The experiences of parents of children diagnosed with cerebral adrenoleukodystrophy

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Received: 2 March 2023 | Revised: 2 October 2023 | Accepted: 4 October 2023

DOI: 10.1111/cch.13184

RESEARCH ARTICLE

WILEY

The experiences of parents of children diagnosed with cerebral adrenoleukodystrophy

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Funding information
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Abstract

Background: Adrenoleukodystrophy (ALD) is a rare X-linked neurodegenerative disease, affecting the brain, spinal cord and adrenal cortex. Childhood cerebral ALD (CCALD) is the most severe form of disease, involving rapidly progressive neurological deterioration. The treatment option for CCALD is allogenic haemopoietic stem cell transplant, which is only successful for early-stage disease. Parents' experiences of CCALD can inform healthcare delivery.

Study aim: To detail the experiences of parents of children diagnosed with cerebral ALD.

Methods: A descriptive qualitative study. Parents were recruited via a UK-based community support organisation. Data collection involved single semi-structured interviews structured around a topic guide and conducted remotely. Data were analysed using the thematic analysis approach.

Findings: Twelve parents from 11 families with a total of 16 children with ALD contributed to the study. Their 16 children with ALD followed one of three disease pathways, determined by the extent of neurological damage at diagnosis. Three themes, and their respective sub themes, describe the pathways and what they meant for parents. 'No possibility of treatment' concerns situations when CCALD was diagnosed at an advanced stage, the landslide of deterioration parents witnessed and their efforts to maintain normality. 'Close to the treatment threshold' describes situations where a small treatment window required parents to make agonising treatment decisions. 'Watching and waiting' explains the challenges for parents when disease was detected early enabling children to benefit from timely treatment.

Discussion: Parents' experiences were largely defined by the extent of cerebral damage at diagnosis, which determined the availability and success of treatment. There were specific challenges related to the three situations, indicating areas where support from health and care services may help parents deal with this devastating diagnosis.

Conclusion: This study indicates support needs of parents across the spectrum of CCALD diagnoses and highlights the critical importance of early diagnosis.

KEYWORDS
adrenoleukodystrophy, childhood cerebral adrenoleukodystrophy, experience, parents, qualitative

1 | INTRODUCTION

Adrenoleukodystrophy (ALD) is a rare X-linked neurodegenerative disease with an estimated population prevalence of one in 15 000–17 000 births (Bezman et al., 2001). The disease is caused by a defect in the ABCD1 gene that codes for a peroxisomal protein required for beta-oxidation of very long chain fatty acids (VLCFA) and consequently leads to an accumulation of VLCFA in plasma and all tissues, including the white matter of the brain, the spinal cord and adrenal cortex (van der Knaap et al., 2019).

ALD is characterised by rapidly progressive inflammatory demyelinating cerebral disease, slowly progressive spinal cord disease and adrenal cortical insufficiency and manifests in terms of several different phenotypes, each with its own clinical features and prognosis (Engelen et al., 2014; Huffnagel et al., 2019). The lifetime prevalence for adrenal insufficiency in approximately 80% in males with the gene defect and develops before the age of 10 years in half of them (Huffnagel et al., 2019). The neurological manifestations vary widely, even among members of the same family, and ranges from rapid and progressive cerebral demyelination to the more slowly progressive adrenomyeloneuropathy (AMN), which manifests in adulthood (Bezman et al., 2001; Engelen et al., 2014).

An estimated 30%–35% of affected males will develop childhood cerebral ALD (CCALD), the most severe form of the disease, before the age of 10 years (Huffnagel et al., 2019). In those children, development is usually normal until 4–10 years of age, when early symptoms appear. These are typically related to behavioural changes and cognitive dysfunction, as well as progressive deterioration of the vision and hearing, a decline in motor skills and epileptic seizures (Engelen et al., 2014). Disease progression is rapid leading to an apparent vegetative state within 2 years and death within a decade of diagnosis (Mahmood et al., 2007).

In the United Kingdom, there is no routine screening for ALD and diagnoses are primarily made on the basis of symptomatic presentation or subsequent extended family testing. In some other countries, including Taiwan, the United States and the Netherlands, ALD has been accepted as part of the newborn screening programme to enable early detection of disease and timely therapeutic intervention (Barendsen et al., 2020; Kemper et al., 2017; Moser et al., 2016).

Adrenal insufficiency is amenable to treatment with adrenal steroid replacement therapy, whilst the possibility of treating the neurological consequences of ALD is much more complex with limited treatment options and difficult treatment decisions. Allogenic haematopoietic stem cell transplant (HSCT) is currently the only treatment that can effectively arrest the progression of CCALD and substantially improve neurological outcomes. However, it has a high rate of morbidity and long-term sequelae related to immunosuppression and graft-versus-host disease (Peters et al., 2004) (Raymond et al., 2019), and is only successful if performed early, when the MRI is abnormal but neurological symptoms are not yet apparent (Matsukawa et al., 2020). A scoring system (the Loes score) is used to make decisions about whether to proceed to transplant. Several multinational prospective studies have assessed treatment outcomes of children receiving HSCT and consistently reported statistically greater rates of survival and rates of survival free of major functional disabilities among those with early disease as compared to those with advanced disease (Kühl et al., 2018; Yalcin et al., 2021).

Research that focuses on the experiences of those affected by rare conditions has a key role informing healthcare delivery because the insights generated enable health and social care providers to develop and deliver responsive services that offer best practice in care. In relation to CCALD, two studies provide some insights into the impact on parents of caring for a child diagnosed with advanced disease. In Taiwan, mothers reported the difficulties they had experienced obtaining a diagnosis of CCALD and securing any treatment and care for their child (Lee et al., 2014), whilst researchers in Japan reported high risk of depression and neurosis among mothers and fathers (Kuratsubo et al., 2008). A more detailed exploration reflecting the wider range of diagnostic and treatment circumstances that parents may experience is indicated.

Key Messages

- Following a diagnosis of ALD, the children followed one of three possible disease pathways. Each pathway was associated with a complex set of intensely difficult emotions for parents and presented them with substantial ongoing challenges, through which they had to navigate.
- The findings offer insight into the enormous emotional toll of caring for a child with ALD, indicating the importance of ensuring parents receive adequate long-term care and support.
- Rapid neurological deterioration in those children diagnosed too late for treatment results in escalating care needs. Health and care services need to recognise this factor and be sufficiently co-ordinated and responsive in order that children and parents receive appropriate aids and support in a timely and co-ordinated fashion.
- The contrasting experiences resulting from early or late diagnosis indicate the value of newborn screening to this population of parents. However, they also indicate the ongoing anxieties and uncertainties for parents generated by an early diagnosis, highlighting the importance of embedding adequate psychological support within such a programme.

2 | STUDY AIM

To provide detailed insights into the experiences of parents of children diagnosed with cerebral ALD.

3 | METHOD

This was a descriptive qualitative study involving parents whose children had been diagnosed with CCALD. Those parents who lived in the United Kingdom and whose child had been diagnosed in the last 20 years, on the basis that this is when HSCT became a recognised treatment for CCALD in the United Kingdom, were eligible to participate. ALEX The Leukodystrophy Charity (ALEX TLC), a UK-based charitable organisation that provides support for families with ALD assisted with recruitment by promoting the study within their membership via their social media platforms and regular newsletters, and by means of a communication briefly outlining the study. Those interested to participate were asked to contact the researchers (using the contact details provided) who provided them with a participant information sheet. A follow-up communication assessed eligibility, enrolled those willing to participate and organised an interview. Fifteen parents expressed interest in the study, one was not eligible, and two decided not to proceed, giving a total of 12 participants.

Although primarily a convenience sampling approach, the number of families we enrolled enabled us to achieve a purposive sample with variability across family characteristics and a range of condition specifics including time since diagnosis, presentation of disease and treatment options. Where both parents wished to participate, they could choose to be interviewed separately or together.

Data collection involved a single semi-structured interview using a topic guide (see Supporting Information). The structure of key questions with follow-up probes was designed to stimulate in-depth discussions with participants having the space and opportunity to share their experiences and viewpoints in their own words and on their own terms (Cresswell, 2008). All interviews were conducted remotely using either Zoom or telephone by a member of the project team (HP or CN). Verbal informed consent was taken and recorded immediately before the interview. The interviews were digitally recorded on a hand-held encrypted device and transcribed verbatim by a commercial company. Interviews lasted from 49 to 97 min with a mean length of 69 min. In a small number of cases, they were conducted in several sessions due to family pressures and demands on parents' time. We anonymised all data and allocated pseudonyms to parents for reporting purposes.

Data were analysed using thematic analysis, a theoretically flexible approach that is readily applicable to applied healthcare research. The six-stage process provides a robust, systematic coding framework within which patterns across the dataset can be identified in relation to the research question, to produce a rich and detailed account of the data (Braun & Clarke, 2006). To ensure rigour of the process, both researchers (HP and CN) contributed fully to all stages of the analysis. Briefly, this involved initially reading and re-reading the transcripts to fully familiarise themselves with the data, followed by independent coding of the entire dataset. We then met to review and compare the coding results and to collectively discuss, identify and agree a set of potential themes. Codes were collated under those candidate themes that were then revised and refined through ongoing iterative analytic processes by both researchers independently and then collectively to produce an overall structure of themes and subthemes. The thematic structure was shared with the project advisory group (comprising parents and consultant paediatricians with experience of CCALD) during the later stage of analysis to clarify aspects of our interpretations.

4 | FINDINGS

A total of 12 parents from 11 families participated in the study. Collectively, those families had 25 children of whom 16 had been diagnosed with ALD. Time since diagnosis ranged from 1 to 20 years. Table 1 provides a summary of routes to diagnosis and treatment.

The analytic structure contains three themes that detail in turn each of three distinct disease pathways we identified in the data. Those pathways were determined by the extent of neurological damage at diagnosis and the consequent treatment options and disease prognosis. All 16 children affected with ALD had followed one of those pathways. In families with more than one affected child, those children had followed different pathways. Table 2 provides an overview of the analytic structure of themes and subthemes.

5 | THEME 1: NO POSSIBILITY OF TREATMENT

5.1 | The route to diagnosis

In several children, the first indications of disease were neurological changes. Parents described a broadly similar pattern of events. The physical, behavioural or cognitive changes they identified triggered investigation but were not unduly concerning because plausible explanations were readily available. Sophie's and Jasmin's sons had both developed a squint that the ophthalmologist had assured them was extremely common. Scarlett had initially assumed that her son's behaviour changes were a response to the recent birth of his brother. James initially attributed his son's uncharacteristic difficulties constructing his lego to social isolation during Covid lockdowns and Sadiq told a similar story, recounting that he had noticed that sometimes his son was struggling to understand or acknowledge what was going on around him and assumed it was 'partly down to the whole Covid situation, kids not being in school'.

TABLE 1 Summary of the children.

Number of families	Number of boys with ALD	Presented with neurological signs	Presented with adrenal failure	Tested as a sibling, after their brother's diagnosis	Number that received HSCT
11	16	7	6	3	7

TABLE 2 Thematic structure.

No possibility of treatment	Close to the treatment threshold	Watching and waiting
Route to diagnosis	The possibility of treatment	Anticipating the need for treatment
A landslide of deterioration	Race against time	Living under a slight shadow
Keeping things normal		

However, the rate of deterioration they witnessed alerted parents to the likelihood that something was seriously wrong as Jasmin explained:

> One day he'd be disorientated, that next day he wouldn't. They were just really variable and very confusing for us to watch …. Over that six-week period of waiting [for investigations] he was becoming more disorientated, started to get more anxious, started to repeat questions. He'd just ask the same things over and over again …. and we noticed his ability to study was getting slower and slower. (Jasmin)

Waiting for a diagnosis, most parents' expectations 'were set at brain tumour or similar terrible event' (Jenny) and they were beginning to anticipate what would happen next, 'that he's going to have to go into hospital and have all sorts of treatments' (Sophie). They were totally unprepared for the CCALD diagnosis they did receive and the fact that there was no possibility of treatment because the cerebral damage was too severe for HSCT to be considered. Hearing that 'there is no real prognosis, it's terminal, there is nothing we can do (Holly)', was overwhelmingly difficult for all parents to comprehend.

> So we weren't given any false hopes or anything like that which, which was good … but, you look, you looked at [him] at that stage of diagnosis and you thought how is this going to happen because this boy who's got this awful scan can walk, talk, you know, how is this going to happen? (Ellie)

5.2 | A landslide of deterioration

Following diagnosis, rapid disease progression resulted in what Sophie described as a 'landslide of deterioration' over just a few months. Sadiq and James explained:

> From May, we had the concerns about schooling and stuff and just a bit clumsy …. But he went from being OK … going to school and doing everything as normal, and then by the end of July he'd actually lost the ability to walk, to talk, to eat or drink. (Sadiq)

> We've gone from a normal nine-year-old boy at the time, so he literally, he can't walk, he can't talk, he can't use his hands, he's being fed through a straw in not even a year, nine months, you know, and that's how aggressive it's been for us. (James)

Witnessing their child lose a succession of functions was intensely difficult and deeply distressing for parents. Each loss effectively served as a separate bereavement event such that 'It's like you're losing your child so many times over in this illness, every time they lose a function' (Scarlett). Holly and Ellie offered some insight into their experience:

> To start with he didn't really lose everything, but he'd lost quite a bit. He couldn't read and write anymore, and you'd have to tell him how to do things or do them for him, things that he'd previously been able to do himself, and that was quite distressing. (Holly)

> Now he isn't really interested in eating, which has been really hard …. it's almost like it's the last thing that he could do and enjoy… that's been really really hard because he loved his food … I feel sad for him because it's just another thing that he can't enjoy. I feel like we're running out of things to keep him happy that he enjoys. (Ellie)

The loss of function meant that there was increasing need for social care packages and aids for daily living. However, the rate of deterioration meant that routine assessment and response times were often too long. In most cases, the rarity of the condition meant that parents were dealing with care providers where 'nobody could quite believe how quickly he was deteriorating' and with services that were 'just always felt like they were a step behind' (Scarlett). Sadiq's example illustrates the point:

> Things like splints, for example, you know, going to the hospital department to get measured for, or moulded for a splint, and then by the time it arrives, it doesn't fit now, because the left foot's dropped even more than it had. (Sadiq)

5.3 | Keeping things normal

Parents were under intense pressure responding to the increasing carer needs of their affected child, and fully occupied with the day-to-day challenges of 'trying to keep all these plates spinning and trying to organise on top of everything else that's happening' (Sadiq).

A central concern for them was to try and maintain some degree of normality for their child. They carefully managed the extent to which others were involved in their care. Healthcare providers were often kept at arm's length and therapist involvement was framed in terms of social interactions as Jasmin explained:

> They're there for us … if we need the physio to come and see him, it's very covert, we'll say this is my friend who's just come to have a little play. We haven't medicalised him, in his life we just try to keep things as normal as possible. (Jasmin)

Parents resisted the involvement of social care as far as possible, commonly absorbing the increasing care demands until they could not cope any longer:

> I couldn't do every night, we couldn't do it between us, we were just on the floor, so we got nurses to cover night shifts. (Holly)

Parents worked hard to 'have as normal a family life as possible' (Scarlett) with social activities that maximised quality of life and where they could be a parent rather than carer. Ellie explained she wanted to be 'doing nice things so I can still be his mum'. Deteriorating cognitive function made this increasingly difficult, further adding to parent's distress as Jenny explained:

> He can't hear very well, he's tired … to be honest he's just generally miserable, which is very hard when we're trying to enjoy everything that we have left … it just limits some of the things that we'd like to do really, which is so gut wrenching when you're trying to do all these nice things and make the time precious. (Jenny)

6 | THEME 2: CLOSE TO THE TREATMENT THRESHOLD

6.1 | The possibility of treatment

Several of those who initially presented with adrenal failure, or who were tested as siblings following their brother's diagnosis, had evidence of cerebral damage at the point of diagnosis. Treatment by HSCT to prevent further cerebral damage was an option, but the MRI severity score (also known as a Loes score) indicated they were close to the treatment threshold as Sadiq explained:

> They'd told us that there is a procedure, a marrow transplant which could be used to halt the disease … our youngest son, even though he had a Loes score of 11, I believe, on his MRI, because neurologically he wasn't showing any symptoms, they said that they would consider the transplant. (Sadiq)

In that situation, treatment outcomes were very uncertain, and parents had to make rapid agonising decisions about whether to proceed, aware that the transplant may not work, and that the treatment could speed up progression of the disease. Roisin explained she had had been 'warned that we may have a very disabled son', and Sophie was similarly advised that 'there was going to be some disability, but [we were] hoping to hold it at a level where he could still live a fairly normal life'.

In most cases, parents were making those decisions for their younger child, acutely aware of the alternative because their older child had been diagnosed too late for treatment. They had all decided to go ahead with the transplant which offered 'that glimmer of hope for him' (Sadiq). Sophie explained their reasoning:

> You've got [your older son] there who is showing you if this treatment doesn't work for [your younger son], this is what we're going through for the second time … and that was extremely hard … We felt we've got to try it, you can't say no because if we hadn't done it, we would have thought he would have been fine if we had done it. (Sophie)

6.2 | A race against time

In this situation, it was a race against time to find a suitable donor and begin the transplant procedure before the window of opportunity for treatment closed. Holly's son deteriorated rapidly before treatment could begin and the glimmer of hope that it had offered for him and his parents was extinguished:

> The first time we saw him [the consultant], he said, we can only do the transplant if there is no further deterioration …. then he [my son] had a really big seizure and was in the intensive care unit. I could tell he'd deteriorated, we all knew as a family … and [when we saw the consultant again] he looked us both in the eye and he said … we're not doing it. … basically he said you just take him home and wait for him to die. (Holly)

All the other children in this situation received transplants but deteriorated rapidly during and after treatment. Parents described the distressing experience of witnessing that loss of function and realising that the transplant was not successful:

> We were already seeing signs that it probably didn't work and if anything had accelerated the disease,

> which was one of the risks associated with it. And since then, he's deteriorated quite considerably …. It's been very difficult at times, because he went into the hospital fine so to speak, and he came out obviously a shadow of his former self. (Sadiq)

> During transplant we realised that he was starting to lose his hearing and his eyesight. He could still read, but he couldn't watch television because he couldn't watch anything fast moving … he's continued to deteriorate…. he's fully dependent for everything … can't speak, … he can hear but it comes and goes. He can't see, he's tube fed, yeah, he can't even scratch his nose … so the transplant didn't work although I think he's in a better place than if he hadn't had the transplant. (Sophie)

7 | THEME 3: WATCHING AND WAITING

7.1 | Anticipating the need for treatment

Among those who were tested as a sibling or who first presented with adrenal insufficiency, several had received their ALD diagnosis at an earlier stage of the disease and had no signs of cerebral damage. A period of regular testing began to monitor disease progression and identify the early signs of cerebral damage that would indicate the need for HSCT. The process of identifying a suitable donor began immediately and parents focused their hopes on knowing that 'steps were being taken so that no time would be wasted' (Scarlett) when treatment was indicated.

This period of waiting was one of prolonged uncertainty for parents, punctuated by heightened anxiety at the time of each scan as Liz explained:

> There is no one path that everybody follows. Some people can deteriorate quite quickly; some don't really deteriorate at all. So really you have no idea which path you're on. And it's a case of you can have MRIs every three months and every three months you're waiting for those results and waiting to see, you know, is he OK this time, is he not OK, are we going to BMT, and it's just, you know, it's just a waiting game. (Liz)

Whilst neurological damage was not inevitable and did not occur in all cases, the mixed emotions parents experienced when the first indications of damage were detected offer insight into the level of anxiety associated with that waiting period:

> That period of time when you're going through monitoring and waiting for results of MRI scans and whether your child needs a bone marrow transplant, the relief when he finally needed a bone marrow transplant was palpable. It was kind of like, oh my God, and also, thanks goodness that we can actually do something about this now. (Scarlett)

7.2 | Living under a slight shadow

The overall experience of HSCT was extremely difficult for parents because, as Liz explained 'you go into hospital with a well child and basically you make them a lot iller'. Aisha described a relatively straightforward experience, but others, including Scarlett's son, had experienced adverse drug reactions and other complications adding further to the trauma for both parent and child.

> He went in and had his bone marrow transplant, and a few little hiccoughs but thankfully he had a very successful transplant. He engrafted hundred percent and was home seven and a half weeks later, which compared to some is very quick. (Aisha)

> I don't think either of us would want to go through bone marrow transplant again. It wasn't that straightforward. He had a massive reaction to cyclosporine and ended up having a massive fit … and that was absolutely terrifying … and then he had a relapse and blew up like a balloon, and then he ended up with bronchiolitis … which was equally terrifying. (Scarlett)

All the children in this group had engrafted successfully and had developed normally, without neurological damage. Parents however acknowledged the limits of the treatment, which was unlikely to offer protection from the other long-term consequences of ALD. This was an ongoing cause of concern as Liz and Scarlett explained:

> There's a lot of things that rumble along in the background, but essentially, he's generally pretty healthy now so, so we're in a good place … but there is still an unknown as to whether he can still get AMN as an adult, nobody really knows, so we still live under a slight shadow, it's always there in the background really. (Liz)

> It (HSCT) removes the risk of cerebral ALD and I think he's still at risk of AMN. I think they don't know yet because the bone marrow transplant is relatively new, so they're still monitoring most boys that are now of an age to get AMN, but maybe a third of the boys that have had transplants might go on to get AMN. (Scarlett)

8 | DISCUSSION

Our findings demonstrate the devastating impact that a diagnosis of CCALD has on parents. The three themes focus in turn on the three

disease pathways children followed. Those pathways were defined by the degree of cerebral damage at diagnosis which determined whether treatment was a possibility and whether that treatment was successful. Each pathway generated a complex set of intensely difficult emotions for parents and presented them with substantial ongoing challenges, through which they had to navigate. Additionally, several parents had more than one affected son, following different disease pathways, and so were dealing simultaneously with the emotions and challenges generated by those pathways and the complex interplay between them. These findings, which provide the first detailed insight into the different circumstances of CCALD and what they mean for parents, have clear relevance to clinicians who need to understand the different circumstances and the distinctions between them in order to offer provide parents with appropriate support.

Others who have studied the experiences of parents whose child is affected by life limiting conditions including CCALD have identified many manifestations of the intense and painful emotions parents experienced, and the roller coaster of daily challenges, leading to feelings of persistent stress, anxiety and isolation and periodic emotional breakdowns (Bally et al., 2018; Lee et al., 2014). The emotional impact is also reflected in the psychological literature that reported poorer levels of functioning among parents of children with a range of life limiting conditions as compared to published norms (Jaaniste et al., 2022) and high levels of depression and neurosis among parents of children with CCALD (Kuratsubo et al., 2008). A study involving parents of children with a range of progressive neurodegenerative conditions similarly identified living grief arising from each successive loss of function, which they identified as chronic sorrow, and parents' focus on maximising quality of life in the short time available to them (Rallison & Raffin-Bouchal, 2013).

Our findings support these findings and provide more detailed insights into specific aspects of particular difficulty for parents, indicating several areas where health and care services might respond to provide appropriate support. The difficulties Scarlett and Sadiq experienced in securing the physical devices and aids they needed to manage their child's deteriorating physical condition, and their frustration when negotiating with services that were 'always behind the curve' and receiving aids that were already inadequate, indicate the limitations of this service. In order to enable parents to continue to provide their child with the care they require, services need to understand the urgency of the situation and be sufficiently responsive to the rapidly changing needs with timely assessment and procurement processes that acknowledge the urgency of the situation. The rapid deterioration of advanced disease placed a substantial and increasing care burden on parents who, despite the physical and emotional toll on themselves, were determined to cope. Their determined focus on keeping things normal for their son and making the most of the limited time they had with him, translated, among other things, into resisting medicalisation by keeping health services at arm's length, and a reluctance to accept input from outside care agencies, until they reached a stage of exhaustion. Our findings suggest the benefits of joined up services that would help to reduce the organisational burden on parents that Sadiq referred to and a flexible and responsive approach to care and support.

As previously reported, treatment by HSCT leads to statistically greater rates of survival and rates of survival free of major functional disabilities among those with early disease as compared to those with advanced disease (Kühl et al., 2018; Yalcin et al., 2021), highlighting the critical importance of early diagnosis. In the United Kingdom and elsewhere, an initial diagnosis of ALD within a family will lead to a programme of extended family testing to identify others at risk of disease (Bezman et al., 2001). When that initial diagnosis is CCALD, the prospects for other children in the family identified at risk of disease through this route will likely be substantially better than for the child who has presented with symptomatic disease because of the possibility of treatment. However, those prospects will be limited for those children with pre-symptomatic disease at the time of testing. Given that CCALD develops between 4 and 10 years of age (Engelen et al., 2014), the age of the child at the time of testing is critical but will be determined by circumstantial factors and primarily the relative ages of the children in a family. In Scarlett's family, the substantial age difference between her sons meant that the youngest was identified as at risk when he was a toddler and could therefore receive HSCT in the early stages of CCALD. By contrast, Sophie's and Sadiq's second sons were close in age to their affected brothers and had signs of disease at the point of testing, presenting parents with agonising treatment decisions. Mekelenkamp et al. (2020) reported similar findings from their study that explored parental experiences of HSCT for a range of conditions. The parents in their study perceived that withholding the transplant was a choice that would result in their child's death and was therefore not considered a realistic option, even in those cases where chances for survival were rated low.

In recent years, several countries including the United States, Taiwan and The Netherlands have incorporated ALD into their national newborn screening programme (NBS) and pilot studies are currently underway in Italy and Japan (Albersen et al., 2023; Bonaventura et al., 2022; Chen et al., 2022; Moser et al., 2016; Shimozawa et al., 2021). Families affected by ALD are supportive of including ALD within the NBS programme that would enable those at risk of disease to be identified and then screened prospectively so they can receive timely treatment (Schaller et al., 2007; Schwan et al., 2019). However, parents whose children had been identified with ALD through NBS struggled with the prolonged uncertainties resulting from a positive result and identified their need for mental health support (Schwan et al., 2019). The stress and anxiety associated with early detection and screening were similarly reported by parents in our study, indicating that the need for ongoing care and support that parents in the Schwan study identified will be equally applicable to all parents in that situation.

9 | STRENGTHS AND LIMITATIONS

We worked with a community-based organisation to promote the study within the ALD community. Whilst this approach necessarily limited recruitment to those who were engaged with that

organisation, the organisation has national coverage and a long-term membership that enabled us to recruit participants who collectively offered a broad range of experiences concerning the different stages of disease at which diagnoses were made. To our knowledge, this is the first study to provide that breadth of insight. Whilst the majority of participants were mothers, two fathers contributed to the study, providing a perspective that is often marginalised. The passage of time since the experiences that parents described varied substantially and may have influenced the data to some degree.

10 | CONCLUSION

A diagnosis of CCALD is devastating for parents and has profound implications. The three possible disease pathways children followed were determined by the stage of disease at diagnosis and the possibility of treatment and largely defined parents' experiences. Parents detailed the substantial challenges and difficulties associated with each pathway, indicating where and how health and social care services might respond to ensure parents receive the support and care they require. The starkly contrasting realities parents described between those diagnoses that heralded a bleak future and those that offered hope contribute to the ongoing policy debates about expanding NBS to include ALD.

AUTHOR CONTRIBUTIONS

Hilary Piercy: Data curation; formal analysis; writing—original draft; methodology; investigation; writing—review and editing; funding acquisition. **Charlotte Nutting:** Data curation; formal analysis; investigation; project administration; writing—review and editing.

ACKNOWLEDGMENTS

The project was funded by ALEX TLC. Our grateful thanks to all those who participated in the study, to the team at ALEX TLC for their assistance with recruitment and to all the members of the advisory group for their input and guidance.

CONFLICT OF INTEREST STATEMENT

None of the authors have a conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The project received approval from the university ethics committee (ER37567144).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Piercy, H., & Nutting, C. (2023). The experiences of parents of children diagnosed with cerebral adrenoleukodystrophy. *Child: Care, Health and Development*, e13184. https://doi.org/10.1111/cch.13184