CHI Congenital Hyperinsulinism International

When Too Little Sugar Hurts, We Help Congenital Hyperinsulinism Patient-Powered Research and Advocacy

Julie Raskin CEO
Congenital Hyperinsulinism International
Brisbane Marriott Hotel, Brisbane, Australia
August 5, 2023

Congenital Hyperinsulinism International
When too little sugar hurts, we help.™

Today's Agenda

- Introduction
- HI Global Registry and Max HIGR
- Collaborative Research Network
- Centers of Excellence

CHI Congenital Hyperinsulinism International

Congenital Hyperinsulinism International (CHI) supports HI research for better treatments and cures, raises awareness of HI to reduce brain damage and death,improves access to care and treatment for those with HI, while providing a community for HI families.

CHI Congenital Hyperinsulinism International

The HI Global Registry

- Launched in 2018, the HI Global Registry (HIGR) is a patient powered registry that can be used to generate natural history data
- Provides a baseline or an overall understanding of the reality of the day-to-day experience of living with HI
- Helps identify the most pressing issues and on-going challenges

CHI Congenital Hyperinsulinism International
When too little sugar hurts, we help.™

Surveys

Submit once

- Pregnancy
- Birth

Longitudinal

- Glucose monitoring - 6 months
- Quality of life (Parent/ LAR) - Annual
- Quality of life (Participant) - Annual

Updatable

- Contact information
- Demographics
- Diagnosis
- Medication management
- Diet & feeding management
- Surgical management
- Other diagnosis
- Developmental

Who can join the HI Global Registry?

- People with HI or their parent can share their experiences with the disease by answering 13 surveys through an online platform
- All information collected is kept on a secure system hosted by NORD
- Questions were developed by HI patients, clinicians, and researchers

Parent of a child living with HI

Respondent

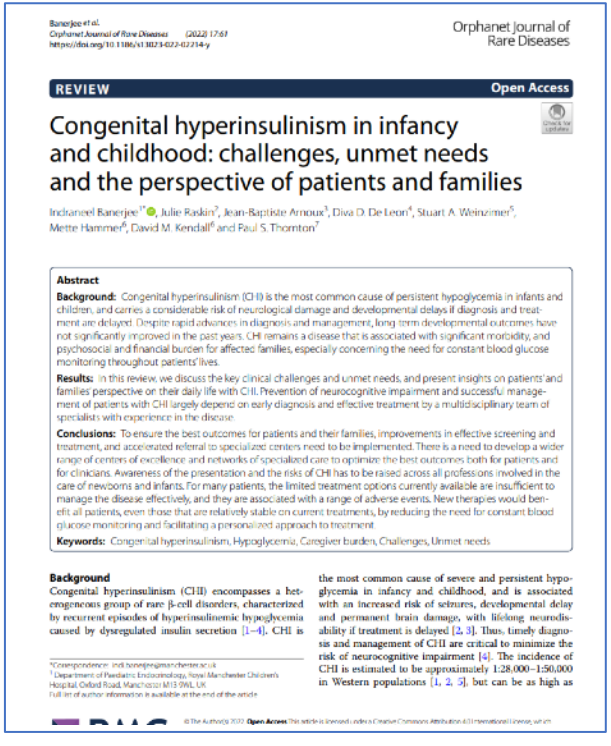
Participant

Adult living with HI

Participant and respondent

CHI Congenital Hyperinsulinism International

Peer-Reviewed Publications Using Registry Data



Banerjee et al.
Orphanet Journal of Rare Diseases (2022) 17:61
https://doi.org/10.1186/s13023-022-02214-y

Orphanet Journal of Rare Diseases

REVIEW Open Access

Congenital hyperinsulinism in infancy and childhood: challenges, unmet needs and the perspective of patients and families

Indraneel Banerjee[1*], Julie Raskin[2], Jean-Baptiste Arnoux[3], Diva D. De Leon[4], Stuart A. Weinzimer[5], Mette Hammer[6], David M. Kendall[6] and Paul S. Thornton[7]

Abstract

Background: Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoglycemia in infants and children, and carries a considerable risk of neurological damage and developmental delays if diagnosis and treatment are delayed. Despite rapid advances in diagnosis and management, long term developmental outcomes have not significantly improved in the past years. CHI remains a disease that is associated with significant morbidity, and psychosocial and financial burden for affected families, especially concerning the need for constant blood glucose monitoring throughout patients' lives.

Results: In this review, we discuss the key clinical challenges and unmet needs, and present insights on patients' and families' perspective on their daily life with CHI. Prevention of neurocognitive impairment and successful management of patients with CHI largely depend on early diagnosis and effective treatment by a multidisciplinary team of specialists with experience in the disease.

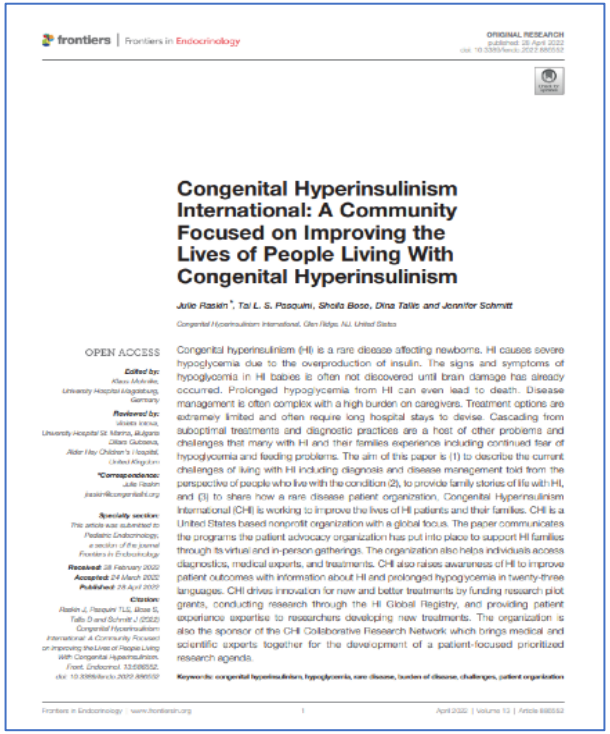
Conclusions: To ensure the best outcomes for patients and their families, improvements in effective screening and treatment, and accelerated referral to specialized centers need to be implemented. There is a need to develop a wider range of centers of excellence and networks of specialized care to optimize the best outcomes both for patients and for clinicians. Awareness of the presentation and the risks of CHI has to be raised across all professions involved in the care of newborns and infants. For many patients, the limited treatment options currently available are insufficient to manage the disease effectively, and they are associated with a range of adverse events. New therapies would benefit all patients, even those that are relatively stable on current treatments, by reducing the need for constant blood glucose monitoring and facilitating a personalized approach to treatment.

Keywords: Congenital hyperinsulinism, Hypoglycemia, Caregiver burden, Challenges, Unmet needs

Background

Congenital hyperinsulinism (CHI) encompasses a heterogeneous group of rare β-cell disorders, characterized by recurrent episodes of hyperinsulinemic hypoglycemia caused by dysregulated insulin secretion [1–4]. CHI is the most common cause of severe and persistent hypoglycemia in infancy and childhood, and is associated with an increased risk of seizures, developmental delay and permanent brain damage, with lifelong neurodisability if treatment is delayed [2, 3]. Thus, timely diagnosis and management of CHI are critical to minimize the risk of neurocognitive impairment [4]. The incidence of CHI is estimated to be approximately 1:28.000–1:50.000 in Western populations [1, 2, 5], but can be as high as

*Correspondence: indraneel.banerjee@manchester.ac.uk
[1] Department of Paediatric Endocrinology, Royal Manchester Children's Hospital, Oxford Road, Manchester M13 9WL, UK
Full list of author information is available at the end of the article



frontiers | Frontiers in Endocrinology

ORIGINAL RESEARCH
published: 28 April 2022
doi: 10.3389/fendo.2022.869532

Congenital Hyperinsulinism International: A Community Focused on Improving the Lives of People Living With Congenital Hyperinsulinism

Julie Raskin*, Tal L. S. Pasquini, Sheila Bose, Dina Tallis and Jennifer Schmitt

Congenital Hyperinsulinism International, Glen Ridge, NJ, United States

OPEN ACCESS

Edited by:
Klaus Mohnike,
University Hospital Magdeburg, Germany

Reviewed by:
Vesela Ivanova,
University Hospital St. Marina, Bulgaria
Zdravko Gudzenko,
Alder Hey Children's Hospital, United Kingdom

*Correspondence:
Julie Raskin
jraskin@congenitalhi.org

Specialty section:
This article was submitted to Pediatric Endocrinology, a section of the journal Frontiers in Endocrinology

Received: 28 February 2022
Accepted: 24 March 2022
Published: 28 April 2022

Citation:
Raskin J, Pasquini TLS, Bose S, Tallis D and Schmitt J (2022) Congenital Hyperinsulinism International: A Community Focused on Improving the Lives of People Living With Congenital Hyperinsulinism. Front. Endocrinol. 13:869532. doi: 10.3389/fendo.2022.869532

Congenital hyperinsulinism (HI) is a rare disease affecting newborns. HI causes severe hypoglycemia due to the overproduction of insulin. The signs and symptoms of hypoglycemia in HI babies is often not discovered until brain damage has already occurred. Prolonged hypoglycemia from HI can even lead to death. Disease management is often complex with a high burden on caregivers. Treatment options are extremely limited and often require long hospital stays to devise. Cascading from suboptimal treatments and diagnostic practices are a host of other problems and challenges that many with HI and their families experience including continued fear of hypoglycemia and feeding problems. The aim of this paper is (1) to describe the current challenges of living with HI including diagnosis and disease management told from the perspective of people who live with the condition (2), to provide family stories of life with HI, and (3) to share how a rare disease patient organization, Congenital Hyperinsulinism International (CHI) is working to improve the lives of HI patients and their families. CHI is a United States based nonprofit organization with a global focus. The paper communicates the programs the patient advocacy organization has put into place to support HI families through its virtual and in-person gatherings. The organization also helps individuals access diagnostics, medical experts, and treatments. CHI also raises awareness of HI to improve patient outcomes with information about HI and prolonged hypoglycemia in twenty-three languages. CHI drives innovation for new and better treatments by funding research pilot grants, conducting research through the HI Global Registry, and providing patient experience expertise to researchers developing new treatments. The organization is also the sponsor of the CHI Collaborative Research Network which brings medical and scientific experts together for the development of a patient-focused prioritized research agenda.

Keywords: congenital hyperinsulinism, hypoglycemia, rare disease, burden of disease, challenges, patient organization

frontiers | Frontiers in Endocrinology

ORIGINAL RESEARCH
published: 02 June 2022
doi: 10.3389/fendo.2022.879503

Global Registries in Congenital Hyperinsulinism

Tal L. S. Pasquini*, Mahlet Merdin, Jennifer Schmitt and Julie Raskin

Congenital Hyperinsulinism International, Glen Ridge, NJ, United States

OPEN ACCESS

Edited by:
Klaus Mohnike,
University Hospital Magdeburg, Germany

Reviewed by:
Rado Vukovic,
The Institute for Health Protection of Mother and Child, Serbia
David Zangen,
Hadassah Medical Center, Israel

*Correspondence:
Tal L. S. Pasquini
tpasquini@congenitalhi.org

Specialty section:
This article was submitted to Pediatric Endocrinology, a section of the journal Frontiers in Endocrinology

Received: 16 February 2022
Accepted: 02 May 2022
Published: 02 June 2022

Citation:
Pasquini TLS, Merdin M, Schmitt J and Raskin J (2022) Global Registries in Congenital Hyperinsulinism. Front. Endocrinol. 13:879503. doi: 10.3389/fendo.2022.879503

Congenital hyperinsulinism (HI) is the most frequent cause of severe, persistent hypoglycemia in newborn babies and children. There are many areas of need for HI research. Some of the most critical needs include describing the natural history of the disease, research leading to new and better treatments, and identifying and managing hypoglycemia before it is prolonged and causes brain damage or death. Patient-reported data provides a basis for understanding the day-to-day experience of living with HI. Commonly identified goals of registries include performing natural history studies, establishing a network for future product and treatment studies, and supporting patients and families to offer more successful and coordinated care. Congenital Hyperinsulinism International (CHI) created the HI Global Registry (HIGR) in October 2018 as the first global patient-powered hyperinsulinism registry. The registry consists of thirteen surveys made up of questions about the patient's experience with HI over their lifetime. An international team of HI experts, including family members of children with HI, advocates, clinicians, and researchers, developed the survey questions. HIGR is managed by CHI and advised by internationally recognized HI patient advocates and experts. This paper aims to characterize HI through the experience of individuals who live with it. This paper includes descriptive statistics on the birthing experience, hospitalizations, medication management, feeding challenges, experiences with glucose monitoring devices, and the overall disease burden to provide insights into the current data in HIGR and demonstrate the potential areas of future research. As of January 2022, 344 respondents from 37 countries consented to participate in HIGR. Parents or guardians of individuals living with HI represented 83.9% of the respondents, 15.3% were individuals living with HI. Data from HIGR has already provided insight into access challenges, patients' and caregivers' quality of life, and to inform clinical trial research programs. Data is also available to researchers seeking to study the pathophysiology of HI retrospectively or to design prospective trials related to improving HI patient outcomes. Understanding the natural history of the disease can also guide standards of care. The data generated through HIGR provides an opportunity to improve the lives of all those affected by HI.

Keywords: rare disease, registry, congenital hyperinsulinism, hypoglycemia, patient-reported outcomes

CHI Congenital Hyperinsulinism International

HIGR Partnerships: MaxHIGR

- Map information between patient-populated HIGR and clinician-derived information
- Clinically validate the Quality-of-Life Questionnaires
- Synchronize patient and clinician populated information to develop a model prototype for an integrated database
- Investigate and utilize data for future research into natural history of the disease
- Define outcome parameters
- Accelerate the development of novel therapies

CHI CRN Mission and Cornerstones

Create a congenital hyperinsulinism (HI) collaborative research network (CRN) that puts patients at the center of a strategy that leads to faster and more accurate diagnosis, drives new evidence-based treatments and cures, standardizes clinical guidelines, and facilitates increased and improved access.

(58 members including physicians, scientists, and patient experts from 18 countries and 5 continents)

The HI CRN has a commitment to:

- supporting **collaboration** across the globe;
- elevating the **patient voice** and ensuring the patient perspective is central to our work;
- guaranteeing **access** to information, medical specialists, and treatments regardless of income and geography;
- engaging **new researchers and ideas** to find innovative concepts and foster additional leaders in the HI network; and
- **addressing diversity, equity, and inclusion** in our work and our community.

CHI Congenital Hyperinsulinism International

Workstreams

Themes

- What is HI?: Nomenclature and Inclusion
- Medical and surgical treatments
- Care Guidelines/centers of excellence
- Diagnostics
- Glucose monitoring
- Clinical trials/industry engagement
- Genetics

Activities and Deliverables

- Clearly defined workstream topics
- Brainstorm to generate a gap analysis document
- Identify the gaps in:
  - Research gaps or needs
  - Infrastructure/ Pooled Research Resources/ Collaboration
  - Knowledge/ Expertise
  - Dissemination/ Funding
- Describe the elements needed to fill the gaps
- Prioritize the elements and create a workplan

Dare to Dream of a Future without Lows

CHI CRN Congenital Hyperinsulinism International Collaborative Research Network

CHI Congenital Hyperinsulinism International

Top 12 Gaps/Needs Prioritized at Lisbon CRN Convening

Workstream	Gap/Need
All	HI Natural History Study
Diagnostics	Identification and adoption of newborn screening approach
Diagnostics	Glucose as a vital sign
Medical and Surgical Treatments	Knowledge of the cause of neurological damage
Care Guidelines & Centers of Excellence	Continually evolving global care guidelines
Clinical Trials & Industry Engagement	An expert group to develop novel clinical trials and outcome measures for regulatory approval
Genetics	Access to genetic testing
Diagnostics	A biomarker for hyperinsulinism
Clinical Trials & Industry Engagement	Meaningful glycemic endpoints
Glucose Monitoring	Device technology for HI patients
Medical and Surgical Treatments	Implementation of personalized medicine
Clinical Trials & Industry Engagement	Expand access and accelerate enrollment in clinical trials

Care Guidelines

- Goal: Create and disseminate continually evolving global care guidelines
- Activities:
  - Raise awareness and encourage adoption of HI care guidelines after publication
  - Create a patient-friendly version of the HI care guidelines
  - Create caregiver home discharge guidelines
  - Begin to review the hypoglycemia guidelines

Newborn Screening

- Goal: to diagnose all babies with congenital hyperinsulinism in a timely manner
  - Scientific Steering Committee to develop study design, creation of RFA, evaluation of study proposals and oversight of sites and data analysis.
  - Advocacy Committee to advocate for NIH and private funding, continue awareness campaign, engage different societies, and drive implementation of screening programs.

Natural History Studies

- Goal: Build a robust registry that collects patient-reported, physician, and real-world data to provide a foundation for HI natural history studies
- Activities:
  - Improve HIGR platform and collect CGM and Glucometer data
  - Increase participation in HIGR and MaxHIGR
  - Increase harmonization of individual and national data repositories

Glucose as a Vital Sign

- Goal: Increase awareness and timely diagnosis of HI
- Activities:
  - Update all HI public facing documentation (e.g. CRN website page, Wikipedia, GARD, Orphanet, NORD) with consistency of messaging across stakeholders
  - Create Ad campaign and partner with PR firm for public awareness campaign
  - Physician/medical professional surveys

CHI Designated HI Centers

- Congenital Hyperinsulinism Center at the Children's Hospital of Philadelphia, PA, United States
- The Hyperinsulinism Center at Cook Children's Medical Center in Fort Worth, TX, United States
- Great Ormond Street Hospital Congenital Hyperinsulinism Service in London, in the United Kingdom
- Charite-Universitatsmedizin Berlin and the University Children's Hospital Duesseldorf partnership in Germany
- Collaborative Alliance on Congenital Hyperinsulinism headquartered in Magdeburg, Germany
- Northern Congenital Hyperinsulinism Service in Manchester and Liverpool, in the United Kingdom

Goals of our Centers of Excellence Designation

- To recognize hospitals/clinics that have excellent multidisciplinary teams that provide the best care for patients with congenital hyperinsulinism
- To make it easier to for patient families to access the best care
- To set patient-focused standards at the leading hospitals
- To foster a pipeline of expert clinicians and researchers
- To encourage collaboration among clinician and researchers to continually improve care and treatment options.

Congenital Hyperinsulinism International
When too little sugar hurts, we help.™

CHI AT A GLANCE

9 MDBR Grants Totaling
$700,000+ Funded

503 HIGR Participants
53 Countries
4 Annual Reports

6 Biotechs in pre-clinical or clinical development for new HI treatments

6 Centers of Excellence Designations

58 Experts and Patient Leaders
19 Countries
7 Workstreams

CHI Family Support Forum
2,255 Members
84 Countries

25 International Family Conferences

3 articles published in peer-reviewed journals

9 Sugar Soirées
38 Awards Given

13 Listening Sessions

HI Genetic Testing
786 Children
60 Countries

CHI Website
15,424 Visitors
155 Countries

38 virtual HI convenings including conferences, meetings and HI community events