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RESEARCH

The *CPT1A Arctic variant*: perspectives of community members and providers in two Alaska tribal health settings

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Abstract

Newborn screening in Alaska includes screening for carnitine palmitoyltransferase 1A (*CPT1A*) deficiency. The *CPT1A* Arctic variant is a variant highly prevalent among Indigenous peoples in the Arctic. In this study, we sought to elicit Alaska Native (AN) community member and AN-serving healthcare providers' knowledge and perspectives on the *CPT1A* Arctic variant. Focus groups with community members and healthcare providers were held in two regions of Alaska between October 2018 and January 2019. Thematic analysis was used to identify recurring constructs. Knowledge and understanding about the *CPT1A* Arctic variant and its health impact varied, and participants were interested in learning more about it. Additional education for healthcare professionals was recommended to improve providers' ability to communicate with family caregivers about the Arctic variant. Engagement with AN community members identified opportunities to improve educational outreach via multiple modalities for providers and caregivers on the Arctic variant, which could help to increase culturally relevant guidance and avoid stigmatization, undue worry, and unnecessary intervention. Education and guidance on the care of infants and children homozygous for the *CPT1A* Arctic variant could improve care and reduce negative psychosocial effects.

Keywords Carnitine palmitoyltransferase 1A (CPT1A) · Alaska Native · Newborn screening · Health education · Arctic variant

Introduction

Across the U S, newborn screening is performed to detect disabling and potentially life-threatening conditions, generally prior to the onset of symptoms, to facilitate early intervention. Testing regimes differ by state, with a core set of conditions that includes 37 primary conditions and 26 secondary conditions (Health Resources & Services Administration 2023).

One such secondary condition is carnitine palmitoyltransferase 1A (CPT1A) deficiency. The severe form of CPT1A deficiency is a rare autosomal recessive disorder of fatty acid oxidation that results from nearly complete loss of enzyme activity, which severely impairs the ability to utilize fatty acids for ketone and energy production. Symptoms include fasting-induced hypoketotic hypoglycemia and liver failure (Bennett and Santani 2016; Bougnères et al. 1981). Identification of infants with CPT1A deficiency and other disorders of fatty acid oxidation via newborn screening allows for education of caregivers regarding the need for avoidance of prolonged fasting and has been shown to reduce morbidity and mortality (Wilcken et al. 2007).

A variant of the *CPT1A* gene associated with a partial loss of function (known as the Arctic variant) is highly prevalent among Indigenous Arctic peoples of Alaska, Canada, Greenland, and northeast Siberia (Collins et al.

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2010; Rajakumar et al. 2009; Clemente et al. 2014; Gessner et al. 2011; Greenberg et al. 2009). Evidence suggests that the high prevalence of the Arctic variant among these populations is the result of positive selection based on beneficial health effects of the variant in combination with a traditional subsistence diet (Rajakumar et al. 2009; Clemente et al. 2014; Lemas et al. 2012). In spite of clear evidence of likely beneficial effects of the Arctic variant, the partial loss of CPT1A activity associated with the variant results in a significant impairment in the ability of infants and young children to utilize fatty acids for ketone and energy production when fasting (Gillingham et al. 2011). Nonetheless, most children homozygous for the Arctic variant never develop any symptoms.

The state of Alaska expanded newborn screening in 2003, and screens for 53 conditions (Alaska Department of Health 2023) which includes the secondary condition of CPT1A deficiency. Alaska reports on newborn screenings that are homozygous for the Arctic variant (Alaska Department of Health 2023). During the first 5 years of screening, 176 infants from western and northern Alaska were identified as homozygous for the Arctic variant (birth prevalence, 0.33%) (Gessner et al. 2011). These regions also reported higher rates of severe respiratory illness among Alaska Native (AN) infants than the general US (Bruden et al. 2015) and an infant mortality rate more than twice that of other parts of Alaska (Blabey and Gessner 2009). Although most infants homozygous for the Arctic variant do not experience negative health outcomes, epidemiologic evidence from Alaska and other circumpolar regions has shown an increased risk for infectious disease, infant mortality, and other adverse health outcomes (Blabey and Gessner 2009; Bruden et al. 2015; Collins et al. 2021a; Collins et al. 2021b; Collins et al. 2012; Gessner et al. 2013; Gessner et al. 2016; Gillingham et al. 2011; Sinclair et al. 2012).

To educate family caregivers and healthcare providers, the state of Alaska and the Alaska Tribal Health System developed an educational DVD, which is mailed together with other informational materials to families of infants identified as homozygous for the Arctic variant via newborn screening (The Other Energy Crisis: Arctic Variant CPT1A 2013). The intent of these efforts was to generate greater awareness regarding the Arctic variant among caregivers and healthcare providers throughout the Alaska Tribal Health System. Key messages of these materials were infants and children with the Arctic variant (1) do not have a disease; (2) need to avoid going long periods of time without eating; (3) should receive carbohydrate rich fluids and foods when ill; and (4) need to be brought in for IV glucose therapy if they develop symptoms and/or are unable to eat for a long period of time. However, the acceptability and effectiveness of this messaging in the AN community have not been formally assessed.

Researchers, providers, and community members recognize the need for culturally tailored healthcare interventions for AN and American Indian (AI) people (Burke et al. 2022; Boyd-Ball 2003; Barrera Jr et al. 2013; Allen et al. 2006). In addition, given the history of discrimination and disparities in healthcare, as well as research that has failed to benefit, and in some cases actively harmed, ANAI peoples (Foulks 1989; Mello and Wolf 2010; Owens 2013), appropriate research protections, and governance structures must be in place (Saunkeah et al. 2021). Using a participatory research approach, this study sought to explore the knowledge and perceptions of AN community members and AN-serving providers regarding the Arctic variant.

Methods

We conducted focus groups with AN community members and healthcare providers in two Tribal health organizations in Alaska.

Setting

The study was carried out in two Tribally-owned non-profit health systems: Southcentral Foundation (SCF) and Norton Sound Heath Corporation (NSHC). SCF provides health and human services to over 65,000 ANAI urban- and rural-dwelling peoples in southcentral Alaska (Gottlieb 2013). SCF is based in Anchorage, a city of nearly 300,000 people. NSHC is based in Nome (population ~3400) and serves 15 rural communities in northern Alaska providing care to more than 10,000 people annually (Norton Sound Health Corporation 2017). Nome and the surrounding communities are not connected to the road system and are only accessible by small airplane; telemedicine and a community health aide/practitioner model are used to provide front-line care (Golnick et al. 2012). In Anchorage and Nome, homozygous newborn screening results for *CPT1A* Arctic variant are shared with the family in the postal mail along with an informational packet that includes a letter from the State of Alaska Newborn Screening Program, a handout, and an informational DVD. Families are encouraged to make an appointment with their primary care provider to discuss further if they have any additional questions.

Sample

Self-identified AN adults served by SCF and/or NSHC and providers employed by SCF and/or NSHC (mid-level family practices providers, physicians, and dieticians) were invited to participate.

Recruitment

Community members were recruited with printed fliers in the SCF primary care center and the NSHC patient lobby areas, at a community health conference, and on health corporation social media. Healthcare providers (e.g. primary care physicians, dieticians) were recruited via printed fliers in clinic staff areas and via email. All participants gave verbal informed consent. Community member participants received a $50 gift card; providers were not compensated.

Data collection

Focus groups occurred from October 2018 to February 2019. A semi-structured focus group guide was used for all focus groups. The focus group guide was co-developed by AN investigators and Arctic variant subject matter experts and was designed to elicit descriptions of participants' familiarity with the Arctic variant. Participants were provided a "Frequently Asked Questions about CPT1A Arctic Variant" document (see Supplemental Information). SCF researchers trained in qualitative methods facilitated the focus groups. In some cases, the SCF researcher(s) knew community members and/or providers who participated in the focus groups, to ensure a balance in potential power differentials, we included two facilitators for each focus group. Focus groups were conducted until theoretical saturation was reached at each site (Hennink et al. 2017) and were audio-recorded and transcribed.

Data analysis

Four investigators reviewed the transcripts and developed a codebook, which were uploaded to ATLAS.ti 8.3.20.0 (Scientific Software Development GmbH, Berlin, Germany). Each investigator coded a sentinel transcript; then, the group reviewed to establish intercoder reliability and identify code revisions. Working in pairs, the remaining transcripts were then dual-coded, and discrepancies were resolved through social moderation. Last, descriptive thematic analysis were used to identify dominant constructs (Nowell et al. 2017).

Ethics statement

The Alaska Area Institutional Review Board reviewed and approved the study protocol. The SCF Research Review committees and Board of Directors (Hiratsuka et al. 2017) and NSHC Research Ethics and Review Board (Norton Sound Health Corporation Research 2022) reviewed and approved the protocol and resulting manuscript prior to journal submission.

Results

We conducted 11 focus groups, with a total of 36 participants (28 community members and 8 providers). Each focus group was about 1-h long. At SCF, we held 5 focus groups (3 with community members, 1 with providers, and 1 with both providers and community members). Note that due to scheduling challenges, one focus group with both providers and community members took place at SCF. At NSHC, we held 6 focus groups (3 with community members and 3 with providers). Table 1 shows the age and gender information. To protect the privacy of participants, we combined demographic information for both sites.

We identified three primary themes: community members' knowledge, providers' knowledge, and participant recommendations, with six sub-themes (Table 2).

Community members' knowledge of the Arctic variant

Community members shared a wide range of knowledge and experiences with the Arctic variant. Many understood it to affect metabolism and that it is prevalent among certain groups of AN people. Community members were especially cognizant of how changes in AN people's eating habits and access to certain foods may interact with the Arctic variant, as shown here:

> …so this gene has to do with our diet, and possibly what we're running into now is because we don't eat the same diet that we did previously in the past, that we're changing our diet, and we're substituting those fats that we used to get that were healthy fats, from fish, from marine mammals, whales, all those animals that have those… good fats … and we're substituting those with fast food,

Table 1 Participant demographic table

	n (%)
All participants	36 (100)
Gender	
Female	29 (81)
Male	7 (19)
Age (years)	
18–34	13 (36)
35–54	8 (22)
55–64	10 (28)
65+	5 (14)

Table 2 Summary of themes

Themes	Sub-themes	Description
Community members' knowledge of the Arctic variant	Knowledge regarding care of children with the Arctic variant	Community members' reports of lived experiences, stories regarding the Arctic variant that they, their families/friends, or their patients have experienced; real-life examples
	Perspectives on newborn screening for the Arctic variant	Participants' views about newborn screening specific to the Arctic variant
Providers' knowledge of the Arctic variant	Knowledge regarding care of children with the Arctic variant	Providers' reports of lived experiences interacting with caregivers of infants with the Arctic variant
Participant recommendations	Education for providers & patients	Participants' recommendations or suggestions about the content, process, form, etc. of messaging, communication, and/or education for parents and/or providers
	Care coordination and referrals	Comments about information provided/received about the Arctic variant specifically, including the return of Arctic variant screening results
	Concern for stigma and cultural responsiveness	Participants' descriptions that could lead to misinterpretation and/or a potential for stigma. Or ways to address potential stigma

> frozen food, and those essentially non-healthy fats…—NSHC Community Member 12

Knowledge regarding care of children with the Arctic variant

Participants whose children screened homozygous for the Arctic variant described feeling fear, confusion, and frustration about the meaning of the test result, and what they needed to do to care for their children. For example, one parent said, "[My son] gets really sleepy if he doesn't eat right away… They said that he can't transfer his fat into energy…" (NSHC Community Member 3). Another described their experience in the neonatal intensive care unit (NICU) as follows:

> [My son] spent 12 hours in the NICU, and it was the same thing, having to track his appetite… just making sure to feed him every couple hours … That sort of really left me scared, because to this day, I still have to make sure he's eating. So I guess in the future, if and when he gets sick, I think that's always going to be a concern…—SCF Community Member 11

Some community members expressed the belief that caregivers of infants and children with the Arctic variant should always keep juice or another convenient, high-sugar source of calories on hand.

Perspectives on newborn screening for the Arctic variant

Many participants shared stories of family members or friends whose children screened homozygous for the Arctic variant. One community member said they were initially worried when informed that their child had the variant but noticed no difference between that child and their other children, who had not screened homozygous. Some recalled experiencing or witnessing others express alarm regarding a homozygous result.

One participant recalled receiving an informational packet and DVD in the mail when their child, who screened homozygous for the Arctic variant, was 1 month old. This participant did not recall any communication from the health system prior to receiving the information packet in the mail. Although not clear where this participant received the information from, and in alignment with what others described, this participant understood prior to receiving the informational material in the mail that the child needed to eat every 2 h.

Providers' knowledge of the Arctic variant

Familiarity and direct experience with the Arctic variant varied among providers. Most knew that the Arctic variant is common in the AN population but rare in the general population. Like community members, they were interested its potential historical role as a protective factor and implications of dietary change, as exemplified here:

> [C]ertainly I think there's many, many people living amongst us that have [the Arctic variant] and, probably have not gotten sick over the many years … So why is that, if you grew up in an area where you had better, more access to a Native diet or to different foods … some of the mammal oils and things like that, was

> that a protective factor? I would assume so, but I don't know for sure.—SCF Provider 1

Knowledge regarding care of children with the Arctic variant

Providers' confidence in giving guidance about feeding infants and children homozygous for the Arctic variant also varied. One said, "… a lot of parents think that they need sugar, which is incorrect, and [parents believe] they need to feed [children] sugary things [to avoid hypoglycemia]" (NSHC Provider 5). One provider who was relatively new to Alaska conveyed a lack of clear guidance about feeding recommendations:

> I just read something about not feeding every two hours but feeding every six hours. It's kind of confusing, because most of the providers that I've known over my last three years in Alaska are from the Lower 48 [states] and have very little interaction or knowledge on this, and it's not really provided in terms of [school] training. It's something that's very specific to this region.—NSHC Provider 3

Providers spoke of identifying patients with the Arctic variant as a high priority to (1) educate parents and caregivers about the need to seek timely care for these infants when they are sick to avoid hypoglycemia and (2) provide appropriate presurgical care (i.e., avoidance of prolonged fasting and provision of IV glucose).

Some providers expressed concern about a perceived lack of understanding among caregivers about how to care for infants with the Arctic variant. Providers noted that although parents often know their child has the variant, many are uncertain of its implications. Providers expressed particular concern around parents bringing their children in for clinic visits more often:

> …that we definitely have parents that bring their kids in sooner, they bring their kids in more often. The kids are not necessarily any more or less sick than the non-CPT1 children because especially the parents who really get it and grasped the education very well a lot of them say that they're very comfortable managing their child's illness at home even in light of the CPT1 but they do a lot of times want that reassurance.—NSHC Provider 4

Another provider reported that many caregivers believe that they should feed infants and children with the Arctic variant frequently, and they may continue this practice beyond infancy. One provider stated, "they [parents] think it's a disease their kid has, and then they feel like they have to feed them constantly so that they don't get sick…" (SCF Provider 3)

Participant recommendations

Education for providers and patients

Participants identified four areas in need of more education and support about the Arctic variant: (1) recommended feeding frequencies by age (e.g., at 1–3 months, 3–6 months, 6–12 months, 12–24 months, and beyond); (2) how *CPT1A* Arctic variant works, and what kinds of foods are best; (3) recommended feeding guidelines according to health status (e.g., when an infant is sick, preparing for surgery, or well); and (4) when to seek medical attention.

Community member and provider participants were concerned about the potential for caregivers to be unnecessarily worried and confused about caring for infants and children with the Arctic variant. Providers said that it should be an explicit goal to help caregivers understand that caring for children with the Arctic variant need not be especially complicated or frightening. One provider said, "We just think the – a reeducation of, if you feed the babies how they want to…[how] they normally eat, they want to eat every three hours when they're new, when they're newborn, and they want to eat every six hours when they're a toddler." (NSHC Provider 5).

Community members described receiving various types of guidance, and their descriptions did not indicate that care plans were updated as the child grew. For example, one parent said:

> They told me that he's going to have a completely different diet and that he wouldn't be able to eat certain things, like a more lean diet. So I had mentally and emotionally prepared myself for that, and then later on I asked about it – they didn't come back with me about it, but I asked about it again – and then they said, "Well, we think that he's just going to have to maybe carry around a candy bar when he gets older…" They did not refer me to anyone about his condition. He's going to be two in January, and most of the information I know is from myself and prodding… But the information is changing, and it's frustrating because it's the health of your baby.—NSHC Community Member 11

It is possible this participant was mistakenly given information about classic CPT1A deficiency, where children born with that condition do require a lean diet low in long-chain fatty acids (Bennett and Santani 2016; Bougnères et al. 1981). Participants also suggested that a variety of professionals in the healthcare setting—including nurses, chaplains, dieticians, behavioral health staff, and health aides should be prepared to educate caregivers about the Arctic variant.

Care coordination and referrals

All participants spoke of the importance of providing clear, timely newborn screening results to families. Providers stressed the need for coordination between the primary care team and specialty providers regarding how caregivers are notified that their infant has the Arctic variant, and the information they are given at that time. Although some providers said that pediatricians or primary care providers routinely discuss homozygous screening results with families, some community member participants reported otherwise. The consensus was that the newborn screening results return process varied by region, and the inconsistency contributes to confusion and misinformation regarding the Arctic variant.

Concern for stigma and cultural responsiveness

Without clear and consistent messaging about the Arctic variant, participants noted that homozygous screening results could instill fear and cause caregivers to believe something is seriously wrong with their child. Participants also suggested that a homozygous result could contribute to racist narratives about AN people being genetically inferior or not caring properly for their children. Participants recommended encouraging, informative, and culturally appropriate messaging from healthcare systems, public health agencies, and providers to increase awareness and understanding of the Arctic variant and its health implications.

Providers' language throughout the focus groups reflected a range of views, referring to patients who screened homozygous for the Arctic variant in various ways, including being "CPT1A positive," to having "CPT1 deficiency," to having an "abnormal test result." Some providers recognized that referring to the genotype as a disease or abnormality is inaccurate and could contribute to stigmatization.

Discussion

This is the first qualitative study to explore stakeholder knowledge and perceptions regarding the *CPT1A* Arctic variant in a circumpolar Indigenous population. Participant's knowledge and understanding about the Arctic variant and its health impact varied and reflected both a lack of information and misinformation with respect to the health implications of the Arctic variant and how it should be managed. Both community members and providers expressed interest in learning more and noted the need for additional education for all healthcare professionals serving AN peoples. Clear and age-appropriate guidelines for providing care for infants and children with the *CPT1A* Arctic variant were recommended by community members and providers.

In this study, community member participants wanted to be able to have support from various healthcare providers to discuss and learn about the care requirements for an infant with the Arctic variant. This finding is consistent with previous study findings from the public on their preferences of receiving genetic testing results (Daack-Hirsch et al. 2013). Similarly, preferences for a variety of professionals within the healthcare system to be able to disclose the results and discuss management were expressed, but it needed to be a person, "…they trusted and someone who was either knowledgeable about the finding itself or who would make a referral to a knowledgeable specialist" (Daack-Hirsch et al. 2013).

Supporting primary care providers in relaying newborn screening results is a documented need (Hayeems et al. 2013), and participants in this study shared similar concerns. Participants described inconsistent messaging and frequent misconceptions regarding the types of foods infants and children with the Arctic variant should or should not eat (sugary drinks, crackers, candy bars, glucose, starch) and the frequency of feeding. With the goal of avoiding hypoglycemia, caregivers may feed high-sugar foods, which can have negative long-term effects on the child's overall health. The development of clear policy guidelines was encouraged to address these concerns.

This study's results suggest that a systematic approach for ongoing provider and caregiver education on care of the child with the Arctic variant is needed, and that the state of Alaska is best positioned to manage and deliver such outreach. Refinement and continued outreach to enhance communication between healthcare professionals and parents will improve the care of infants and children with the Arctic variant. Moreover, outreach and communication across developmental stages and ages should be explored. In Iowa, for example, a systematic approach focusing on educational outreach improved access to hearing evaluation after a failed newborn hearing test (Sapp et al. 2021). Such an approach could help to meet the needs of both family caregivers and providers. Since these focus groups were conducted, the educational video for parents of infants that test homozygous for the Arctic variant by newborn screening has been updated based on feedback from parents and other stakeholders (Living with the Arctic Variant 2020; The Other Energy Crisis: Arctic Variant CPT1A 2013). In addition, a new training video specifically for healthcare providers has been produced (CPT1A Arctic Variant for Health care providers 2020). Additional qualitative assessments with providers and family caregivers will be necessary to assess the impact of these materials.

Limitations

The community member sample was not limited to caregivers or individuals of child-bearing age; some participants had never been parents, and others' children were long grown. Participants' views were limited to two regions and may not be representative of the larger AN population. In addition, participation may have been dampened in the mixed community member and provider focus group: providers may have said less out of concern about overpowering community member voices, and community members may have said less due to positional power differences.

Public health implications

This study identified several opportunities for improvement in the communication and education on care for infants and children with the Arctic variant: (1) ongoing communication and education about the Arctic variant and its health effects; (2) feeding guidelines including food types and fasting limits specific to infant/child age and health status; and (3) guidelines for providers and family caregivers about when to seek medical attention. Offering ongoing educational opportunities via multiple modalities for providers and caregivers on the Arctic variant could help improve the care of infants and children with the Arctic variant by providing culturally relevant recommendations and avoiding stigmatization, undue worry, and unnecessary intervention.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12687-023-00684-6.

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Declarations

Conflict of interest The authors declare no competing interests.

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