodes of <2.0 mmoL/L), or severe hypoglycemic episodes (<1.0 mmoL/L).[3]

The NHSGGC guideline was based on the BAPM consensus, but was published recently after the study patients were discharged. The authors in the study by Chai, *et al.*, have taken a cutoff of 3.0 mmoL/L (54 mg/dL) for all age groups, including neonates.[4] If their neonatal unit had adopted the BAPM consensus recommendations, their cutoffs for screening might be different and could partially explain the lack of evaluation or follow-up of some of the babies in the mild hypoglycemia group. The NHSGGC guidelines also mention that babies with hypoglycemia who have risk factors need not undergo extensive evaluation as they are likely hyperinsulinemic and would be sufficient to have an estimation of insulin, C-peptide, free fatty acids, and beta-hydroxybutyrate. However, additional tests should be included if any other etiology is suspected based on clinical and other biochemical results.

In our center, we use a cutoff of 3.0 mmoL/L (54 mg/dL) for neonatal hypoglycemia, and the screening investigations include all the tests mentioned in this study. We prioritize insulin, C-peptide, ketones (bedside), beta-hydroxybutyrate, glucose, lactate, cortisol, growth hormone, and free fatty acids. In addition to the above, we also check ammonia, amino acids, blood spots for acylcarnitine, and urine organic acids. It is important to remember that the former list is critical and needs to be done during hypoglycemia to be interpretable and, hence, prioritized.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.
©2023 Published by Scientific Scholar on behalf of Journal of Pediatric Endocrinology and Diabetes

Once hyperinsulinism is highly suspected or confirmed, we target a blood glucose cutoff of 3.5 mmoL/L (63 mg/dL). All babies with confirmed hyperinsulinism undergo six hours of fasting before discharge to ensure safety. Any neonate with confirmed hyperinsulinism will be followed up in the outpatient clinic after discharge. It is important to ensure close-up with the multi-disciplinary team. It is good that the authors have investigated the follow-up data along with the investigations, highlighting the importance of follow-up.

Hypoglycemia in the post-neonatal age group is different in presentation and etiology. As opposed to neonates, this age group is generally symptomatic with hypoglycemia, and it is typically due to an underlying illness. Most children present with ketotic hypoglycemia, and it is important to check ketones at the time of hypoglycemia to guide further evaluation. The bedside ketones using point-of-care devices give immediate results to narrow down the causes. The NHSGGC guidelines recommend a cutoff of 2.6 mmoL/L (46 mg/dL) for defining hypoglycemia in this age group.[5] Our center uses a cutoff of 3.0 mmoL/L (54 mg/dL) to ensure adequate evaluation of all cases.

History and examination can give important clues toward diagnosis in addition to the investigations. As mentioned in this study, the investigations planned are similar, but priority is always given to the critical samples.[5] A "hypoglycemia order set" on the electronic medical record system to facilitate completeness of testing and ease of requesting the tests during emergencies is available in our center. Some centers also have readymade packs (hypo packs) with required blood bottles to avoid delay.

Although idiopathic ketotic hypoglycemia is common, it is important to note that this is a diagnosis of exclusion and needs complete evaluation before giving this diagnosis. In situations where this has not been possible in the acute presentation, an elective admission for controlled fasting and evaluation is conducted, especially in children who have recurrent hypoglycemic episodes or have an unusual presentation. It is important for these children to have at least one follow-up appointment to review all the results and discuss future measures to prevent and manage hypoglycemia, especially during intercurrent illness. A glucose polymer (e.g., polycal or maxijul)-based emergency regimen with the help of an experienced dietician could be offered along with parental training for blood glucose monitoring to aid hypoglycemia management at home.

Although hypoglycemia is very common in emergency presentations, it is important that adequate evaluation is performed as hypoglycemia is never a stand-alone diagnosis and is only a sign of some underlying illness. This study has highlighted this by evaluating the adequacy of investigations and highlighting the gaps in care. Although not included in the study design, the authors have helpfully discussed the neonatal and post-neonatal groups separately. It is important that the hypoglycemia cutoffs and investigation lists are shared and discussed widely with the neonatal and emergency teams to ensure adequate compliance with guidelines.

REFERENCES

1. Hawdon JM. Identification and management of neonatal hypoglycemia in the full-term infant. British Association of perinatal medicine framework for practice, 2017. J Hum Lact 2019;35:521-3.
2. Shaikh MG, Lucas-Herald AK, Dastamani A, Estebanez MS, Senniappan S, Abid N, *et al*. Standardized practices in the networked management of congenital hyperinsulinism: A UK national collaborative consensus. Front Endocrinol (Lausanne) 2023;14:1231043.
3. NHSGGC Paediatrics for Health Professionals. Hypoglycaemia: Term infants. 2023. Available from: https://www.clinicalguidelines.scot.nhs.uk/nhsggc-guidelines/nhsggc-guidelines/neonatology/hypoglycaemia-term-infants [Last accessed on 2024 Feb 20].
4. Chai XY, Shaikh MG, McNeilly JD. Etiology and outcome of hypoglycemia in young children: A retrospective cohort study using laboratory data. J Pediatr Endocrinol Diabetes 2023;3:100-5.
5. NHSGGC Paediatrics for Health Professionals. Hypoglycaemia management, paediatric emergency department; 2021. Available from: https://www.clinicalguidelines.scot.nhs.uk/nhsggc-guidelines/nhsggc-guidelines/emergency-medicine/hypoglycaemia-management-paediatric-emergency-department [Last accessed on 2024 Feb 20].

How to cite this article: Senniappan S, Ramakrishnan A. Evaluation of the etiology and outcome of hypoglycemia in young children – A challenging task. J Pediatr Endocrinol Diabetes. 2023;3:95-6. doi: 10.25259/JPED_7_2024