Tuberous Sclerosis Health Care Utilization Based on the National Inpatient Sample Database: A Review of 5655 Hospitalizations

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■ INTRODUCTION: **Tuberous sclerosis complex (TSC) has an incidence of 1/6000 in the general population. Overall care may be complex and costly. We examine trends in health care utilization and outcomes of patients with TSC over the last decade.**

■ METHODS: **The National Inpatient Sample (NIS) database for inpatient hospitalizations was searched for admission of patients with TSC.**

■ RESULTS: **During 2000–2010, the NIS recorded 5655 patients with TSC. Most patients were admitted to teaching hospitals (71.7%). Over time, the percentage of craniotomies performed per year remained stable ($P = 0.351$). Relevant diagnoses included neuro-oncologic disease (5.4%), hydrocephalus (6.5%), and epilepsy (41.2%). Hydrocephalus significantly increased length of stay and hospital charges. A higher percentage of patients who underwent craniotomy had hydrocephalus (29.8% vs. 5.3%; $P < 0.001$), neuro-oncologic disease (43.5% vs. 3.4%; $P < 0.001$), other cranial diseases (4.2% vs. 1.2%; $P < 0.001$), and epilepsy (61.4% vs. 40.1%; $P < 0.001$).**

■ CONCLUSIONS: **Our study identifies aspects of inpatient health care utilization, outcomes, and cost of a large number of patients with TSC. These aspects include related diagnoses and procedures that contribute to longer length of stay, increased hospital cost, and increased in-hospital mortality, which can inform strategies to reduce costs and improve care of patients with TSC.**

INTRODUCTION

Tuberous sclerosis complex (TSC) is a multisystem disease that causes benign tumors in the brain and elsewhere. It can result from de novo mutation or, more frequently, autosomal dominant inheritance. TSC occurs in approximately 1/6000 births, and there are approximately 25,000 Americans living with TSC.[1,2] TSC results from mutation of either the TSC1 or the TSC2 gene, encoding the proteins hamartin and tuberin, respectively.[3,4] These genes are involved with regulation of cellular growth and differentiation via the mammalian target of rapamycin (mTOR) pathway.[3-5] Clinically, TSC presents with a broad spectrum of disease, ranging from minimal symptoms to severely disabling neurologic disorders. Neurologic manifestations of TSC include epilepsy, developmental impairment, and autism.[4,6,7] Other major, nonneurologic manifestations of the disease include cutaneous angiofibromas, renal angiomyolipomas, pulmonary lymphangiomyomatosis, and cardiac rhabdomyomas.[5-7]

Neurosurgical care of patients with TSC may include treatment of epilepsy, hydrocephalus, and subependymal giant cell astrocytoma (SEGA).[6,8,9] Given the prevalence and potential severity of this illness, care of these patients is often complex, requiring considerable health care resources. Assessing the overall costs of treatment and identifying specific variables associated with

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- Epilepsy
- Health care utilization
- Hydrocephalus
- National Inpatient Sample
- Neurosurgical care
- Subependymal giant cell astrocytoma
- Tuberous sclerosis complex

Abbreviations and Acronyms
IQR: International quartile range
LOS: Length of stay
mTOR: Mammalian target of rapamycin
NIS: National Inpatient Sample
PEG: Percutaneous endoscopic gastrostomy
SEGA: Subependymal giant cell astrocytoma
TSC: Tuberous sclerosis complex
UTI: Urinary tract infection

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higher costs may help guide allocation of research funding and direct future strategies to reduce utilization without diminishing effectiveness. Lennert et al.[10] characterized the resource utilization in a small cohort over a 5-year period and reported extensive health care utilization for 3 years after diagnosis, with waning costs thereafter. Over the last decade, several advances in treatment, such as mTOR inhibitors and the proliferation of stereotactic radiosurgery, have likely affected trends on care.[4,11-14] There is a paucity of evidence to assess the impact of these innovations as well as a lack of overall evidence to estimate and characterize the national economic toll.[10] Thus, we examine trends in health care utilization and outcomes of patients with TSC over the last decade using the National Inpatient Sample (NIS) database. Discussion of these novel treatments is out of the scope of this article; however, the data collected and analyzed in this study may be used as a baseline to compare how effects of these novel treatments affect treatment and outcomes in patients with TSC, when these data become available.

METHODS

The NIS is a database obtained from the Agency for Healthcare Research and Quality. This database includes approximately 8 million hospitalizations annually. It represents a stratified sample of approximately 20% of all hospital admissions per year and serves as a representative sample of inpatient admissions in the United States (http://www.hcup-us.ahrq.gov/nisoverview.jsp). For the purposes of this study, the NIS was queried using ICD-9 (International Classification of Diseases, Ninth Revision) codes to identify individual cases of patients with the diagnosis of tuberous sclerosis from 2000 to 2010. ICD-9 codes were also used to identify relevant diagnoses and procedures (Table 1).

The TSC cohort was described according to their demographic characteristics, diagnoses, procedures, and outcomes. The teaching status of the hospital was noted. Diagnoses of interest included hydrocephalus, neuro-oncologic diseases, other cranial diseases, epilepsy, and moyamoya syndrome. Procedures of interest included ventricular shunt placement and craniotomy. Outcomes of interest were percutaneous endoscopic gastrostomy (PEG), tracheostomy, mechanical ventilation continuously for 96 hours or longer, urinary tract infection,[15] pneumonia, in-hospital death, length of stay (LOS),[11] and total hospital charges. Trends in patient characteristics, diagnoses, procedures, and outcomes were evaluated by comparing the patients across years. Total hospital charges were not compared across years because of the bias created by inflation. Multivariate analysis was performed to identify predictors of the various outcomes. Binary logistic regression was used for the categorical outcome variables, and linear regression was used for the continuous outcome variables.

A subset of patients with TSC with hydrocephalus and a second subset who underwent craniotomies were also described according to the characteristics mentioned earlier. They were compared with the group of patients with TSC who did not have hydrocephalus or a craniotomy, respectively. Categorical variables were compared using the χ^2 test for independence. Continuous variables were compared using the Student *t* test or the Mann-Whitney U test, where appropriate. Multivariable logistic regression analysis was also performed to identify predictors of outcomes.

Table 1. ICD-9 Codes

Codes for diagnoses	
Tuberous sclerosis	759.5
Neuro-oncologic disease	191.0, 191.1, 191.2, 191.3, 191.4, 191.5, 191.6, 191.7, 191.8, 191.9, 192.0, 192.1, 192.2, 192.3, 192.8, 192.9, 194.3, 194.4, 198.3, 198.4, 225.0, 225.1, 225.2, 225.3, 225.4, 225.8, 225.9, 227.3, 227.4, 237.5, 237.6, 239.6
Hydrocephalus	331.3, 331.4, 377.00, 377.01, 742.3, V45.2
Epilepsy	345.00, 345.01, 345.10, 345.11, 345.2, 345.3, 345.40, 345.41, 345.50, 345.51, 345.60, 345.61, 345.70, 345.71, 345.80, 345.81, 345.90, 345.91
Other cranial disease	348.4, 348.5, 348.8, 349.82, 349.89, 742.4
Moyamoya disease	434.90, 434.91, 747.81
Pneumonia	480.0, 480.1, 480.2, 480.3, 480.8, 480.9, 481, 482.0, 482.2, 482.30, 482.31, 482.32, 482.39, 484.40, 482.41, 482.42, 482.49, 482.81, 482.82, 482.83, 482.84, 482.89, 482.9, 483.0, 483.1, 483.8, 484.1, 484.3, 484.5, 484.6, 484.7, 484.8, 485, 486, 487.0, 487.1
Urinary tract infection	595.0, 595.89, 595.9, 597.8, 597.89, 599.0
Codes for procedures	
Craniotomy	01.09, 01.13, 01.14, 01.18, 01.24, 01.25, 01.31, 01.32, 01.39, 01.51, 01.52, 01.53, 01.59, 02.03, 02.05, 02.12, 02.99
Shunt	02.21, 02.22, 02.31, 02.32, 02.33, 02.34, 02.35, 02.39, 02.41, 02.42, 02.43
Percutaneous endoscopic gastrostomy	43.11, 43.19, 46.32
Tracheostomy	31.1, 31.2, 31.21, 31.29
Mechanical ventilation >96 hours	96.72

RESULTS

Patients with TSC

From 2000 to 2010, the NIS recorded 5655 hospitalizations for patients with TSC (Table 2). The mean age at time of admission was 22.3 ± 19.5 years. Slightly more patients were female (52.5% female, 47.5% male) and most were white (66.6% white, 14.7% Hispanic, 11.6% black, 7.1% other). Most patients were admitted to teaching hospitals (71.7%). There were 305 (5.4%) patients with TSC with a known diagnosis for neuro-oncologic disease, and 1.3% ($n = 74$) of these patients had a diagnosis of other cranial diseases. Hydrocephalus was reported in 6.5% of cases ($n = 367$). Of patients with TSC, 41.2% had epilepsy. Of patients