

# Practice Variations in Diagnosis and Treatment of Hypoglycemia in Asymptomatic Newborns

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## ABSTRACT

**OBJECTIVES:** To describe variations in the practice of hypoglycemia screening and treatment in asymptomatic infants in the United States.

**METHODS:** During the time period from February 2018 to June 2018, we surveyed representatives of hospitals participating in the Better Outcomes through Research for Newborns Network, a national research network of clinicians providing hospital care to term and late-preterm newborns. The survey included 22 questions evaluating practices related to hypoglycemia screening and management of asymptomatic infants.

**RESULTS:** Of 108 network sites, 84 (78%) responded to the survey; 100% had a hypoglycemia protocol for screening at-risk infants in the well-baby nursery. There were wide variations between sites regarding the definition of hypoglycemia (mg/dL) (<45 [24%]; <40 [23%]; <40 [0–4 hours] and <45 [4–24 hours] [27%]; <25 [0–4 hours] and <35 [4–24 hours] [8%]), timing of first glucose check (<1 hour [18%], 1–2 hours [30%], 30 minutes post feed [48%]), and threshold glucose level for treatment (<45 [19%]; <40 [18%]; <40 [0–4 hours] and <45 [4–24 hours] [20%]; <25 [0–4 hours] and <35 [4–24 hours] [15%]). All respondents used breast milk as a component of initial therapy. Criteria for admission to the NICU for hypoglycemia included the need for dextrose containing intravenous fluids (52%), persistent hypoglycemia despite treatment (49%), and hypoglycemia below a certain value (37%).

**CONCLUSIONS:** There is a significant practice variation in hypoglycemia screening and management across the United States.

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Persistent hypoglycemia in the newborn has the potential to cause brain injury and long-term neurologic sequelae.<sup>1</sup> Whereas routine blood glucose screening for all newborns is not currently recommended, blood glucose screening in high-risk newborns allows timely diagnosis and appropriate treatment to minimize the risk of morbidity related to hypoglycemia. Screening is recommended for asymptomatic newborns who lack metabolic stores (preterm, small for gestational age [SGA]) and those who potentially have high insulin levels (large for gestational age [LGA] and infants of diabetic mothers [IDMs]).<sup>2,3</sup>

There is a lack of consensus regarding which glucose level should be used during screening to define and treat hypoglycemia.<sup>4</sup> The 2011 American Academy of Pediatrics (AAP) clinical report on screening and treatment of neonatal hypoglycemia suggests that blood glucose values <47 mg/dL (the value used in some previously published outcome studies) are normally acceptable values because these low values are often transient during the first few hours of life.<sup>2,5</sup> However, the Canadian Pediatric Society uses blood glucose values <47 mg/dL as a threshold for treatment,<sup>3</sup> whereas the British Association of Perinatal Medicine uses blood glucose values <2 mmol/L (<36 mg/dL) as the operational threshold for asymptomatic infants.<sup>6</sup> Swenne et al<sup>7</sup> showed blood glucose levels could drop below 36 mg/dL within the first 24 hours after delivery in healthy newborns. The Pediatric Endocrine Society reevaluated transitional neonatal hypoglycemia and suggested that neonatal hypoglycemia is a hypoketotic state.<sup>8</sup> Because of the potential lack of other energy sources, such as ketones, the Pediatric Endocrine Society recommends target thresholds for high-risk infants to be >50 mg/dL for <48 hours and >60 mg/dL for >48 hours.<sup>9</sup>

Standardization of practice in the health care setting has been revealed to improve safety and patient outcomes.<sup>10,11</sup> Given the differing recommendations from the various pediatric associations, as well as the sparse evidence regarding screening, diagnosis, and treatment of hypoglycemia, it is unclear

how varied newborn hypoglycemia practices are across nurseries in the United States.<sup>2,3,6,8</sup>

The Better Outcomes through Research for Newborns (BORN) Network had identified hypoglycemia as an area needing further evaluation.<sup>12</sup> We surveyed BORN member hospitals to identify current practice variations related to screening and management of hypoglycemia across nurseries.

Our objective is to describe variations in the practice of screening and treatment of asymptomatic hypoglycemic newborns among US nurseries.

## METHODS

The BORN Network is a national group of clinicians providing care for well newborns during the birth hospitalization.<sup>12</sup> Our cross-sectional study surveyed representatives of BORN member hospitals between February 2018 and June 2018. At the time of the survey, the network included 108 newborn nurseries located in 35 states in the United States. Together, these sites provide care for ~365 000 newborns annually or ~10% of national annual births. We obtained delivery volume and geographical location of all BORN member hospitals from the BORN Network on the basis of information given after joining the network.

The institutional review board at our medical center determined this study was exempt from human subjects research review.

## Survey Methods

The survey was conducted by using the online Qualtrics Survey Tool and consisted of a total of 22 questions. This included 3 questions describing the center demographics; 13 questions evaluating practices related to hypoglycemia screening guidelines, diagnosis, and treatment of hypoglycemia in asymptomatic newborns; and 6 questions related to maternity practices that may have an influence on hypoglycemia in newborns, namely breastfeeding, skin-to-skin contact, and delayed cord clamping (DCC). Each BORN site received a unique survey link by e-mail with instructions for survey completion, after which they received up to 5 reminder

e-mails over a 3-month period. The questions required either yes or no or multiple-choice responses. Most of the questions had an “other” option for open-ended narrative comments. Additionally, participating sites had the option of submitting aggregated audit data on the prevalence of screening, diagnosis, and treatment of hypoglycemia at each site obtained from either a 1-week audit of patients or a random sample of 50 patients over the previous year, which represented the mean 1 week patient census at BORN member hospitals.

## Analysis

We summarized the data using descriptive statistics. We compared annual delivery volume and site location between survey respondents and nonrespondents. Hypoglycemia definition and treatment threshold were compared by the highest level of nursery and by the type of providers (family practice, pediatrician, neonatologist) caring for newborns. Treatment options were compared by the highest level of nursery. Breastfeeding rates were compared between sites after  $\geq 5$  of the World Health Organization (WHO) Ten Steps to Successful Breastfeeding<sup>13</sup> and sites that did not.  $\chi^2$  or Fisher's exact test was used to compare categorical variables. The response to each question was summarized as the percentage of sites that selected each choice. We compared the annual delivery volume, location of site, and highest level of nursery between audit respondents and nonrespondents. Data analysis was conducted by using Stata 14.2 (Stata Corp, College Station, TX).

## RESULTS

### Demographics

Of the 108 sites surveyed, a total of 84 (78%) sites responded. The responding sites are located in 33 states (17 from the Midwest, 22 from the Northeast, 26 from the South, and 19 from the West), representing ~185 000 annual deliveries. The majority of responding sites (61%) had annual deliveries of 2000–5999. There was no difference in the location or annual delivery volumes between the responding and the nonresponding sites (Table 1). Among the

**TABLE 1** Site Demographics: Survey Responders and Nonresponders

	Survey Responders, <i>n</i> = 84	Survey Nonresponders, <i>n</i> = 24	<i>P</i>
Location, %			ns
Midwest	20	29	—
Northeast	26	33	—
South	31	13	—
West	23	25	—
Delivery volume (births per year), %			ns
<1000	5	4	—
1000–1999	17	13	—
2000–3999	51	46	—
4000–5999	18	25	—
6000–9999	7	16	—
>10 000	2	0	—

ns, not significant; —, not applicable.

survey respondents, 83 sites (98%) had general pediatricians caring for the well newborns and 65 sites (77%) reported having the highest level 3 nursery at their institution. The survey questions and the percentage of sites selecting each response are presented in Table 2.

### Hypoglycemia Guideline

All sites reported having a hypoglycemia protocol in their well-baby nursery. Hospital screening protocols consistently included SGA (98%), premature (96%), and LGA infants (98%), and IDMs (100%) as high-risk factors for hypoglycemia screening. Of the 31 sites that selected the “other” category for hypoglycemia screening, 10 screened because of exposure to certain maternal medications, 9 screened on the basis of absolute birth weight (<2500 g or >4 kg), and the remaining 12 had various other reasons (eg, anomalies, postdates, symptoms). Most sites used <10th (78%) and >90th (81%) percentiles as criteria for SGA and LGA; however, some defined these categories using different growth charts.

There was a wide variation across sites regarding the level of blood glucose that is defined as hypoglycemia. The majority of sites (62%) used one of the following 3 thresholds to define hypoglycemia in the first 24 hours: (1) <40 mg/dL, (2) <45 mg/dL, or (3) a time-dependent definition of <40 mg/dL in the first 4 hours and <45 mg/dL in the next 4 to 24 hours. Fifteen

(18%) sites reported defining hypoglycemia in the first 24 hours without using one of these 3 thresholds. Of those 15 sites, 12 reported time-dependent definitions that were different from these 3 thresholds. Regarding hypoglycemia after 24 hours of age, 79% of the sites responded that the definition of hypoglycemia after 24 hours was <40, <45, or <50 mg/dL. Of the 18 (21%) sites that reported a different definition of hypoglycemia after 24 hours of age, 8 stated that their hypoglycemia protocol did not include a definition for hypoglycemia after 24 hours of age, 2 reported a definition of <47 mg/dL, and the remaining centers had time-dependent definitions. The definition of hypoglycemia did not differ by the highest level of nursery reported at a site (Table 3).

Fifty-four (65%) sites reported that the minimum number of glucose checks according to their hypoglycemia screening protocol or policy was  $\geq 3$ . Twenty-six (31%) sites reported that they never confirm point-of-care testing (POCT) results with laboratory plasma glucose values, whereas 4 (5%) and 9 (11%), respectively, reported that they always confirm POCT with laboratory testing or that they always confirm POCT before treatment. Of the remaining 45 (54%) sites, 31 reported a value below which they confirm a POCT result with plasma glucose values, which varied between centers from <20 to <55 mg/dL.

### Treatment Strategies

The threshold for treatment differed across the sites. There was no difference in the treatment threshold values based on the highest level of nursery (Table 3) or provider level available at the site. All sites used breastfeeding or breast milk feeding as a treatment option. There was a wide variation in other hypoglycemia treatment options, including dextrose gel, dextrose containing intravenous (IV) fluids, and formula. There was no significant difference in the treatment options based on the highest level of nursery.

### NICU Admission

Criteria for admission to the NICU for hypoglycemia reported by respondents included the need for dextrose containing IV fluids (52%), persistent hypoglycemia despite treatment (49%), and hypoglycemia below a specific blood glucose value (37%) that ranged from 15 to 40 mg/dL.

### Breastfeeding and Maternity Practices

Whereas 99% of sites reported using breast milk as a treatment of hypoglycemia, 83% followed  $\geq 5$  of the WHO's Ten Steps to Successful Breastfeeding.<sup>13</sup> Sites that stated following  $\geq 5$  of the WHO's Ten Steps reported higher breastfeeding initiation and exclusive breastfeeding rates compared with sites that did not. Skin-to-skin contact (holding the unwaddled infant next to a parent's bare skin) was allowed in the delivery room in 73% of the sites, with 58% sites reporting skin-to-skin contact for >60 minutes. DCC for >30 seconds was performed in 94% of all responding sites, with 31% performing DCC for >60 seconds.

### Aggregated Audit Data

Fifty percent of sites (*n* = 42) provided aggregated data audit responses. There was no significant difference between sites that provided and those that did not provide data audit responses in terms of location, delivery volume, and highest level of nursery (Table 4). The survey revealed that the majority of sites screened between 10% and 40% of all asymptomatic newborns for hypoglycemia, diagnosed  $\leq 10\%$  of all asymptomatic newborns with hypoglycemia, and admitted <10% of hypoglycemic

**TABLE 2** Survey Results (*n* = 84)

	<i>n</i> (%)
1. Approximately how many deliveries does your hospital have each year?	
<1000	6 (7)
1000–1999	17 (20)
2000–3999	35 (42)
4000–5999	16 (19)
6000–9999	8 (10)
>10 000	2 (2)
2. What level of nurseries do you have at your hospital (select all that apply)?	
Level 1	74 (88)
Level 2	46 (55)
Level 3	65 (77)
3. Which of the following services provide care for well newborns at your institution (select all that apply)?	
Family practice	36 (43)
Pediatricians	82 (98)
Neonatology	24 (29)
4. Does your institution have an existing hypoglycemia guideline or protocol in the well-baby nursery or postpartum unit?	
Yes	84 (100)
No	0 (0)
5. How do you define hypoglycemia for infants aged <24 h?	
<40	19 (23)
<45	20 (24)
<25 (0–4 h); <35 (4–24 h)	7 (8)
<40 (0–4 h); <45 (4–24 h)	23 (27)
Other	15 (18)
6. How do you define hypoglycemia for infants aged >24 h?	
<40	12 (14)
<45	38 (45)
<50	16 (19)
Other	18 (21)
7. What asymptomatic infants require routine hypoglycemia screening at your institution (select all that apply)?	
SGA	82 (98)
Late preterm	81 (96)
IDM	84 (100)
LGA	82 (98)
IUGR	31 (37)
Infants with poor feeding or feeding gap more than a specified length of time	21 (25)
Other	29 (35)
8. How do you define SGA?	
<2500 g	13 (16)
Use Fenton growth chart	46 (57)
Use Olsen growth chart	10 (12)
Use WHO growth chart	9 (11)
9. How do you define LGA?	
>4000 g	14 (17)
Use Fenton growth chart	45 (56)
Use Olsen growth chart	9 (11)
Use WHO growth chart	9 (11)
10. For those infants that meet your institution's criteria for screening, when is the first glucose check done?	
<1 h	15 (18)

TABLE 2 Continued

	<i>n</i> (%)
1–2 h	25 (30)
30 min after first feed	40 (48)
Other	4 (5)
11. What is the minimum number of glucose checks done in an asymptomatic infant at risk for hypoglycemia?	
1	2 (2)
2	3 (4)
3	25 (30)
4–8	29 (35)
Depends on risk category	23 (27)
Other	2 (2)
12. When are subsequent glucoses checked in asymptomatic infants at risk for hypoglycemia if >1 is required in the protocol?	
Before feeding	70 (83)
After feeding	0 (0)
Varies	6 (7)
Other	8 (10)
13. What is the glucose threshold level for which treatment is recommended?	
<40	15 (18)
<45	16 (19)
<25 (0–4 h); <35 (4–24 h)	13 (15)
<40 (0–4 h); <45 (4–24 h)	17 (20)
Depends on risk category	3 (4)
Other	20 (24)
14. When do you confirm POCT with serum glucose at your institution (select all that apply)?	
Always	4 (5)
Never	26 (31)
Before initiating therapy	9 (11)
Other	45 (54)
15. Considering all levels of hypoglycemia, what are the possible treatment strategies used at your institution (select all that apply)?	
Breastfeeding	83 (99)
Expressed breast milk	83 (99)
Formula	53 (63)
IVF	72 (86)
Dextrose gel	47 (56)
Glucose water (Sweet-Ease)	0 (0)
Donor human milk	7 (8)
16. What are the criteria for NICU admission for hypoglycemia (select all that apply)?	
Needing IVF	44 (52)
Glucose level below threshold	31 (37)
Glucose level below threshold despite first-line treatments	41 (49)
17. Does your institution practice DCC?	
No	0 (0)
Yes	79 (94)
30 s	17 (22)
31–60 s	33 (43)
61–120 s	22 (29)
>120 s	4 (5)
Unsure	5 (6)
18. Does your institution practice early skin-to-skin contact in the delivery room?	

**TABLE 2** Continued

	<i>n</i> (%)
No	1 (1)
Yes, only for vaginal deliveries	22 (26)
Yes, for all deliveries	61 (73)
<30 min	3 (4)
30–60 min	32 (39)
>60 min	48 (58)
Unsure	0 (0)
19. Are the infants separated from mother after birth during the newborn admission process before the glucose checks (bathing, vitamin K or Hepatitis B vaccine, etc)?	
No	77 (92)
Unsure	5 (6)
Yes, <30 min	2 (0)
Yes, ≥30 min but <60 min	0
20. Is your institution a Baby-Friendly designated hospital?	
Unsure	0 (0)
Yes	45 (54)
No, but follow ≥5 of the WHO's Ten Steps to Successful Breastfeeding	25 (30)
21. What percentage of infants initiate breastfeeding in your institution?	
<25%	0 (0)
25%–50%	3 (4)
51%–75%	18 (21)
>75%	56 (67)
Unsure	7 (8)
22. What percentage of infants are exclusively breastfed or breast milk fed during the initial birth hospitalization in your institution (never received any type of milk other than breast milk)?	
<25%	4 (5)
25%–40%	10 (12)
41%–60%	25 (30)
61%–80%	28 (33)
>80%	8 (10)
Unsure	9 (11)

IUGR, intrauterine growth restriction; IVF, intravenous fluids.

newborns to the NICU for treatment (Table 5).

## DISCUSSION

To our knowledge, this is the first survey evaluating the practice variations in the care of asymptomatic newborns at risk for hypoglycemia in nurseries across the United States. Our results reveal that considerable practice variation exists among the survey sites.

Notably, in our survey, all sites reported having a guideline for screening asymptomatic newborns and managing hypoglycemia. The main variation in the screening guideline related to the definition of hypoglycemia reflects limitation in the

literature regarding normal glucose levels for healthy newborns. Whereas studies have revealed normal values as low as 30 mg/dL in healthy newborns in the first 24 hours of life,<sup>7,14–17</sup> Harris et al<sup>18</sup> conducted a randomized control trial (RCT) in New Zealand using 47 mg/dL as the definition and treatment threshold for hypoglycemia. A recent multicenter RCT revealed that a cutoff value of 36 mg/dL was noninferior to a cutoff value of 47 mg/dL when looking at neurodevelopmental outcomes at 18 months.<sup>19</sup> Cornblath et al<sup>20</sup> highlight that a single number cannot be applied universally and suggest that the operational threshold should be different from the therapeutic goal. The 2011 AAP clinical

report provides time-sensitive blood glucose values (feed for <40 mg/dL at 0–4 hours and <45 mg/dL at 4–24 hours and dextrose containing IV fluids for <25 mg/dL at 0–4 hours and <35 mg/dL at 4–24 hours).<sup>2</sup> Whereas 25% of the sites used the time-sensitive definition of hypoglycemia recommended by the AAP, only 15% used the AAP-recommended time-sensitive treatment thresholds for initiating dextrose containing IV fluid therapy. There is no literature evaluating whether the use of the AAP-recommended time-sensitive blood glucose values may decrease overdiagnosis and treatment or may increase decision-making complexity, resulting in errors in screening, clinical notification, and treatment.

**TABLE 3** Hypoglycemia Definition, Treatment Threshold

	Nursery Level 1, <i>n</i> = 10	Nursery Level 2, <i>n</i> = 9	Nursery Level 3, <i>n</i> = 65	<i>P</i>
Hypoglycemia definition <24 h (mg/dL), %				ns
<25 (0–4 h); <35 (4–24 h)	20	0	8	—
<40	10	33	23	—
<40 (0–4 h); <45 (4–24 h)	20	33	28	—
<45	50	11	22	—
Other	0	22	20	—
Treatment threshold (mg/dL), %				ns
<25 (0–4 h); <35 (4–24 h)	20	11	15	—
<40	10	11	20	—
<40 (0–4 h); <45 (4–24 h)	30	33	17	—
<45	30	0	20	—
Depends on risk	0	11	3	—
Other	10	33	25	—

ns, not significant; —, not applicable.

Intermittent blood glucose checks may underestimate the true number of hypoglycemic episodes when compared with continuous interstitial monitoring.<sup>5,21</sup> However, McKinlay et al<sup>5</sup> revealed that, although one-quarter of infants had low glucose concentrations measured by continuous interstitial glucose monitoring that were not detected by intermittent blood glucose monitoring, children who had unrecognized low glucose levels (only

detected by continuous monitoring) did not have any increased risk of abnormal neurodevelopment compared with those with no evidence of low glucose concentrations. In our survey, most sites indicated 10% to 40% of asymptomatic newborns were screened for hypoglycemia, and 65% of sites reported a minimum of 3 glucose checks for each newborn per screening algorithm. This describes a large number of newborns affected by

institutional policies and the burden of potentially unnecessary diagnosis or treatment. A recent study reported the practice at a single institution and found that the screening for hypoglycemia potentially had a negative impact on a large population of newborns, suggesting that the process of screening for hypoglycemia as well as the diagnosis of hypoglycemia was associated with decreased exclusive breastfeeding and increased formula feeding.<sup>22</sup>

Despite the large number of newborns screened, <10% were diagnosed with hypoglycemia and <10% of those with hypoglycemia required NICU admission. In the RCT conducted by Harris et al,<sup>18</sup> 47% of at-risk newborns were hypoglycemic. Of the hypoglycemic newborns, 14% (experimental glucose gel group) and 25% (control group) were admitted to the NICU for hypoglycemia. In our study, 90% of the sites that responded to data audit questions reported that their NICU admission criteria included the need for dextrose containing IV fluids and/or hypoglycemia treatment failure. These were similar to the reasons for NICU admission reported in the Harris et al<sup>18</sup> study. Our survey respondents reported lower NICU admissions compared with admissions published by the Harris et al<sup>18</sup> study, likely because of the lower cutoff values for the definition for hypoglycemia. Harris et al<sup>18</sup> used 47 mg/dL as the cutoff value for the definition of hypoglycemia as well as treatment failure, whereas the majority (62%) of the survey sites use values <45 mg/dL for the definition of hypoglycemia and for treatment failure. When the threshold for the definition and treatment of hypoglycemia is higher, we expect that there will be more patients who are hypoglycemic with treatment failure, requiring further treatment (such as with dextrose containing IV fluids). The availability of different treatment options in the newborn nursery may play a role in avoiding NICU admissions. In our survey, 56% of sites use dextrose gel as a treatment option for hypoglycemia and 43% of the audits reported using dextrose gel for the treatment of hypoglycemia.

**TABLE 4** Site Demographics: Audit Responders and Nonresponders

	Audit Responders, <i>n</i> = 42	Audit Nonresponders, <i>n</i> = 42	<i>P</i>
Location, %			ns
Midwest	14	26	—
Northeast	24	29	—
South	43	19	—
West	19	26	—
Delivery volume (births per year), %			ns
<1000	5	5	—
1000–1999	20	14	—
2000–3999	49	52	—
4000–5999	15	21	—
6000–9999	12	2	—
>10 000	0	5	—
Highest nursery level, %			ns
Level 1	12	12	—
Level 2	12	10	—
Level 3	76	78	—

ns, not significant; —, not applicable.

**TABLE 5** Aggregated Audit Data on the Prevalence of Screening, Diagnosis, and Treatment of Hypoglycemia at Each Site (*n* = 42)

	<i>n</i> (%)
1. What is the estimated percentage of all asymptomatic infants who are screened for hypoglycemia at your institution per your guidelines or protocol?	
<10%	1 (2)
11%–20%	15 (36)
21%–30%	11 (26)
31%–40%	7 (17)
41%–50%	3 (7)
>50%	2 (5)
Unsure	3 (7)
2. What is the estimated percentage of all asymptomatic infants who are diagnosed with hypoglycemia?	0 (0)
<1%	2 (5)
1%–5%	16 (38)
6%–10%	8 (19)
>10%	9 (21)
Unsure	7 (17)
3. What is the estimated percentage of infants treated with supplemented feeds with formula for hypoglycemia?	0 (0)
Never	1 (2)
<10%	8 (19)
10%–25%	10 (24)
26%–50%	13 (31)
51%–75%	5 (12)
>75%	5 (12)
4. What is the estimated percentage of infants treated with glucose gel for hypoglycemia?	0 (0)
Never	24 (57)
<10%	5 (12)
10%–25%	1 (2)
26%–50%	2 (5)
51%–75%	4 (10)
>75%	6 (14)
5. What is the estimated percentage of infants admitted to the NICU for hypoglycemia?	
<10%	31 (74)
10%–25%	11 (26)
26%–50%	0 (0)
51%–75%	0 (0)
>75%	0 (0)
6. What is the estimated percentage of infants treated with IV fluids for hypoglycemia?	
Never	2 (5)
<10%	31 (74)
10%–25%	9 (21)
26%–50%	0 (0)
51%–75%	0 (0)
>75%	0 (0)

Another important area of variation lies in the laboratory confirmation of POCT glucose values by repeating a plasma glucose measurement. Our study revealed approximately one-third of the sites never confirm POCT glucose values with a plasma measurement. In our survey, we did not ask

which glucometer each institution uses and whether the type of glucometer affects the decision to confirm with plasma blood glucose measurements. Point-of-care devices have different accuracies, with some having a better correlation to laboratory values than others.<sup>23</sup> Some

studies have suggested that the glucometers are not reliable in the hypoglycemic ranges and should not be used alone for blood glucose measurements in neonates.<sup>24,25</sup> The AAP 2011 recommendations state that bedside blood glucose measurements should be

confirmed by laboratory values<sup>2</sup> but do not specify at which level of POCT glucose values confirmation is needed. Moreover, there is a real challenge in balancing the benefits of treating hypoglycemia in newborns in a timely manner with waiting to confirm hypoglycemia through plasma laboratory measurements.<sup>2</sup>

The priority of management should be to prevent hypoglycemia. Delivery room practices can affect neonatal transition after birth. DCC increases blood volume and cardiac output and allows for a smooth transition from fetal to neonatal circulation, thereby stabilizing the infant's hemodynamic status.<sup>26,27</sup> Moreover, the increased blood volume attributable to DCC provides additional blood glucose to the newborns, reducing their risk for hypoglycemia. In a recent study<sup>28</sup> of late-preterm infants gestational ages 35 + 0/7 weeks to 36 + 6/7 weeks whose mothers received betamethasone, DCC was revealed to protect these newborns from early neonatal hypoglycemia. Ninety-four percent of sites in our survey reported performing DCC, with 70% delaying >30 seconds. Early and prolonged (>60 minutes) skin-to-skin contact has been revealed to decrease the incidence of hypoglycemia as well as increase breastfeeding rates in the hospital.<sup>29–31</sup> It is reassuring to see that 99% of survey sites reported skin-to-skin practices in the delivery room; however, only 58% of sites practiced skin-to-skin contact for >60 minutes, as recommended by the WHO's<sup>13</sup> Baby-Friendly Hospital Initiative, which has been associated with increased in-hospital breastfeeding rates.<sup>32,33</sup> There is a direct relationship between the number of Baby-Friendly Hospital Initiative steps a hospital practices and breastfeeding rates.<sup>34</sup> In our survey, 54% of respondents reported their institution has received the Baby-Friendly Designation and an additional 30% reported their institution following  $\geq 5$  of the WHO's Ten Steps.

The main strength of our study is that this is the first nationwide survey evaluating the management of hypoglycemia in newborns. The BORN Network represents sites providing care to ~10% of US births

annually. Our survey had a high response rate of 78%, representing care of ~8% of all births occurring in sites from 33 geographically diverse states across the country.

Our study has some limitations. Only 1 clinician from each site was asked to respond to the survey, which may underestimate provider-level variations that could exist within sites and may introduce misclassification error if an individual respondent did not understand their institution's policy in its entirety or did not answer a survey item correctly or comprehensively. Because written protocols were not obtained, we did not capture the differences between a hospital's written policy and a responding clinician's understanding of or adherence to the policy in this study, which might introduce bias. In addition, in our survey, we did not explore variation in the primary treatment modality for hypoglycemia or the myriad of reasons that a particular site might use given glucose threshold values for defining and treating hypoglycemia.

## CONCLUSIONS

This study reveals that wide variations exist in practice for the diagnosis and management of hypoglycemia in asymptomatic newborns. The Institute for Healthcare Improvement has brought awareness that standardization in practices has been revealed to improve outcomes for many conditions.<sup>10</sup> However, standardization without proven outcome improvements may pose a significant burden to a large number of healthy newborns and put them at risk for unnecessary interventions. The challenge is balancing the risk of overscreening and treatment of those newborns with normal transient lower blood glucose levels with the risk for potential poor long-term neurodevelopmental outcomes due to persistent hypoglycemia.<sup>18</sup> Studies with long-term outcomes related to screening and management strategies in this population are needed to inform the revision and standardization of hypoglycemia practice guidelines and potentially reduce unnecessary treatments.

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## REFERENCES

1. Wickström R, Skiöld B, Petersson G, Stephansson O, Altman M. Moderate neonatal hypoglycemia and adverse neurological development at 2-6 years of age. *Eur J Epidemiol.* 2018;33(10):1011–1020
2. Adamkin DH; Committee on Fetus and Newborn. Postnatal glucose homeostasis in late-preterm and term infants. *Pediatrics.* 2011;127(3):575–579
3. Narvey MR, Marks SD. The screening and management of newborns at risk for low blood glucose. *Paediatr Child Health.* 2019;24(8):536–554
4. Tin W. Defining neonatal hypoglycaemia: a continuing debate. *Semin Fetal Neonatal Med.* 2014;19(1):27–32
5. McKinlay CJD, Alsweiler JM, Ansell JM, et al; CHYLD Study Group. Neonatal glycemia and neurodevelopmental outcomes at 2 years. *N Engl J Med.* 2015;373(16):1507–1518
6. 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(3):521–523
7. Swenne I, Ewald U, Gustafsson J, Sandberg E, Ostenson CG. Inter-relationship between serum concentrations of glucose, glucagon and insulin during the first two days of life in healthy newborns. *Acta Paediatr.* 1994;83(9):915–919
8. Stanley CA, Rozance PJ, Thornton PS, et al. Re-evaluating “transitional neonatal hypoglycemia”: mechanism and implications for management. *J Pediatr.* 2015;166(6):1520–1525.e1
9. Thornton PS, Stanley CA, De Leon DD, et al; Pediatric Endocrine Society.

- Recommendations from the Pediatric Endocrine Society for evaluation and management of persistent hypoglycemia in neonates, infants, and children. *J Pediatr*. 2015;167(2):238–245
10. Rozich JD, Howard RJ, Justeson JM, Macken PD, Lindsay ME, Resar RK. Standardization as a mechanism to improve safety in health care. *Jt Comm J Qual Saf*. 2004;30(1):5–14
  11. Rotter T, Kinsman L, James E, et al. Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs. *Cochrane Database Syst Rev*. 2010;(3): CD006632
  12. Simpson E, Goyal NK, Dhepyasuwan N, et al. Prioritizing a research agenda: a Delphi study of the Better Outcomes through Research for Newborns (BORN) Network. *Hosp Pediatr*. 2014;4(4): 195–202
  13. World Health Organization. Ten steps to successful breastfeeding. Available at: <https://www.who.int/activities/promoting-baby-friendly-hospitals/ten-steps-to-successful-breastfeeding>. Accessed September 15, 2020
  14. Srinivasan G, Pildes RS, Cattamanchi G, Voora S, Lilien LD. Plasma glucose values in normal neonates: a new look. *J Pediatr*. 1986;109(1):114–117
  15. Hoseth E, Joergensen A, Ebbesen F, Moeller M. Blood glucose levels in a population of healthy, breast fed, term infants of appropriate size for gestational age. *Arch Dis Child Fetal Neonatal Ed*. 2000;83(2):F117–F119
  16. Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 hours of life. *J Pediatr*. 1987;110(1): 119–122
  17. Diwakar KK, Sasidhar MV. Plasma glucose levels in term infants who are appropriate size for gestation and exclusively breast fed. *Arch Dis Child Fetal Neonatal Ed*. 2002;87(1):F46–F48
  18. Harris DL, Weston PJ, Signal M, Chase JG, Harding JE. Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2013;382(9910): 2077–2083
  19. van Kempen AAMW, Eskes PF, Nuytemans DHGM, et al; HypoEXIT Study Group. Lower versus traditional treatment threshold for neonatal hypoglycemia. *N Engl J Med*. 2020;382(6):534–544
  20. Cornblath M, Hawdon JM, Williams AF, et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. *Pediatrics*. 2000;105:1141–1145
  21. Harris DL, Battin MR, Weston PJ, Harding JE. Continuous glucose monitoring in newborn babies at risk of hypoglycemia. *J Pediatr*. 2010;157(2):198–202.e1
  22. Mukhopadhyay S, Wade KC, Dhudasia MB, et al. Clinical impact of neonatal hypoglycemia screening in the well-baby care. *J Perinatol*. 2020;40(9):1331–1338
  23. Reddy V R S, M E S, Gowda Y C B, Suhail S M. Comparison of point of care (POC) testing of glucose by B Braun Glucometer and Hemocue Glucose 201+ analyser versus centralised testing in Neonatal Intensive Care Unit (NICU). *J Clin Diagn Res*. 2014;8(7):PC10–PC13
  24. Ho HT, Yeung WKY, Young BWY. Evaluation of “point of care” devices in the measurement of low blood glucose in neonatal practice. *Arch Dis Child Fetal Neonatal Ed*. 2004;89(4):F356–F359
  25. Turnquist M, Haskins A, Holt C. Validity of neonatal POC glucose testing. Available at: <http://knowledgeconnection.mainehealth.org/mmc/699>. Accessed December 3, 2020
  26. Hooper SB, Polglase GR, te Pas AB. A physiological approach to the timing of umbilical cord clamping at birth. *Arch Dis Child Fetal Neonatal Ed*. 2015;100(4): F355–F360
  27. Ceriani Cernadas JM. Timing of umbilical cord clamping of term infants. *Arch Argent Pediatr*. 2017;115(2): 188–194
  28. Hitchings L, Rodriguez M, Persaud R, Gomez L. The effect of delayed cord clamping on blood sugar levels on 34–36 week neonates exposed to late preterm antenatal steroids [published online ahead of print October 12, 2020]. *J Matern Fetal Neonatal Med*. doi: 10.1080/14767058.2020.1832074
  29. Chiruvolu A, Miklis KK, Stanzo KC, et al. Effects of skin-to-skin care on late preterm and term infants at-risk for neonatal hypoglycemia. *Pediatr Qual Saf*. 2017;2(4):e030
  30. Dalsgaard BT, Rodrigo-Domingo M, Kronborg H, Haslund H. Breastfeeding and skin-to-skin contact as non-pharmacological prevention of neonatal hypoglycemia in infants born to women with gestational diabetes; a Danish quasi-experimental study. *Sex Reprod Healthc*. 2019;19:1–8
  31. Christensson K, Siles C, Moreno L, et al. Temperature, metabolic adaptation and crying in healthy full-term newborns cared for skin-to-skin or in a cot. *Acta Paediatr*. 1992;81(6–7): 488–493
  32. Pérez-Escamilla R, Martínez JL, Segura-Pérez S. Impact of the Baby-friendly Hospital Initiative on breastfeeding and child health outcomes: a systematic review. *Matern Child Nutr*. 2016;12(3): 402–417
  33. Gomez-Pomar E, Blubaugh R. The Baby Friendly Hospital Initiative and the ten steps for successful breastfeeding: a critical review of the literature. *J Perinatol*. 2018;38(6):623–632
  34. DiGirolamo AM, Grummer-Strawn LM, Fein SB. Effect of maternity-care practices on breastfeeding. *Pediatrics*. 2008;122(suppl 2):S43–S49

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