

Parent-reported disease burden in Krabbe disease: Evaluating outcomes of hematopoietic stem cell transplant



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Background

Methods

oKrabbe disease (KD) is a rapidly progressive neurodegenerative disorder caused by β -galactocerebrosidase deficiency.

oThe only approved disease modifying therapy for infantile KD (IKD) and late-infantile KD (LIKD) is hematopoietic stem cell transplantation (HSCT) when performed in pre-symptomatic stages.

oWhile KD was recently added to the RUSP, only 12 states have an active KD newborn screening (NBS) program.

oIt is uncertain at what rate states will conform to the RUSP recommendations, with a frequently cited barrier being the absence of studies addressing the impact of HSCT on quality-of-life.

oThe purpose of this study was to investigate patient/parent reported outcomes of HSCT by comparing qualitative and quantitative data collected during structured caregiver interviews.

o90-minute caregiver interview was designed to evaluate patient/family-centered outcomes of HSCT in relation to quality-of-life.

oComparisons were made between 1) children not transplanted or transplanted after symptom onset **against** 2) those transplanted before symptom onset.

oInfantile KD (IKD; onset <12 months) and late infantile KD (LIKD; onset 13-36 months) were analyzed independently.

oQuantitative data was collected using the validated Leukodystrophy quality-of-life assessment (LQLA) .

oThe LQLA consists of 43 questions divided into 4 domains. Non-paired t-test were used to compare total score and sub-scores for each domain for non/late-transplanted versus early transplanted patients.

oQuantitative data was collected using open-ended data with common themes identified using two independent coders.

Results

Table 1: Demographics (N=40)

Cohort	N =	Deceased	Mean Age	Mean age of diagnosis	Diagnosed with NBS
IKD Late/Non-transplant	19	14 (64%)	67.3 mo	7.1 mo	1 (5%)
IKD Early transplant	10	2 (20%)	74.6 mo	0.3 mo	9 (90%)
LIKD Late/Non-transplant	7	0 (0%)	120 mo	29.7 mo	1 (14%)
LIKD Early transplant	4	0 (0%)	219 mo	13.8 mo	0 (0%)

Table 2: IKD LQLA

Domain	Early Transplant	Non/Late Transplant	P-value
Overall	Mean: 30.7; Range 23-38	Mean: 20.57; Range: 13-27	p<0.00001**
Communication	Mean: 8.7; Range 5-10	Mean: 4.84; Range 1-10	p=0.000284**
Daily Living	Mean: 11.7; Range 9-14	Mean: 8.79; Range 5-12	p=0.001188**
Social/Family	Mean: 6.7; Range 4-9	Mean: 5.79; Range 3-9	p=0.089792
Motor	Mean: 2; Range 0-5	Mean: 1.16; Range 0-4	p=0.089792

Table 3: LIKD LQLA

Domain	Early Transplant	Non/Late Transplant	P-value
Overall	Mean 33; Range 26-40	Mean: 25.29; Range 15-29	p=0.022086**
Communication	Mean: 8; Range 6-10	Mean: 8.29; Range 5-10	p=0.4305
Daily Living	Mean: 12.75; Range 11-14	Mean: 9.43; Range 4-13	p=0.031743**
Social/Family	Mean: 7; Range 6-10	Mean: 5.71; Range 3-8	p=0.103511
Motor	Mean: 4.75; Range 3-6	Mean: 1.86; Range 0-5	p=0.007441**

Figure 1. Caregiver physical burdens

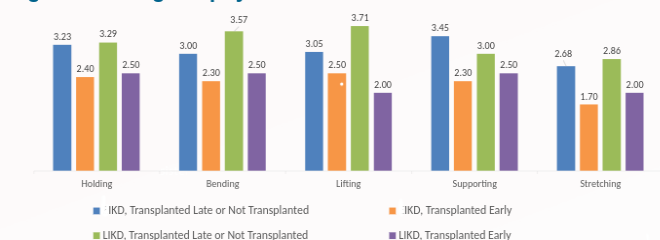
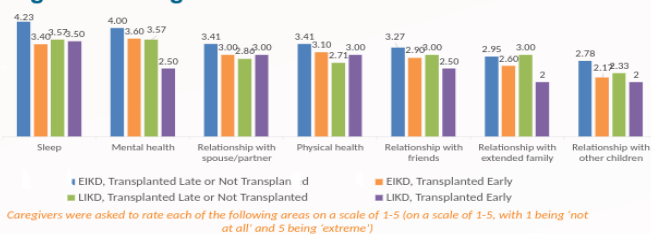


Figure 2. Caregiver emotional and social burden



Illustrative quotes show the various ways the diagnosis has impacted caregivers' relationship

"Overall, we have grown a lot stronger. We have moments when we deal with this disease very differently... I push it out of my mind and he analyzes over and over, so we balance each other out. There are moments, though, like during transplant, I wasn't sure our marriage would make it. You are in a hospital for 6 months, the amount of anger this disease brings gets taken out on your spouse. Thankfully we have gotten stronger and it has made us here where there's no way I could do anything without him. He understands everything related to this disease which is not something anybody else gets". (LIKD, Transplanted Late or Not)

"The diagnosis and being away for transplant tied into my divorce. We both handled it a lot differently, he was away from him for 9 months while he got the transplant, wasn't there during a lot of it and didn't understand a lot of it. He was shell shocked when he got back and couldn't handle all the changes in medical care. I was traumatized and so tired... I had lived in a hospital for 9 months and needed help but I wasn't getting help and he shut himself off with video games. We coped a lot differently and still do to this day. For me I see my son as a blessing and for him it's more like he's going to die and doesn't want to think about the good stuff...but you can't think about just the good stuff. I wouldn't say the diagnosis was the only reason, but it pushed us towards that. We had issues before that." (EIKD, Transplanted Late/Not)

Discussion

oThis study provides convincing evidence that HSCT improves quality-of-life and reduces caregiver burden in IKD and LIKD.

oIn general, early transplanted families benefitted from improved familial and social relationships, less missed educational opportunities, less financial strain, better sleep, and less time providing care. They also felt a greater sense of control over their life.

oAlthough there was variability between individual responses, parents of early transplanted patients often suffered less physical stress.

oThis data will be invaluable to states debating whether to add KD to their NBS panels with hopes to facilitate early diagnosis and treatment.

oIt will also allow families to weigh the risks and benefits of HSCT more confidently when making the life-altering decision of whether to proceed with transplant.



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References

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