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Determinants of Health Care Utilization in a Population-Based Leukodystrophy Cohort

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Abstract

Objectives—To determine the costs for children with leukodystrophies, and whether high costs were associated with characteristic clinical features or resources utilization.

Study design—We determined health care costs in a population cohort of 122 patients with leukodystrophy including inpatient, outpatient, and emergency department use, over a 9 year period. We analyzed differences in patients with high costs (>85th percentile) and their health care utilization.

Results—Patients with leukodystrophy had significant variability in resource utilization, with the top 15th percentile of patients accounting for 73% of costs ($9.6 million). The majority of costs, 81% ($10.8 million), arose from inpatient hospitalization. High-cost patients had more and longer hospitalizations, increased requirements for intensive unit care and mechanical ventilation, and significantly more infections. Importantly, bone marrow transplantation did not solely account for the difference between high-cost and low-cost groups.

Conclusion—Inpatient hospitalization is the greatest source of health care resource utilization in patients with leukodystrophy. A minority of patients account for the majority of costs, primarily due to an increased volume of hospitalization. Strategies to improve care and reduce costs will need to reduce inpatient stays and target modifiable reasons for hospitalization.

Keywords

Leukodystrophy; cost analysis; hospitalization; pediatric; bone marrow transplant

Inherited leukodystrophies are diverse diseases, including abnormal myelin development, hypomyelination, and myelin degeneration.[1,2] Over the past two decades the characterization and diagnosis of leukodystrophies has been aided tremendously by magnetic resonance imaging (MRI) and improved genetic testing,[3] but up to 51% of patients

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still do not receive a specific diagnosis.[4,5] Treatment for leukodystrophies is largely supportive. Bone marrow transplantation (hematopoietic cell transplantation), umbilical cord blood transplantation, and enzymatic therapies are currently used for a subset of diseases, and only benefit a minority of patients.[6–8] For the great majority of patients with leukodystrophy, however, care is not curative, and only a very few experience therapies that significantly alter the course of disease.

Even though the current standard of therapy for most patients is supportive, the costs of these treatments can be substantial. Children with neurological impairments, including leukodystrophies, account for a significant disease cohort for children's hospitals' admissions and costs, making up 29% of all hospital charges in 2006.[9] It is important to determine what the reasons for hospitalization were, and how inpatient costs contribute to the overall health care costs.

The objective of our study was to determine the health care costs of pediatric patients with leukodystrophy. We used detailed hospital billing data to characterize the resources involved in caring for these children. We sought to determine what the major costs for patients with leukodystrophy were, and whether there were clinical characteristics associated with increased health care costs. We analyzed whether different patients accounted for different proportions of the costs, and if there were potentially modifiable reasons for health care utilization.

METHODS

This study was approved by the Institutional Review Boards at the University of Utah and Intermountain Healthcare. A cohort of 122 patients with confirmed inherited leukodystrophies seen over a nine-year period at a children's hospital providing both primary and tertiary care was compiled through June 30, 2009.[5] Cases were identified through a computerized search of diagnosis codes and confirmed by manual chart review.[5] The primary study hospital is the sole tertiary care pediatric hospital in Utah, and receives referrals from Wyoming, Idaho, Montana, and parts of Nevada, Colorado, and Arizona. The study hospital is part of Intermountain Healthcare (IH). IH is a large, vertically integrated not-for-profit health care system in the Intermountain West encompassing 23 hospitals (including the single children's hospital) and more than 185 physician clinics. IH maintains records including admissions, emergency room visits, clinic visits to pediatric neurology, testing, pharmacy, and home health visits, in an electronic record format for its hospitals and clinics and affiliated providers. Data were extracted for each patient in the cohort from the Enterprise Data Warehouse (EDW) maintained by IH. The EDW contains financial data from inpatient, outpatient, and emergency room visits and can be searched by patient, encounter, date range, or ICD-9 code, among other variables. We queried the EDW using unique identifiers assigned to each of the 122 patients with leukodystrophy.

The EDW contains detailed cost data for the IH system.[10–12] Costs were derived from IH's cost accounting program, the Standard Cost Master, which is a single activity-based cost accounting system that spans all of IH care delivery locations (inpatient, outpatient and ED). It reflects the costs of individual units of care (e.g., a single dose of a drug, a single lab test, an acuity-adjusted hour of nursing services, or a specific radiologic exam). The costs are also standardized across the system irrespective of location of care, and incorporate fixed and variable costs. The EDW is organized with detailed line-item costs for all diagnostic tests, therapeutics, supplies, room fees, and facility fees, as well as the dates and location of service.

The cost data were analyzed in two ways: 1) patient setting: outpatient vs. inpatient vs. emergency department; and 2) individual charge group costs. 59 different individual charge group costs were available from the EDW, which were then organized into three categories: diagnostic, room/supply, and therapeutics (Table I; available at www.jpeds.com) for all settings. The "high-cost" group was identified after ordering the cohort by total cost per patient, then analyzing patients who were above the 85th percentile.

Characteristics of both the high-cost group and the remainder of the cohort were examined in an effort to discover if certain clinical or etiologic features were able to predict a "high-cost" patient with leukodystrophy. The differences in respective proportions were evaluated for statistical significance using *p* values. Number of days requiring mechanical ventilation was determined by querying for daily charges for mechanical ventilation support. Patients who received a bone marrow transplantation was determined both by manual inspection of medical records, as well as cross-referencing patient records using the 41.x procedure code.

Once costs had been collected, aggregated, and stratified by encounter type and service year, they were adjusted to 2009 constant U.S. dollars using inflators for western states from the medical product price index on the Department of Commerce Web site.[13] Cost data for practitioner professional fees are not available in the EDW. Descriptive statistics were used to characterize the study cohort. Two-tailed *p* values were calculated using Fisher's exact test. Mean, median, and interquartile ranges (IQRs) and total hospital costs were determined and compared for each group.

RESULTS

Total costs were calculated for the group as a whole as well as for individual patients. The total cost for the entire cohort was $13.1 million. The mean cost of medical care of a patient with leukodystrophy during the study period was $107,225 US dollars (Table II). The majority of costs, 81%, or $10.8 million, arose from inpatient stays. The causes of leukodystrophy in these patients were diverse, with more than 20 different diagnoses. The most common diagnoses were (described in Bonkowsky et al.),[5] in descending order of frequency: unknown/no diagnosis; metachromatic leukodystrophy; Pelizaeus-Merzbacher disease; mitochondrial; and x-linked adrenoleukodystrophy.

To determine what services and utilization accounted for the costs, we compiled and organized all line-item charge data into one of three categories: Diagnostic; Therapeutics; or Room/Supplies (Table I). Cost data for each line-item was extracted from the EDW and placed into the categories. Room/Supplies accounted for $7.1 million or greater than 50% of costs, and Diagnostic and Therapeutic categories comprised $2.6 million and $3.3 million respectively, each close to 25% of total costs (Table III). Other significant contributors to cost included pharmacy costs (part of Therapeutics costs), totaling greater than $1 million, or 11.1% of total costs; and laboratory costs (part of Diagnostic costs), accounting for 15% of all costs.

The distribution of costs was skewed, with a small number of patients accounting for the majority of costs. We evaluated characteristics of patients accounting for the top 15th percentile of costs: the "high-cost" group consisted of 18 patients. Patients in the high-cost group had a per patient mean cost of $531,555, and the remaining 85% of patients (the "low-cost" group) had a per patient mean cost of $33,783 (Table II). We then assessed the cost group profiles for the two groups separately (Table IV). Interestingly, even though overall costs were very different in the high- versus low-cost groups, the relative proportions of costs remained practically identical. For example, in the high-cost group of 18 patients total costs for Room/Supplies was $5,289,160, compared with $1,859,164 in the low-cost group

for 104 patients. However, the percentage of total costs accounted for by Room/Supplies was almost exactly the same, at 55.3% compared with 52.9%, respectively. Therefore, at least in the structure of costs, the high-cost and low-cost groups were indistinguishable.

We also analyzed costs by time, to determine whether overall length of time, for example from time of presentation, or length of time to death, might significantly influence costs. We found that average per patient per year cost was $24,495, with ranges from $1/year to $601,429/year. There was no direct correlation between costs/year and length of time that care was provided. For example, 10 of the 18 high-cost patients had an average length of care in the system of 2.7 years, compared with 5.2 years for the entire cohort.

We next assessed whether there were clinical factors that were characteristic of high-cost patients with leukodystrophy (Table V). We evaluated factors that we had previously shown to be associated with variation in clinical outcomes in patients with leukodystrophy.[5] In addition, we also evaluated variable such as bone marrow transplantation or need for intensive unit care that would be expected to lead to higher costs. Five clinical characteristics were predictive of patients in the cohort who had a cost profile greater than the 85th percentile: “walk ever;” “at least one word ever”; endocrine abnormalities; diagnosis of metachromatic leukodystrophy (because these patients commonly receive bone marrow transplanation); and underwent bone marrow transplant. However, in addition to clinical characteristics, hospitalization-associated costs were highly associated with being in the high-cost leukodystrophy group (Table V). These features included both the overall length of stay and the number of hospital admissions; whether intensive care unit (ICU) care was needed; whether mechanical ventilatory support was required; and whether a patient had an infection (either viral or bacterial).

To determine whether hospitalization-associated charges were still associated with high costs in the absence of bone marrow transplant, we evaluated these charges without the subgroup of transplant-recipient patients (Table VII; available at www.jpeds.com). A total of six patients received bone marrow transplantation for metachromatic leukodystrophy and for x-linked adrenoleukodystrophy. Strikingly, hospitalization-associated costs were still significantly associated with the high costs group, including length of stay, number of admissions, percent and number of ICU admissions, percent and number of ventilator days, and percent and number of infections.

DISCUSSION

This study evaluates health care burden and costs for pediatric patients with leukodystrophy. Our data show that the primary determinant of costs for pediatric patients with leukodystrophy is inpatient hospitalization (81% of all costs). The top 15th percentile of patients accounted for 73% of costs, and a high-cost patient had average costs 15-fold greater than a low-cost patient. This high-cost group was defined by a severe disease course, with more and longer admissions as well as ICU admissions. This was true regardless whether they had received a bone marrow transplant. Although recipients of bone marrow transplants accounted for a third of the high-cost group, they did not solely account for the high costs. Further, because we were able to determine the length of time that patients were cared for, we demonstrated that length of time of care did not correlate with the costs patient incurred.

We found that infections, and requirements for ventilatory support, were significantly associated with high cost. Both infections and need for ventilatory support are potentially modifiable risk factors. For example, more aggressive respiratory care improves survival rates of children with spinal muscular atrophy, a chronic neurological disease.[14] Whether

this pro-active respiratory care model results in lower costs is currently unknown, but would be important to characterize for the development of any clinical care process pathway.

In contrast, other clinical factors that one might expect to be associated with high cost because of presumed more severe disease course did not reveal a clear trend. Two of these clinical characteristics, “at least one word ever” and “walk ever” may reflect a group of patients with more severe disease. These patients may have significant bulbar dysfunction, spasticity, or orthopedic issues leading to increased hospitalizations and need for surgical procedures, as well as more frequent clinical follow-up. However, it is surprising then that two other clinical features associated with a severe disease course - death, and requirement for a gastrostomy tube - were not significantly elevated in the high-cost group. Although a diagnosis of metachromatic leukodystrophy was associated with higher costs, this was due to the association with bone marrow transplantation. Other diagnoses not receiving bone marrow transplantation also were represented in the high-cost group, but the very low numbers of patients did not permit statistical analyses.

Our data on costs are unique because we had the ability to comprehensively track and identify patients as a majority of pediatric patients in Utah are cared for by the same health care system. The health care system maintains records including admissions, emergency room visits, clinic visits to pediatric neurology, testing, pharmacy, and home health visits, in an electronic record format for its 23 hospitals and numerous clinics and affiliated providers.

Another significant innovation of our work is that it was not based simply on end-user charges.[15] This was because the activity-based cost accounting system allowed detailed analyses on the location and unit costs, which was internally standardized across the IH system. In turn, the data are not skewed by adjustments, for example, billing to insurance or the patient, which can affect methods that use the charge/cost ratios.[16] We chose to analyze the data by splitting our analysis into high-cost versus low-cost groups, which revealed the differences in health care utilizations. Costs for patients with leukodystrophy are not distributed in a normal fashion,[5] but the disproportionately very high costs of a small number of patients weighted the analysis in such a fashion that regardless of the exact percentile chosen to represent the high-cost group the results were very similar.

Limitations of this study include that it represents a single health-care system, and it is possible that some data were lost if patients sought services from other providers. All data were collected retrospectively, and cost data may have been affected by total duration of the patient in the study as we did not annualize costs data. The limited sample size precluded multivariate analysis of characteristics for comparing patient groups, and imposes restrictions on the statistical significance of our findings. Another limitation is that physician services were not included in the cost analyses. Even though we expect that physician service costs would mirror overall costs, such that high cost patients would also require more physician services, we do not have data on this question. In addition, we have no data on costs from the family perspective, including out-of-pocket or caregiver costs associated with caring for these children. Future studies on leukodystrophy health care costs and utilization would thus ideally include multi-center and/or national data sets, as well as on costs from physician services and the family perspective. However, the low specificity of ICD-9 codes for correctly identifying inherited leukodystrophies has been a barrier to these studies.[5]

Our findings for cost data mirror the health care burden for patients with leukodystrophy, as well as for children with other chronic neurological diseases. Children with neurological diseases have increasingly longer survival because of improved management of co-morbid conditions such as oromotor dysfunction and chronic lung disease.[17,18] Further, children

with neurological impairments account for one-quarter of hospital days, and almost a third of charges within children's hospitals.[9]

To summarize, our findings demonstrate that most of the medical burden in leukodystrophies arises from a minority of patients. Inpatient hospitalization volume is the primary reason for the high costs for this group of patients. Two potentially modifiable risk factors, infections and need for ventilatory support, could be targeted to reduce the need for hospitalization. With a goal of improving the quality and efficiency of medical care in patients with leukodystrophy, efforts to investigate if increased costs lead to improved outcome or quality of life may be helpful.

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ABBREVIATIONS

EDW	electronic data warehouse
IH	Intermountain Healthcare
MRI	magnetic resonance imaging

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Table 1

Charge groups for EDW billing, categorized into either “Room/Supplies,” “Therapeutics,” or “Diagnostics” cost groups.

Room/Supplies	Therapeutics	Diagnostics
Room and Care	Operating Room	Imaging-General (Radiology)
Nursing Ancillary	OR Supplies	Imaging-CT
Nursing Supplies	Anesthesia	Imaging-Interventional
Recovery (PACU)	Pain Management	Angiography
Same Day Services	Dialysis/Renal	Imaging-MRI
Transport/Life Flight	Transplant	Imaging-Nuclear Medicine
Emergency Room	Oncology/Bone Marrow	Imaging-Ultrasound
Labor and Delivery	Radiation Therapy	EEG/EMG/Sleep Lab
Neonatology	Respiratory Therapy	EKG
Dental Clinic	ET Therapy	CV Lab (Cardiology)
Medical Office Building	Physical Therapy	CV Monitoring
Instacare/Clinic #1	Occupational Therapy	Endoscopy
Instacare/Clinic #2	Occupational Therapy-(Industrial)	Lab-Immunology
Instacare/Clinic #4	Lactation Tech	Lab-Chemistry
Hospital-based Clinics	Audiology/Speech Pathology	Lab-Cytology/Pathology
Home Health	Orthotics	Lab-Hematology
	Retail Pharmacy	Lab-Microbiology
	Pharmacy	
	IV Therapy/Nutritional Support	

Table II

Total costs by setting; and mean per capita costs for high, low, and overall population patient groups.

Setting	**Total Costs ($ US)**	**Percent of Total**
Inpatient	10,796,385	81%
Outpatient	2,329,966	18%
Emergency	128,814	1%
Patient Group	**Per Capita Costs ($ US)**	**Number**
High cost (>85%ile)	531,555	18
Low cost (<85%ile)	33,783	104
Overall population	107,225	122

Table III

Health-care costs of patient with leukodystrophy, evaluated by cost groups for all cost settings.

Category	Total	Percent of total	Mean	Median	25th Quartile	75th Quartile
Total	**13,081,454**		**107,225**		**6,747**	**74,192**
Diagnostic	2,608,257	19.9%	21,379	5,728	2,378	15,039
Imaging	603,954		5,033	2,067	858	6,840
Laboratory	1,960,432		16,337	3,228	1,002	9,124
Other	43,872		366	-	-	327
Room and Supplies	7,148,324	54.6%	58,592	9,964	959	42,679
Care	6,571,225		54,760	8,359	936	33,522
Supplies	577,098		4,809	299	-	1,748
Therapeutics	3,324,873	25.4%	27,253	4,280	912	25,564
Acute	728,618		6,072	635	-	2,796
Chronic	1,148,211		9,568	1,900	262	13,220
Pharmacy	1,448,044		12,067	805	108	6,422

Amounts shown are inflation-adjusted to 2009 U.S. dollars. Mean, Median, and 25th and 75th Quartile values are given per patient.

Table IV

"High-cost" (top 15th percentile, n=18 patients) health-care of patient with leukodystrophy, evaluated by cost groups compared with low-cost patients (bottom 85th percentile, n=104 patients) for all cost settings.

High-cost						
Category	**Total**	**Percent of total**	**Mean**	**25th Percentile**	**75th Percentile**	**Median**
Total	**9,567,995**		**531,555**	**243,135**	**644,818**	
Diagnostic	1,889,591	19.7%	104,977	40,709	110,280	50,816
Imaging	310,465		17,248	11,914	19,012	16,574
Laboratory	1,558,603		86,589	24,795	82,477	34,290
Other	20,522		1,140	-	839	325
Room and Supplies	5,289,160	55.3%	293,842	152,840	382,037	226,707
Care	5,071,916		281,773	144,645	364,558	223,770
Supplies	217,244		12,069	1,812	21,505	3,381
Therapeutics	2,389,245	25.0%	132,736	39,110	163,306	101,471
Acute	533,267		29,626	2,375	27,835	6,048
Chronic	609,267		33,848	19,219	38,833	29,510
Pharmacy	1,246,711		69,262	15,795	106,207	29,722
Low-cost						
Category	**Total**	**Percent of total**	**Mean**	**25th Quartile**	**75th Quartile**	**Median**
Total	**3,513,459**		**33,783**	**5,597**	**49,928**	
Diagnostic	718,667	20.5%	6,910	1,641	9,596	4,607
Imaging	293,488		2,877	743	3,683	1,637
Laboratory	401,829		3,940	751	5,659	2,318
Other	23,349		229	-	209	-
Room and Supplies	1,859,164	52.9%	17,877	637	26,667	5,679
Care	1,499,309		14,699	561	15,725	4,571
Supplies	359,855		3,528	-	858	179

High-cost						
Category	**Total**	**Percent of total**	**Mean**	**25th Percentile**	**75th Percentile**	**Median**
Total	**9,567,995**		**531,555**	**243,135**	**644,818**	
Therapeutics	935,628	26.6%	8,996	653	14,354	3,037
Acute	195,351		1,915	-	1,928	391
Chronic	538,944		5,284	94	6,857	1,216
Pharmacy	201,333		1,974	61	1,952	340

Amounts shown are inflation-adjusted to 2009 U.S. dollars. Mean, Median, and 25th and 75th Percentile values are per patient (except for the Total).

Table V

Clinical characteristics evaluated for patients with leukodystrophy to be of high-cost.

Clinical characteristic	High Cost Patients n=18	Low Cost Patients n=104	*p*
Gastrostomy tube (%)	50	43	0.581
Microcephaly (%)	28	21	0.508
Macrocephaly (%)	0	4	0.508
Dysmorphic features (%)	39	24	0.182
Developmental regression (%)	17	34	0.152
At least one word ever (%)	22	53	**0.015**
Walk ever (%)	22	57	**0.006**
Endocrine abnormality (%)	28	11	**0.044**
Age of presentation (months)	22.6	36.3	0.29
Seizures (%)	61	49	0.347
Death (%)	44	34	0.413
MLD (%)	28	5	**0.001**
Bone Marrow Transplant (%)	33.3	0	**<0.0001**
Length of stay (avg. days)	145	9	**<0.0001**
Number of admissions (avg.)	12	2	**0.002**
Number of ICU admissions (avg.)	2.6	0.46	0.128
Pts requiring ICU (%)	61	29	**0.004**
Ventilator days (avg.)	17.8	1.8	**0.001**
Pts requiring ventilator (%)	61	23	**<0.0001**
Number of infections (avg.)	12	2	**0.002**
Pts with infection (%)	94	66	**0.008**

Fisher exact test was used to calculate two-tailed *p* values. Significant changes ($p<0.05$) are shown in bold. Abbreviations: avg.-average; pts-patients; ICU-intensive care unit; MLD-metachromatic leukodystrophy.

Table VI

List of ICD-9-CM diagnosis codes used to search for infections.

Code
008.x
009.x
036.x
038.x
040.x
041.x
047.x
048.x
049.x
058.x
078.x
079.x
320.x-326.x
460.x-466.x
480.x-488.x
590.x
599.0
790.7
995.x
996.60–996.69
997.31
998.51–998.59
999.3

Table VII

Clinical characteristics of high-cost patients with leukodystrophy compared with the low-cost cohort, excluding patients who received a bone marrow transplant.

Clinical characteristic	High Cost Patients n=12	Low Cost Patients n=104	*p*
Length of stay (avg. days)	120	9	**0.001**
Number of admissions (avg.)	13	2	**0.002**
Number of ICU admissions (avg.)	3.8	0.46	**0.043**
Pts requiring ICU (%)	61	29	**<0.0001**
Ventilator days (avg.)	17.8	1.8	**0.001**
Pts requiring ventilator (%)	83	23	**<0.0001**
Number of infections (avg.)	13	2	**0.001**
Pts with infection (%)	92	66	**0.036**