Healthcare Resource Utilization and Cost Burden of Facial Angiofibroma Associated with Tuberous Sclerosis Complex: A Real-World Claims Database Analysis in the United States

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Hebert AA[1], Paydar C[2], Das AK[2], **Boggarapu S**[3], Beresford E[3]; [1]*UTHealth McGovern Medical School, Houston, TX, USA;* [2]*Partnership for Health Analytic Research (PHAR), LLC, Beverly Hills, CA, USA;* [3]*Nobelpharma America, LLC, Bethesda, MD, USA*

BACKGROUND

- Tuberous sclerosis complex (TSC) is a rare, multisystemic, autosomal dominant genetic disorder that affects ~2 million globally and up to 80,000 individuals in the US.[1] Facial angiofibromas are one of the most predominant skin manifestations reported in TSC patients, which present as multiple small, pink papules that grow gradually, often impacting facial appearances.[2]
- Inhibitors of the mechanistic target of rapamycin, such as everolimus and sirolimus, have previously been effective in treating facial angiofibromas. They are used as a standalone therapy, or combined with procedures such as cryotherapy, laser, or surgery.[3]
- TSC requires multiple long-term healthcare-associated visits, causing significant psychological and economic burdens to patients, caregivers, and society.[4,5] Elucidating the burden of illness for facial angiofibroma associated with TSC is challenging due to limited data on the healthcare resource utilization (HCRU; i.e., visits to hospitals, emergency department [ED], and offices, outpatient services, and prescription fills), therapies (procedures and/or medication) and related costs for affected children and adults in the US.
- Here, we used real-world data from a healthcare claims database to document HCRU and costs associated with the management of TSC, especially in subset of the patients related to facial angiofibroma.

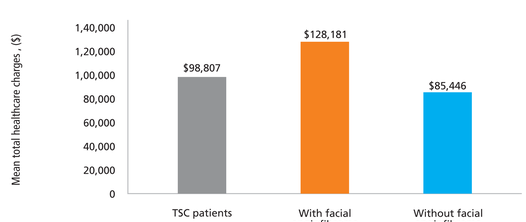
METHODS

- This cross-sectional, retrospective study obtained 3-year data (Nov. 2018 - Oct. 2021) from the Symphony Health Solution Integrated Dataverse database of 10,358 patients with TSC. Of these patients, we included 4,446 with existing or newly diagnosed TSC. A subset of patients with facial angiofibroma was identified based on the medication and/or procedures. Patients were included in the study if they had ≥1 inpatient or ≥2 outpatient medical claims for TSC (International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM] diagnosis code: Q85.1), and continuous medical and pharmacy data coverage for 1 year from the index date (randomly chosen TSC claim date for patients with multiple TSC claims during study period).
- Estimation of the HCRU (inpatient hospitalizations, office and ED visits, outpatient services, and fills) and costs (per visit and total cost) were estimated based on medical claims with TSC as the primary diagnosis. All data were stratified by overall TSC patients and TSC patients with or without facial angiofibroma.
- Study parameters were assessed during the 1-year follow-up period. The results were stratified by age groups (children, <18 years and adults, ≥18 years), payer/insurance type, and therapy options for facial angiofibroma.
- The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies[6] were used for conducting and reporting data. Descriptive statistics were reported for continuous and categorical data for all patients.

RESULTS

- Overall, 4,446 TSC patients were included in this real-world retrospective analysis, of which 31.3% (1,390) were classified as having facial angiofibroma. TSC patients faced substantial healthcare charges ($98,807), with the average cost to those with facial angiofibroma being much higher ($128,181) than those without facial angiofibroma ($85,446) **(Figure 1)**.

Figure 1. Total healthcare charges of TSC patients, stratified by those with and without facial angiofibroma



Note: *Charges are adjusted to the US dollar value ($) for 2021. TSC, tuberous sclerosis complex*

- The Charlson Comorbidity Index (CCI) of the overall TSC patient population (with and without facial angiofibroma) is shown in **Table 1**. The most commonly observed comorbidities for overall TSC patients, those with facial angiofibroma and those without facial angiofibroma, were related to the kidney, heart, and brain, respectively **(Table 1)**.

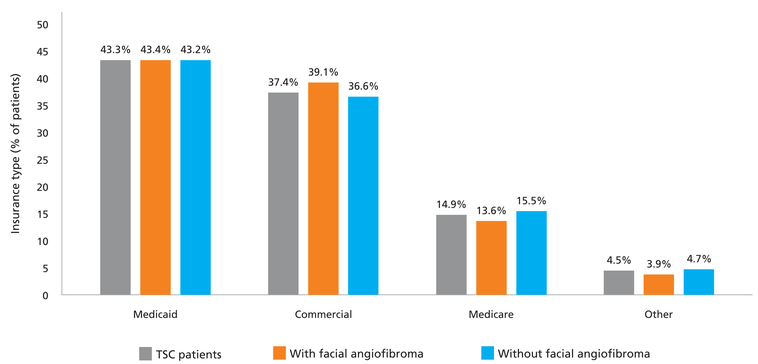
Table 1. Comorbidities in TSC patients, stratified by those with and without facial angiofibroma

Variables	TSC patients	With facial angiofibroma	Without facial angiofibroma
Charlson Comorbidity Index, Mean	0.8	0.9	0.8
	(% of patients)		
Kidney	16.4	23.7	13.1
Heart	8.4	10.6	7.4
Brain	7.5	15.4	4.0
Lung	3.9	7.5	2.3
Behavior problems	3.8	5.3	3.1
Cutaneous manifestations other than facial angiofibroma	3.4	4.3	2.9
Cognitive disability	1.2	0.8	1.4

TSC, tuberous sclerosis complex

- Medicaid (43.3%), followed by Commercial (37.4%), and Medicare (14.9%) were the most commonly utilized insurance types by the TSC patients. The variety of insurance services utilized by the TSC patients was similar across all three cohorts **(Figure 2)**.

Figure 2. Insurance types used by TSC patients, stratified by those with and without facial angiofibroma



TSC, tuberous sclerosis complex

- While inpatient hospitalizations were the most expensive, with a per hospitalization charge of $29,254, the cost to TSC patients was predominantly attributed to a large number of outpatient services (50,235) and pharmacy claims (152,013) **(Table 2)** for those with and without facial angiofibroma.

Table 2. Number of hospital, emergency department, office and outpatient visits, and pharmacy claims by TSC patients, and associated costs, stratified by those with and without facial angiofibroma

Variables	**TSC patients** No. of visits (cost per visit)	**With facial angiofibroma** No. of visits (cost per visit)	**Without facial angiofibroma** No. of visits (cost per visit)
Inpatient hospitalizations	3,352 ($29,254)	987 ($29,293)	2,370 ($29,237)
Emergency department visits	3,538 ($3,529)	1,042 ($3,041)	2,496 ($3,733)
Office visits	26,232 ($410)	9,113 ($475)	17,119 ($375)
Non-emergency department/Outpatient services	50,235 ($3,746)	17,393 ($3,552)	32,842 ($3,849)
Pharmacy claims	152,013 ($3,352)	56,664 ($982)	95,349 ($2,370)

Note: *Charges are adjusted to the US dollar value ($) for 2021. TSC, tuberous sclerosis complex*

- The majority of TSC patients with facial angiofibroma were prescribed medication only (87.9%), with everolimus (57.3%) being prescribed most often, followed by sirolimus (20.2%). The total mean healthcare charges were highest with tacrolimus prescriptions ($350,885).

CONCLUSIONS

- In the US, TSC patients with and without facial angiofibroma face substantial HCRU and cost burden.
  - The total healthcare expenses for TSC patients (with and without facial angiofibroma) were predominantly driven by outpatient pharmacy claims and other outpatient services costs, reflecting the multifactorial nature of the illness and various diagnostic tests and procedures required to manage such patients.
  - These data highlight the immediate treatment needs of TSC patients (with and without facial angiofibroma) in the healthcare setting.
- Most TSC patients with facial angiofibroma were treated with medication alone, indicating the milder nature of facial angiofibroma in this cohort.

LIMITATIONS

- Since the primary purpose of the database was to collect claims data and not characterizing TSC patients with or without facial angiofibroma, it is likely that the number of cases was underreported. This is mainly dut to the lack of a specific ICD code for facial angiofibroma. Our analysis was conducted based on a claims database using therapy options for facial angiofibroma. In contrast, the number of pharmacy claims may have been overrepresented as it does not provide information on actual medication consumption. Additionally, the data does not report out-of-pocket expenses, including expenses incurred on formulations. Finally, data was only collected over 3 years; while TCS being a chronic condition, patients are likely to face substantial economic burden in the long term.

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