SCIENCEHOOD

Research Article

Neurology and Neurological Research

Open access

David J. Alexander *

Incidence and Risk Factors of Transient Global Amnesia at High Altitudes: A Population-Based Analysis

David J. Alexander [1*], Alexander Kaizer [2], Gary Luckasen [3], and Sean Pauzauskie [1]

[1] University of Colorado School of Medicine, Colorado, USA

[2] Colorado School of Public Health Department of Biostatistics & Informatics, Colorado, USA

[3] Heart Center of the Rockies, USA

***Corresponding Author: David J. Alexander,** University of Colorado School of Medicine, Colorado, USA

Citation: David J. Alexander, Alexander Kaizer, Gary Luckasen, Sean Pauzauskie (2026), Incidence and Risk Factors of Transient Global Amnesia at High Altitudes: A Population-Based Analysis; J. Neurology and Neurological Research, 3(1): DOI: 10.64585/3065-0097-3-1-20.

s

Research Article

Volume 03; Issue 01

Received Date: January 15, 2026

Accepted Date: February 02, 2026

Published Date: February 13, 2026

DOI: 10.64585/3065-0097-3-1-20

ABSTRACT

Objective:
Report risk factors and incidence of transient global amnesia (TGA) in Northern Colorado. Compare vascular health of Colorado TGA patients with the broader TGA patient population. Discuss altitude-related hypoxia as a potential contributor to TGA pathophysiology.

Background:
TGA is a rare syndrome of sudden anterograde and occasional retrograde amnesia, resolving within 24 hours. Its mechanism remains unclear. Based on EHR data, incidence of TGA in Northern Colorado is significantly higher than the national average, providing a setting to confirm risk factors while raising a question of altitude-related hypoxia in the pathophysiology of TGA.

Design/Methods:
Using Epic Cosmos data, we retrospectively enrolled 246 patients between 2019-2023 based on having a diagnosis of TGA in Northern Colorado, assessing single vs recurrent episodes, vascular/emotional risk factors, and demographics. Additionally, the database was utilized to compare prevalence of TGA within the state of Colorado with the broader population, as well as contrasting comorbidities between Colorado TGA patients and TGA patients in the broader population.

Results:
In the Northern Colorado cohort, the prevalence of hypertension, hyperlipidemia, coronary artery disease, anxiety, depression, and seizure disorder was significantly higher than U.S. general population estimates (all $p<0.001$). Separately, using the Epic Cosmos database, TGA prevalence was significantly higher in Colorado than in the broader Epic Cosmos population ($p<0.0001$). Among patients with TGA, Colorado cases exhibited lower rates of hypertension (ages 40-85, $p<0.005$) and hyperlipidemia (ages 50-85, $p<0.0005$) than TGA cases outside Colorado.

Conclusions:
Significant differences in vascular and emotional risk factors between TGA patients and the general population support vascular and catecholamine-stress mechanisms. Higher seizure-disorder prevalence supports EEG to exclude transient epileptic amnesia. Despite a lower vascular comorbidity burden, TGA was more prevalent in Colorado than in the broader population, indicating a mechanistic gap, possibly associated with altitude-related hypoxia unmasking TGA in susceptible individuals.

KEYWORDS:

transient global amnesia, vascular risk factors, altitude, hypoxia.

INTRODUCTION

Transient global amnesia (TGA) was initially described by Fisher and Adams in 1958 [1]. TGA is characterized by a sudden-onset anterograde amnesia with temporary retrograde amnesia that is unrelated to seizure or stroke.

Many etiologies have been posited in that time, including venous congestion, arterial ischemia, catecholamine stress, cortical spreading depression, and epileptic mechanisms [2-6]. The commonality between these competing theories is dysfunction at the hippocampus.

TGA is a relatively benign diagnosis, as studies have shown that short- and long-term risk of stroke, seizures, and cognitive impairment do not increase [7,8].

Epidemiology

The majority of individuals presenting with TGA are between the ages of 50-80. Amnestic episodes last for several hours, typically resolving within 1-24 hours. TGA is a relatively rare syndrome, with reported incidence ranging 3.4 – 10.4/100,000 [9]. The incidence of TGA in Northern Colorado is elevated at 13.8 per 100,000, based on Epic data from 2 counties in 2019. Data from other health systems was not included, so this figure may underestimate the true prevalence.

TGA recurrence occurs in up to 13.7% of patients based on a 2020 study [10]. TGA is often associated with a precipitating event involving emotional or physical stress, including scenarios such as receiving difficult news, sexual intercourse, or submerging in a body of hot or cold water. Such events may precede up to 89% of TGA episodes [11].

Altitude

Previous population studies of transient global amnesia have been conducted with limited attention to environmental modifiers of incidence. Higher-altitude regions differ from sea-level populations in effective oxygen availability and altitude-related exposures, including acute stress and physical exertion, which are commonly reported antecedents to TGA episodes [12,13].

Despite a growing body of research, no one mechanism has sufficiently explained the development of TGA. It is possible that TGA as a syndrome is a shared end point with a multifactorial pathogenesis. Our study aims to identify incidence of TGA in Northern Colorado and compare associated risk factors with national data, while identifying discrepancies potentially related to regional altitude-related hypoxic exposure.

METHODS

We conducted a retrospective cross-sectional observational study using de-identified electronic health record data from Epic Cosmos (COMIRB#: 21-2777). Patients with a diagnosis of TGA based on ICD-10 codes in Northern Colorado between June 2019 and June 2023 were identified. After manual chart review, 21 cases were excluded for insufficient documentation, ambiguous diagnosis, or duplicate entries, yielding a final cohort of 246 patients.

For this Northern Colorado cohort, categorical data were collected encompassing comorbidities, social history, context of TGA episode, and other biological and demographic data. Comorbidities were determined from concurrent diagnoses at the time of TGA diagnosis encounter. Sample comorbidity prevalence was compared to US or CO-specific populations via a one-sample, two-sided test of proportions. Two-sample tests for equality of proportions with continuity correction were performed, assuming independence between groups, random sampling from the respective populations, binary outcome variables, and sufficiently large sample sizes to justify approximation to a normal distribution. US and CO estimates were derived from various governmental surveys and reports for the variables hypertension (HTN), hyperlipidemia (HL), diabetes mellitus (DM), coronary artery disease (CAD), anxiety, depression, bipolar disorder, alcohol use disorder, seizure disorder, and TGA recurrence [14-22].

Separately, Epic Cosmos was used to compare the prevalence of TGA diagnoses in Colorado with the broader Epic Cosmos population, stratified by age. Among patients with TGA within Epic Cosmos, Colorado cases were compared with TGA cases outside of Colorado to assess differences in vascular risk factors, specifically HTN and HL. Epic Cosmos is a dataset created in collaboration with a community of health systems using Epic representing more than 300 million patient records from over 1,762 hospitals and 40,700 clinics as of September 2025. This community represents patients from all 50 states, D.C.,

Canada, Lebanon, and Saudi Arabia. Analyses were completed with R v4.1.0 (Vienna, Austria).

Comparison populations were selected based on the best available public data for each variable, prioritizing Colorado-specific estimates when available and U.S. estimates otherwise. Epic Cosmos data is a proprietary,

HIPAA-limited dataset from participating healthcare organizations. Data cannot be downloaded, removed, or directly accessed without affiliation to a member organization and proper authorization.

RESULTS

Variable	TGA Prevalence	US Prevalence	CO Prevalence
Hypertension	**53.2%**	**32.5% (p<0.001)**	**25.8% (p<0.001)**
Hyperlipidemia	**52.8%**	**33.3% (p<0.001)**	**29.9% (p<0.001)**
Diabetes	**10.6%**	**10.6% (p=1.000)**	**7.6% (p=0.076)**
Coronary artery disease	**16.1%**	**6.7% (p<0.001)**	**No data**
Anxiety	**27.8%**	**19.1% (p<0.001)**	**No data**
Depression	**28.4%**	**4.7% (p<0.001)**	**No data**
Bipolar	**1.4%**	**2.8% (p<0.001)**	**No data**
Alcohol Use Disorder	**2.8%**	**5.3% (p=0.127)**	**No data**
Seizure Disorder	**10.1%**	**1.2% (p<0.001)**	**No data**
TGA Recurrence	**15.8%**	**5.8-13.7%**	**No data**

Table 1. Prevalence of variables among Northern Colorado TGA group vs U.S./Colorado general population prevalence.

The Northern Colorado TGA group (n = 246) had a mean age of 69.8 years (SD = 10.9) and a mean BMI of 27.6 (SD = 4.92). Compared with U.S. and Colorado population estimates, the Northern Colorado TGA cohort had significantly higher prevalence of HTN, HL, CAD, anxiety, depression, and seizure disorders (all p<0.001). National TGA recurrence ranges from 5.8 to 13.7% including both annual and lifetime rates of recurrence. Lifetime TGA recurrence was found to be 15.8% in our dataset.

Age (years)	US Sample	Colorado Sample	P value
≥18 - <30	0.0021%	0.0030%	0.110
≥30 - <40	0.0032%	0.0044%	0.090
≥40 - <50	0.0080%	0.0098%	0.134
≥50 - <65	0.0360%	0.0570%	2.20E-16
≥65 - <75	0.0772%	0.1184%	2.20E-16
≥75- <85	0.0770%	0.1089%	8.76E-08
≥85	0.0430%	0.0702%	0.000353

Table 2. Proportion of TGA diagnoses within the Epic Cosmos sample.

Within the Epic Cosmos dataset, the proportion of patients diagnosed with TGA was significantly higher in Colorado compared to the nationwide sample in the age groups 50-85+ ($p<0.001$).

Age (years)	US Sample	Colorado Sample	P value
≥18 - <30	13.6%	NA	NA
≥30 - <40	25.5%	NA	NA
≥40 - <50	39.7%	24.8%	0.00335
≥50 - <65	51.4%	39.2%	8.13E-10
≥65 - <75	61.3%	51.4%	2.33E-09
≥75- <85	69.9%	58.2%	1.28E-08
≥85	76.2%	69.6%	0.110

Table 3. Prevalence of HTN among TGA patients within the Epic Cosmos sample (US vs. CO).

Among patients with TGA in the Epic Cosmos dataset, the prevalence of HTN among CO TGA patients was found to be significantly lower than the US TGA groups in the age groups 40-85.

Age (years)	US Sample	Colorado Sample	P value
≥18 - <30	7.7%	NA	NA
≥30 - <40	17.2%	NA	NA
≥40 - <50	34.7%	30.7%	0.461
≥50 - <65	54.6%	39.5%	2.28E-14
≥65 - <75	68.0%	60.2%	7.36E-07
≥75- <85	72.5%	65.4%	0.000460
≥85	69.4%	62.4%	0.113

Table 4. Prevalence of HL among TGA patients within the Epic Cosmos sample (US vs. CO).

Among patients with TGA in the Epic Cosmos dataset, the prevalence of HL among CO TGA patients was found to be significantly lower than the US TGA groups in the age groups 40-85.

DISCUSSION

Vascular

Comorbidities such as HTN, HL, and CAD are well known risk factors for TGA [23]. Our data shows significantly elevated prevalence of vascular risk factors (HTN, HL, CAD) in the Northern Colorado TGA group when compared to national and Colorado state averages. These results both confirm and strengthen previous studies in support of a vascular mechanism for TGA.

The first region of the cornu ammonis (CA1) of the hippocampus is a vascular watershed susceptible to hypoperfusion and metabolic stress [24]. This poor perfusion can be triggered by Valsalva maneuvers, wherein the resulting venous congestion may lead to transient ischemia in key memory structures, a cascade that may be exacerbated by the presence of vascular risk factors [25]. Diffusion-weighted imaging (DWI) has demonstrated focal CA1 lesions following TGA episodes, supporting a vascular ischemic etiology [26].

Cerebrovascular reactivity (CVR), a marker of cerebral blood flow regulation, declines most prominently in the temporal lobe with age, potentially facilitating impaired hemodynamic responsiveness within hippocampal memory circuits and resulting transient hypoperfusion [27].

Emotional stress

Psychiatric comorbidities like depression and anxiety have been associated with TGA, with resultant stress states that impair memory encoding and retrieval [28,29]. Takotsubo syndrome (TTS), or stress cardiomyopathy, is thought to occur due to an increased level of circulating catecholamines [30,31]. Excess catecholamine stimulation may also underly TGA, causing cerebral vasospasm and hippocampal dysfunction, supported by reports of concurrent TGA and TTS [32].

The significantly elevated prevalence of depression and anxiety in the Northern Colorado TGA group when compared to the national average supports the etiology of

catecholamine stress for TGA that is also implicated in TTS. Individuals with these conditions are predisposed to experiencing elevated stress states, serving as an impetus for TGA. This could open the door for future therapies targeted at reducing circulating catecholamine levels in individuals experiencing TGA, such as beta-blocker therapy.

Seizure disorders

The increased prevalence of seizure disorders in the Northern Colorado TGA group compared to national averages may indicate that clinicians are missing transient epileptic amnesia (TEA) presentations. Another retrospective study found that 18% of suspected TGA cases had TEA after workup [33].

This finding has substantial clinical significance as management for TEA patients is entirely different than TGA patients regarding initiation of anti-epileptic therapy. Based on these findings, an argument could be made for continuous EEG monitoring for suspected TGA patients to rule out focal temporal lobe epilepsy causing amnesia.

Altitude/hypoxia

The higher prevalence of TGA in Northern Colorado compared with national estimates warrants consideration of regional factors. Effective atmospheric oxygen decreases with increasing altitude, and the majority of Northern Colorado is situated at elevations greater than 5,000 feet above sea level. Altitude-related hypoxic stress itself may be a relevant regional factor. Additionally, behaviors and exposures associated with altitude, including physical exertion and acute stress, may also be relevant, both of which have been reported as common antecedents to TGA episodes. This observed association may reflect a combination of these factors rather than a single causal mechanism.

Tables 2-4 show that the proportion of patients diagnosed with TGA was significantly higher in Colorado than in the broader Epic Cosmos sample among individuals aged 50-85+. The lack of statistical significance in younger age groups is attributable to the very low incidence of TGA in younger individuals. However, despite the higher prevalence, Colorado TGA patients had lower rates of hypertension and hyperlipidemia compared with TGA patients outside of Colorado, known risk factors for TGA. This discordance suggests that factors beyond vascular comorbidities contribute to the increased incidence of TGA in Colorado. Altitude-related hypoxia in addition to altitude-related exposures and behaviors may lower the physiologic threshold for hippocampal hypoperfusion, unmasking episodes in susceptible individuals that might not occur at sea level. Given the observational nature of these findings, studies in other high-altitude regions are needed to confirm this association and exclude alternative explanations such as regional diagnostic bias.

Study Limitations and Next Steps

This study has several limitations. There is potential for bias in the retrospective design. The Epic Cosmos database is a sample of EHR data, not full population data, potentially limiting the generalizability of this study. Confounding variables for comorbidities such as migraine or vascular disease were not available within the national databases and not addressed in the analysis performed for this study. The heterogeneity of data sources for population comparison creates the potential for ascertainment bias. The observational nature of the study limits the strength of conclusions drawn regarding the altitude-hypoxia theory. Future studies could be strengthened with matched controls, additional objective data (EEG, DWI), and more granular data to stratify TGA patients by altitude such as zip codes.

CONCLUSIONS

Although the etiology of TGA has not been proven, the significant findings of our study including the elevated prevalence of vascular and emotional stress risk factors may point towards a shared mechanism for TGA. There is a possibility that this syndrome is the shared end point of

multiple mechanisms. Catecholamine-induced vasospasm, venous congestion and arterial insufficiency may all lead to transient ischemia and dysfunction of the hippocampus and related memory structures. The discordance generated by higher incidence of TGA in Colorado despite lower prevalence of classic TGA risk factors creates a gap in our understanding of the mechanism, which can potentially be explained by altitude-related hypoxia.

At present, treatment of TGA largely involves ruling out other diagnoses and reassurance while waiting for the amnestic episode to resolve. Our findings combined with the body of evidence supporting vascular and catecholamine stress etiologies highlight the potential for interventions targeting these mechanisms. Low-cost and low-risk interventions to reduce amnestic time could change the management of TGA. Prospective studies employing interventions targeted at the proposed mechanisms may prove useful in reducing amnestic time in TGA patients.

Although TGA is relatively rare and is considered to be a benign diagnosis, it remains a frightening experience for patients and their families considering the more sinister items on a differential for altered mental status and amnesia. Bolstering the ability of clinicians to recognize this syndrome and further research on TGA makes a real difference in the lives of those that experience it.

Statements and Declarations

The authors declare that they have no conflict of interest.

REFERENCES

1. Fisher C (1958). Transient Global Amnesia. *Trans Am Neurol Assoc*;83:143-146.

2. Han K, Chao AC, Chang FC, et al (2015). Obstruction of Venous Drainage Linked to Transient Global Amnesia. *PLoS ONE*;10(7):e0132893.

3. GÜNGÖR TUNÇER Ö, AKSAY KOYUNCU B, VİLDAN OKUDAN Z, ALTINDAĞ E, TOLUN R, KRESPİ Y (2015). Vascular Ischemia as a Cause of Transient Global Amnesia: A Patient Series. *Nöro Psikiyatri Arş*;52(1):59-63.

4. Michaelson NM, Friedman SA, Ch'ang JH (2023). Update on Transient Global Amnesia (TGA): Current Theories Underlying the Etiology, Diagnosis, Prognosis, and Management of TGA. *Curr Treat Options Neurol*;25(8):231-239.

5. Olesen J, Jørgensen MB (1986). Leao's spreading depression in the hippocampus explains transient global amnesia. *Acta Neurol Scand*;73(2):219-220.

6. Miller JW, Yanagihara T, Petersen RC, Klass DW (1987). Transient Global Amnesia and Epilepsy: Electroencephalographic Distinction. *Arch Neurol*.;44(6):629-633.

7. Garg A, Limaye K, Shaban A, Adams HP, Leira EC (2021). Transient global amnesia does not increase the risk of subsequent ischemic stroke: a propensity score-matched analysis. *J Neurol*.;268(9):3301-3306.

8. Arena JE, Brown RD, Mandrekar J, Rabinstein AA (2017). Long-Term Outcome in Patients With Transient Global Amnesia: A Population-Based Study. *Mayo Clin Proc*;92(3):399-405.

9. Spiegel DR, Smith J, Wade RR, et al (2017). Transient global amnesia: current perspectives. *Neuropsychiatr Dis Treat*.;13:2691-2703.

10. Morris KA, Rabinstein AA, Young NP (2020). Factors Associated With Risk of Recurrent Transient Global Amnesia. *JAMA Neurol*;77(12):1551-1558.

11. Quinette P, Guillery-Girard B, Dayan J, et al (2006). What does transient global amnesia really mean? Review of the literature and thorough study of 142 cases. *Brain*.;129(7):1640-1658.

12. Dong J qing, Zhang J hang, Qin J, et al (2013). Anxiety correlates with somatic symptoms and sleep status at high altitudes. *Physiol Behav*.;112-113:23-31.

13. Forrer A, Gaisl T, Sevik A, et al (2023). Partial Pressure of Arterial Oxygen in Healthy Adults at High Altitudes: A Systematic Review and Meta-Analysis. *JAMA Netw Open*.;6(6):e2318036.

14. Explore High Blood Pressure in Colorado | AHR. Accessed September 3, 2025.

15. Explore High Cholesterol in Colorado | AHR. Accessed September 3, 2025.

16. Explore Diabetes in Colorado | AHR. Accessed September 3, 2025.

17. CDC. Heart Disease Facts. Heart Disease. July 10, 2025. Accessed September 3, 2025.

18. Any Anxiety Disorder - National Institute of Mental Health (NIMH). Accessed September 3, 2025.

19. FastStats. July 11, 2025. Accessed September 3, 2025.

20. Bipolar Disorder - National Institute of Mental Health (NIMH). Accessed September 3, 2025.

21. Alcohol Facts and Statistics | National Institute on Alcohol Abuse and Alcoholism (NIAAA). Accessed September 3, 2025.

22. CDC. Epilepsy Facts and Stats. Epilepsy. October 3, 2024. Accessed September 3, 2025.

23. Jang JW, Park SY, Hong JH, Park YH, Kim JE, Kim S (2013). Different Risk Factor Profiles between Transient Global Amnesia and Transient Ischemic Attack: A Large Case-Control Study. *Eur Neurol*.;71(1-2):19-24.

24. Tatu L, Vuillier F (2014). Structure and Vascularization of the Human Hippocampus. Published online April 22,.

25. Lewis SL (1998). Aetiology of transient global amnesia. *The Lancet*;352(9125):397-399.

26. Szabo K, Hoyer C, Caplan LR, et al (2020). Diffusion-weighted MRI in transient global amnesia and its diagnostic implications. *Neurology*;95(2):e206-e212.

27. Kapoor A, Dutt S, Engstrom AC, et al (2025). Association of Medial Temporal Lobe Cerebrovascular Reactivity and Memory Function in Older Adults With and Without Cognitive Impairment. *Neurology*;104(1):e210210.

28. Shields GS, McCullough AM, Ritchey M, Ranganath C, Yonelinas AP (2019). Stress and the medial temporal lobe at rest: Functional connectivity is associated with both memory and cortisol. *Psychoneuroendocrinology*.;106:138-146.

29. Machahary N, Thakran S, Thampi G, et al (2025). Association of endogenous hormones with major depressive disorder phenotype: A systematic review and meta-analysis of drug-free case and control cross-sectional study. *Biochem Biophys Res Commun*;793:153007.

30. Assad J, Femia G, Pender P, Badie T, Rajaratnam R (2022). Takotsubo Syndrome: A Review of Presentation, Diagnosis and Management. *Clin Med Insights Cardiol*.;16:11795468211065782.

31. Lyon AR, Rees PS, Prasad S, Poole-Wilson PA, Harding SE (2008). Stress (Takotsubo) cardiomyopathy—a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. *Nat Clin Pract Cardiovasc Med*.;5(1):22-29.

32. Stöllberger C, Finsterer J (2024). Simultaneous occurrence of transient global amnesia and Takotsubo syndrome triggered by caring for a terminally ill relative. *Clin Case Rep*.;12(5):e8797.

33. Lanzone J, Ricci L, Assenza G, Ulivi M, Di Lazzaro V, Tombini M (2018). Transient epileptic and global amnesia: Real-life differential diagnosis. *Epilepsy Behav EB*;88:205-211.

Neurology and Neurological Research

David J. Alexander, Alexander Kaizer, Gary Luckasen, Sean Pauzauskie (2026), Incidence and Risk Factors of Transient Global Amnesia at High Altitudes: A Population-Based Analysis; J. Neurology and Neurological Research, 3(1): DOI: 10.64585/3065-0097-3-1-20.