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ORIGINAL ARTICLE

Characterising Glanzmann Thrombasthenia in the United States: Real-World Data From the EPIC Cosmos Dataset

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ABSTRACT

Background: Glanzmann Thrombasthenia (GT) is a rare autosomal recessive bleeding disorder characterised by defective platelet aggregation due to abnormalities in the glycoprotein IIb/IIIa complex. With a lack of large real-world database studies, our study aimed to characterise the demographic, clinical and treatment profiles of GT patients using a large, national database.

Methods: A retrospective cohort study was conducted using the EPIC Cosmos database from 1 January 2013 to 31 December 2024. Patients with at least one encounter coded with the SNOMED code for GT (32942005) were included. The primary outcome was the prevalence of GT, calculated using the total database population as the denominator. Secondary outcomes included bleeding manifestations, comorbidities, transfusion utilisation, medication use, sex-based differences and mortality, with statistical comparisons performed using Chi-squared tests.

Results: A total of 1059 GT patients were identified, 58.5% female. The estimated prevalence of GT was 1 in 352,435, higher than prior US estimates. The most frequent bleeding manifestations were abnormal uterine bleeding (29.7% of females aged 11–45), epistaxis (22.6%) and hematuria (16.1%). Anaemia was the most common comorbidity (35.6%), with iron deficiency anaemia present in 31.0%. Transfusion dependency was frequent, with 16.4% of patients requiring blood or component transfusions. No significant sex-based differences were observed. Mortality increased with age, with an overall annualised rate of 1222 per 100,000 GT patients, exceeding that of the general US population.

Conclusion: GT is more prevalent in the United States than previously recognised and is associated with substantial clinical burden from recurrent bleeding, anaemia and transfusion dependency.

1 | Introduction

Glanzmann Thrombasthenia (GT) is a rare autosomal recessive bleeding disorder resulting from a deficiency or dysfunction of the platelet glycoprotein IIb/IIIa complex [1] and is characterised by mucocutaneous bleeding manifestations [2, 3]. Due to the rarity of the condition, studies in GT are limited to retrospective single or small multi-institution studies with small cohorts of patients with GT [4–7]. This has limited the broader understanding of GT's clinical presentation, treatment practices and associated comorbidities, hindering efforts to optimise disease management and inform clinical guidelines.

A comprehensive understanding of the clinical characteristics and treatment patterns in GT requires large, population-level data, which has been historically difficult to obtain for rare diseases. The use of extensive, real-world healthcare datasets provides an opportunity to address these knowledge gaps by

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offering insights into the demographic and clinical profiles of affected individuals. To address this, our study aims to analyse data from a large, multi-institutional database to better characterise the GT population and contribute to a more comprehensive understanding of this rare bleeding disorder.

2 | Methods

Study Design and Objectives: This retrospective cohort study aimed to estimate the prevalence and clinical characteristics of patients with GT from 1 January 2013 to 31 December 2024. The primary objective was to describe the demographic and clinical features of GT patients using a large, real-world dataset. Secondary objectives included assessment of bleeding events, comorbidities, treatment patterns and sex-based clinical differences.

Data Source: Data were obtained from Epic Cosmos (Epic Systems Corporation, Verona, WI, USA), a national, deidentified dataset that includes inpatient, outpatient (including telehealth) and emergency department encounters. As of December 2024, the database comprised over 289 million patient records from 1626 hospitals and 37,700 clinics across all 50 states, the District of Columbia, Lebanon and Saudi Arabia. Due to the deidentified nature of the dataset, the study qualified as non-human subjects research and did not require IRB approval. Queries were executed on 30 July 2025.

Data extraction was performed using Cosmos SlicerDicer for cohort identification and the Data Science platform for detailed variables such as date of death. Cosmos employs 'groupers'—customizable sets of clinical codes and terminology, including ICD, SNOMED, diagnosis names and medications—to define clinical concepts, and maps ICD-9 codes to their corresponding ICD-10 codes to ensure capture of events across the entire study period (2013–2024). Full grouper definitions are provided in Table S1. In compliance with Epic policy, which also refers to the CMS cell suppression policy, values fewer than 10 are reported as '<11' [8]. Where such values could be inferred, categories were grouped to maintain confidentiality. For example, for age-based mortality, patients aged <18 and 18–45 both had <11 patients, so we grouped them with the 45–65 group as <65, preventing back-calculation of actual values based on other data reported. This is consistent with the CMS cell suppression policy standards for minimum cell sizes to protect confidentiality.

Patient Selection and Validation: Cases were included in the GT cohort if they had at least one encounter coded with the SNOMED concept code for GT (32942005) during the study period in the United States (Country of care and country of residence as USA). Cosmos automatically reconciles duplicate entries and merges patient records across institutions. The control group consisted of all patients with a healthcare encounter during the same period, excluding those with bleeding disorders as defined in Table S2. While the control population was large (over 241 million patients), it preserved the real-world distribution and enabled high statistical power. For AUB and Contraceptive data, the GT and control populations were further limited to Female patients 11–45 years of age at the time of any encounter within the study period.

2.1 | Outcome Definitions and Assessment

The primary outcome was GT prevalence, calculated as the number of identified GT patients divided by the total database population during the study period, expressed per 100,000 individuals.

Secondary outcomes included bleeding manifestations, comorbidities, transfusion utilisation, medication use, sex-based differences and mortality:

i. Bleeding manifestations: Identified using a predefined list of ICD-10 codes (Table S3) and categorised by anatomical location. Patients were counted once per category if they had a qualifying code during the study period; repeat events were not captured.

ii. Comorbidities: Selected from the 20 most frequent non-bleeding diagnoses among GT patients, resulting in 11 comorbidities for analysis.

iii. Transfusions: Included packed red blood cells (pRBC), platelets and other blood components identified using procedure codes. Patients were counted once per transfusion type if a documented event occurred.

iv. Medications: Captured from prescription and administration records, including desmopressin, tranexamic acid, aminocaproic acid and factor VII preparations. Medications were assessed separately for outpatient prescriptions and clinic/hospital administrations.

v. Sex-based differences: Outcomes for bleeding, comorbidities, transfusion utilisation and medication use were compared between males and females.

vi. Mortality: Determined from documented death dates through 30 December 2024, accessed via the Data Science platform. Mortality counts were aggregated by year and age group. When any single-year total or age group contained fewer than 11 patients, values were reported as '<11' or combined into broader categories in accordance with Epic/CMS cell suppression policies.

Statistical Analysis: Descriptive statistics were used to summarise baseline characteristics. Comparisons between GT and control populations, as well as sex-based differences within the GT cohort, were performed using Chi-squared tests applied to 2×2 contingency tables. Statistical significance was defined as a two-sided α of 0.05. In addition to p values, absolute differences in event rates were calculated to aid interpretation of clinical relevance. The scipy.stats Python package (version 1.12.0) was used to perform statistical testing [9].

3 | Results

3.1 | Demographics

Between 2013 and 2024, 1059 patients with GT were identified in the dataset. Among the cohort, 624 patients (58.9%) were female, while 435 patients (41.1%) were male. Among 1059 patients with GT, 123 patients (11.6%) were less than 18 years old. Most

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TABLE 1 | Demographic characteristics of patients with Glanzmann thrombasthenia compared with the general population without bleeding disorders.

	Glanzmann		General Population		*p* value
	$N = 1059$	%	$N = 267{,}513{,}353$	%	
Age group					<0.001
0–5 years	20	1.9%	12,414,149	4.6%	
6–12 years	53	5.0%	19,815,259	7.4%	
13–17 years	50	4.7%	14,138,420	5.3%	
18–29 years	148	14.0%	39,779,541	14.9%	
30–44 years	195	18.4%	54,565,327	20.4%	
45–64 years	227	21.4%	62,824,142	23.5%	
65–80 years	239	22.6%	42,447,285	15.9%	
> 80 years	127	12.0%	21,526,153	8.0%	
Sex					<0.001
Female	624	58.9%	140,527,273	52.5%	
Male	435	41.1%	126,642,672	47.3%	
Race					0.085
White	785	74.1%	171,654,050	64.2%	
Black	149	14.1%	38,201,280	14.3%	
Asian and Pacific Islander	58	5.5%	12,929,498	4.8%	
Other (includes AIAN)	171	16.1%	32,886,322	12.3%	
Ethnicity					0.908
Hispanic	141	13.3%	35,170,685	13.1%	
US CENSUS REGIOn					0.053
South	417	39.4%	103,980,257	38.9%	
Midwest	291	27.5%	63,973,085	23.9%	
West	174	16.4%	48,386,952	18.1%	
Northeast	177	16.7%	47,595,100	17.8%	

Source: Data pulled from Cosmos on 30 July 2025.

patients were Caucasian (74.1%), followed by African American (14.1%) (Table 1). The distribution of patients by US Census region is detailed in Table 1, and the comparison of geographical distribution of patients with GT and controls is shown in Figure 1. Table 2 summarises the frequency of bleeding manifestations, non-bleeding comorbidities, transfusion utilisation and medication use in patients with Glanzmann Thrombasthenia compared with the general population.

3.2 | Bleeding Symptoms

Among 1059 GT patients, Epistaxis was the most common bleeding symptom ($n = 239$, 22.6%), followed by hematuria ($n = 170$, 16.1%) and melena ($n = 138$, 13%). Among females aged 11–45 years, abnormal uterine bleeding (AUB) was documented in 29.7% (94/316) of patients with GT, significantly higher than the 7.4% observed in controls.

3.3 | Comorbidities

Among the top 11 non-bleeding comorbidities in GT (Table 2), anaemia emerged as the most frequent. Anaemia, unspecified, was present in 35.6% of patients, while iron deficiency anaemia affected 31.0%. Both were significantly more common than in the general population (5.2% and 3.3%, respectively; $p < 0.001$).

3.4 | Transfusions

135 (12.7%) received packed red blood cell (pRBC) transfusions and 120 (11.3%) received platelet transfusions, reflecting the most common transfusion needs in this population. Fresh frozen plasma (FFP) was used in 26 patients (2.5%).

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TABLE 2 | Frequency of bleeding events, comorbidities, transfusions and medication use in patients with Glanzmann thrombasthenia compared with the general population without bleeding disorders.

	Glanzmann		General Population		*p* value	RR, 95% CI
	N = 1059	%	*N* = 267,513,353	%		
1. BLEEDS						
AUB*	94	29.7%	5,173,533	7.4%	<0.001	4.02 ± 0.68
Epistaxis	239	22.6%	3,583,652	1.3%	<0.001	16.85 ± 1.88
Hematuria	170	16.1%	12,351,571	4.6%	<0.001	3.48 ± 0.48
Melena	138	13.0%	5,311,784	2.0%	<0.001	6.56 ± 1.03
Soft TISSUE INjury	131	12.4%	1,409,584	0.5%	<0.001	23.48 ± 3.78
Hematemesis	74	7.0%	1,268,933	0.5%	<0.001	14.73 ± 3.26
Hemoptysis	36	3.4%	1,256,638	0.5%	<0.001	7.24 ± 2.36
Intracranial Hemorrhage	24	2.3%	824,630	0.3%	<0.001	7.35 ± 2.98
Hemarthosis	20	1.9%	132,580	0.0%	<0.001	38.11 ± 17.07
Any Bleeding	550	51.9%	28,993,352	10.8%	<0.001	4.79 ± 0.28
Anaemia, unspecified	377	35.6%	13,940,851	5.2%	<0.001	6.83 ± 0.55
Essential (primary) hypertension	367	34.7%	45,243,403	16.9%	<0.001	2.05 ± 0.17
Iron deficiency anaemia (ICD-10-CM: D50.*)	328	31.0%	8,952,407	3.3%	<0.001	9.26 ± 0.83
Hyperlipidemia, unspecified	260	24.6%	27,104,580	10.1%	<0.001	2.42 ± 0.26
Vitamin D deficiency, unspecified	233	22.0%	20,974,737	7.8%	<0.001	2.81 ± 0.32
Anxiety	229	21.6%	27,627,884	10.3%	<0.001	2.09 ± 0.24
Other chronic pain	224	21.2%	25,808,923	9.6%	<0.001	2.19 ± 0.26
GASTROESOPHAGEAL reflux disease without esophagitis	210	19.8%	22,564,313	8.4%	<0.001	2.35 ± 0.29
Acute upper respiratory infection, unspecified (ICD-10-CM: J06.9)	195	18.4%	31,737,429	11.9%	<0.001	1.55 ± 0.2
Low back pain, unspecified(ICD-10-CM: M54.50)	194	18.3%	21,071,224	7.9%	<0.001	2.33 ± 0.3
Depression	172	16.2%	21,057,175	7.9%	<0.001	2.06 ± 0.28
pRBC Transfusion	135	12.7%	2,340,592	0.9%	<0.001	14.57 ± 2.31
Platelet Transfusion	120	11.3%	403,317	0.2%	<0.001	75.16 ± 12.73
FFP	26	2.5%	322,805	0.1%	<0.001	20.35 ± 7.91
Cryoprecipitate	<11		87,278	0.0%		
Whole BLOOD TRANSFUsion	<11		51,962	0.0%		
Any Transfusion	174	16.4%	2,531,327	0.9%	<0.001	17.36 ± 2.37
Oral Iron	224	21.2%	8,251,783	3.1%	<0.001	6.86 ± 0.8
Aminocaproic acid	200	18.9%	30,777	0.0%	<0.001	1641.55 ± 206.26
Tranexamic acid	180	17.0%	355,526	0.1%	<0.001	127.89 ± 17.08
Factor VII Preparations	90	8.5%	441	0.0%	<0.001	51552.94 ± 11357.27
Desmopressin acetate	28	2.6%	235,817	0.1%	<0.001	29.99 ± 11.21
IV Iron	<11		74,489	0.0%		
CONTRACEPTIVES, ORAL	104	32.9%	8,707,185	12.4%	<0.001	2.64 ± 0.42
CONTRACEPTIVES, INJECTABLE	11	3.5%	692,211	1.0%	<0.001	3.52 ± 2.16
CONTRACEPTIVES, IMPLANTABLE	<11		187,435	0.3%		

(Continues)

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TABLE 2 | (Continued)

	Glanzmann		General Population		*p* value	RR, 95% CI
CONTRACEPTIVES, TRANSDERMAL	<11		496,133	0.7%		
CONTRACEPTIVES, INTRAVAGINAL	<11		90,052	0.1%		
CONTRACEPTIVES, INTRAVAGINAL, SYSTEMIC	<11		655,261	0.9%		
CONTRACEPTIVES, ANY	111	35.1%	10,052,620	14.4%	<0.001	2.44 ± 0.37
Tranexamic acid	174	16.4%	4,128,984	1.5%	<0.001	10.65 ± 1.45
IV Iron	172	16.2%	2,962,285	1.1%	<0.001	14.67 ± 2.01
Oral Iron	163	15.4%	6,058,489	2.3%	<0.001	6.8 ± 0.96
Factor VII Preparations	148	14.0%	34,295	0.0%	<0.001	1090.14 ± 163.92
aminocaproic acid	140	13.2%	570,238	0.2%	<0.001	62.02 ± 9.61
desmopressin acetate	71	6.7%	438,110	0.2%	<0.001	40.94 ± 9.28
CONTRACEPTIVES, INTRAVAGINAL	24	7.6%	1,581,496	0.6%	<0.001	3.36 ± 1.32
CONTRACEPTIVES, ORAL	17	5.4%	288,268	0.1%	<0.001	13.05 ± 6.25
CONTRACEPTIVES, IMPLANTABLE	<11		3724	0.0%		
CONTRACEPTIVES, TRANSDERMAL	<11		932,919	0.3%		
CONTRACEPTIVES, INJECTABLE	<11		11	0.0%		
CONTRACEPTIVES, INTRAVAGINAL, SYSTEMIC	<11		1530	0.0%		
CONTRACEPTIVES, ANY	64	20.3%	4,217,060	1.6%	<0.001	3.36 ± 0.74

Abbreviations: AUB, abnormal uterine bleeding; CI, confidence interval; dof, degrees of freedom; FFP, fresh frozen plasma; GT, Glanzmann thrombasthenia; IM, intramuscular; IV, intravenous; PO, oral; PRBC, packed red blood cells; RR, relative risk; SQ, subcutaneous.
Source: Data pulled from Cosmos on 30 July 2025.

3.5 | Medications

Iron Supplementation: Oral iron was prescribed to 224 GT patients (21.2%) compared to 3.1% of controls ($p < 0.001$; RR = 6.86), with clinic-administered oral iron also higher (15.4% vs. 2.3%; RR = 6.8). IV iron was given to 172 GT patients (16.2%) versus 1.1% of controls ($p < 0.001$; RR = 14.67).

Hormonal Therapy/Contraceptives: Among women aged 11–45 years, oral contraceptives were prescribed more often in GT (32.9% vs. 12.4%; RR = 2.64), as were injectables (3.5% vs. 1.0%; RR = 3.52). Overall, 35.1% of GT patients received any contraceptive compared to 14.4% of controls (RR = 2.44). In the clinic setting, intravaginal (7.6% vs. 0.6%; RR = 3.36) and oral contraceptives (5.4% vs. 0.1%; RR = 13.05) were also significantly higher.

Antifibrinolytics and Recombinant Factor VIIa: Aminocaproic acid was used in 200 patients (18.9%) and tranexamic acid in 180 (17.0%), with similar rates for clinic administration (13.2% and 16.4%, respectively). Factor VII preparations were prescribed in 90 patients (8.5%) and administered in 148 (14.0%) in hospital/clinic. Desmopressin acetate was less common, prescribed in 28 patients (2.6%) and administered in 71 (6.7%) in in hospital/clinic.

3.6 | Sex Based Differences in Patients With GT

Figure 2 illustrates sex-based differences in Glanzmann Thrombasthenia patients across multiple domains, including bleeds, comorbidities, transfusions and medication use.

a. Bleeding Symptoms: Males had significantly higher rates of epistaxis (26.9% vs. 19.5%), hematuria (19.8% vs. 13.4%), hematemesis (9.7% vs. 5.8%) and hemoptysis (4.8% vs. 2.4%). Soft tissue injury and melena were similar across sexes. Among females aged 11–45 years, abnormal uterine bleeding was observed in 29.7%, underscoring the clinical impact of gynecologic bleeding in this population.

b. Comorbidities: Females were more likely to have vitamin D deficiency, low back pain, depression, chronic pain, anxiety and iron deficiency anaemia, all with significant relative risks favouring higher prevalence in females. Other comorbidities showed no significant sex differences.

c. Transfusions: Platelet, pRBC and FFP transfusion rates were broadly similar across sexes, with no statistically significant differences.

d. Medications (Prescriptions): Tranexamic acid was prescribed more often to females, while aminocaproic acid and Factor VII preparations were more commonly prescribed to males. Oral iron and desmopressin use did not differ significantly.

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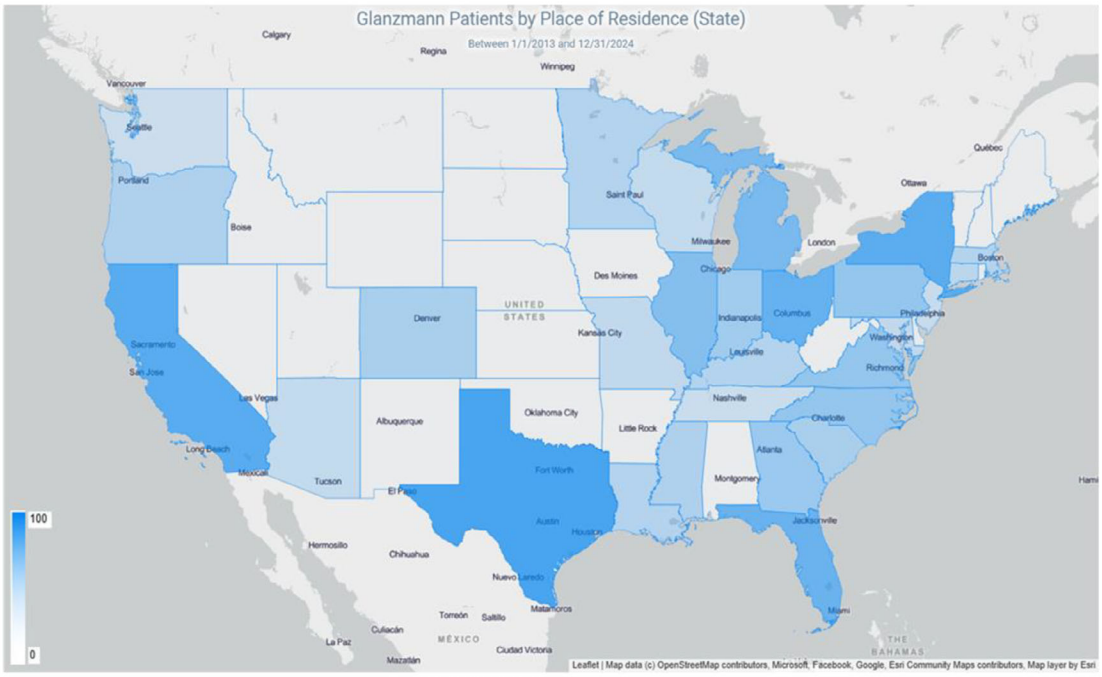


FIGURE 1 | Geographic distribution of GT patients versus control population.

e. Medications (Clinic or Hospital Administered): IV iron was more common in females, whereas aminocaproic acid and Factor VII preparations were more frequently administered to males. No significant differences were seen in tranexamic acid, oral iron or desmopressin use.

3.7 | Mortality

A total of 117 deaths were recorded among GT patients, including 29 in those under 65 years, 51 in the 65–80 years group and 37 in patients older than 80. Only patients with a documented date of death in the EMR were included. Figure 3 summarises annual mortality from 2013 through September 2024. Between 2013–2024, 117 deaths occurred among 1059 individuals with GT, corresponding to an average '**annual crude death rate of ~0.94% (≈944 per 100,000 GT persons per year)**.'

4 | Discussion

This national cohort study represents one of the largest analyses of Glanzmann Thrombasthenia (GT) to date, adding critical

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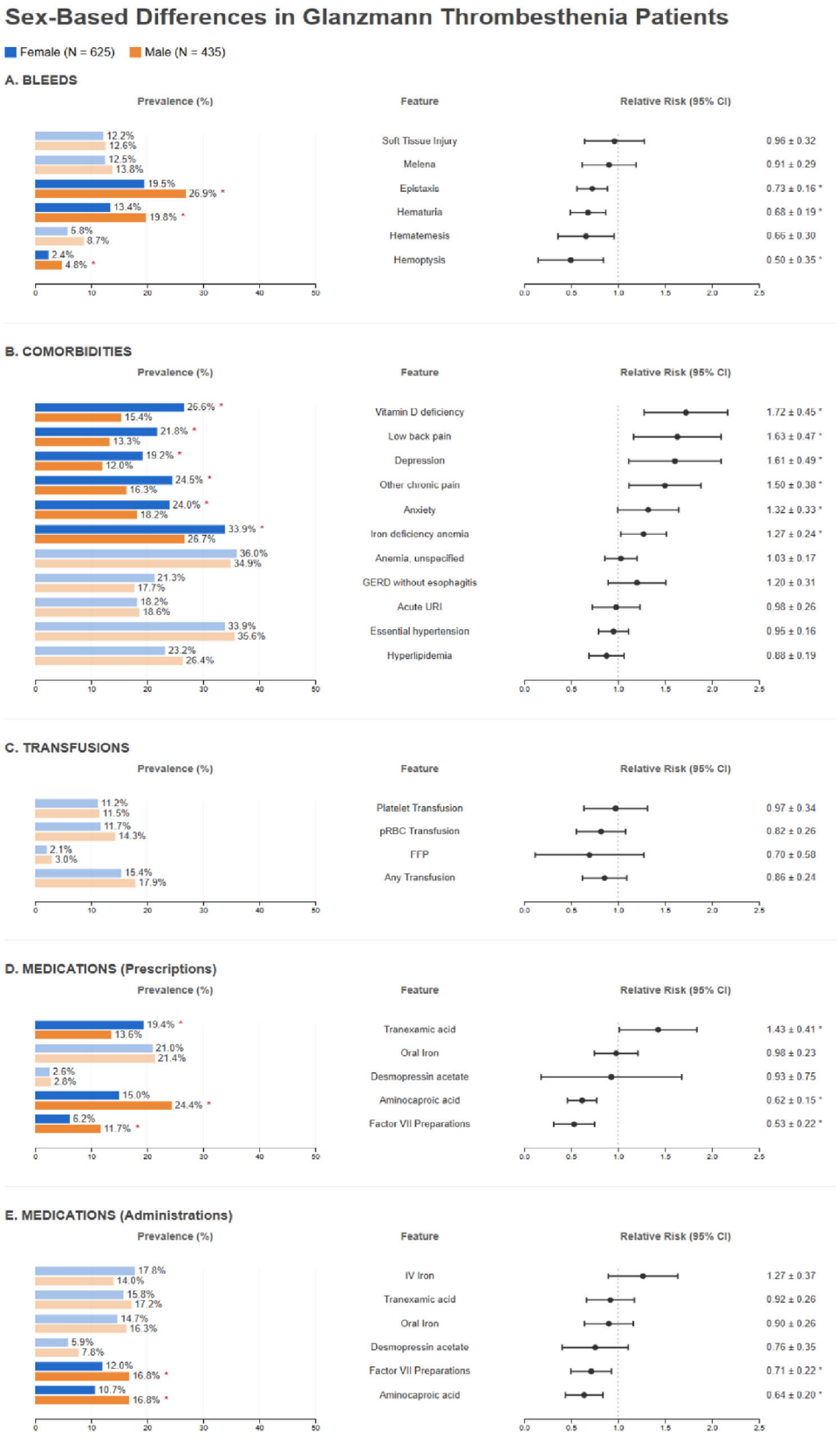


FIGURE 2 | Sex based differences in clinical characteristics of patients with Glanzmann thrombasthenia. Comparisons with significant p values < 0.05 are highlighted and marked by *.

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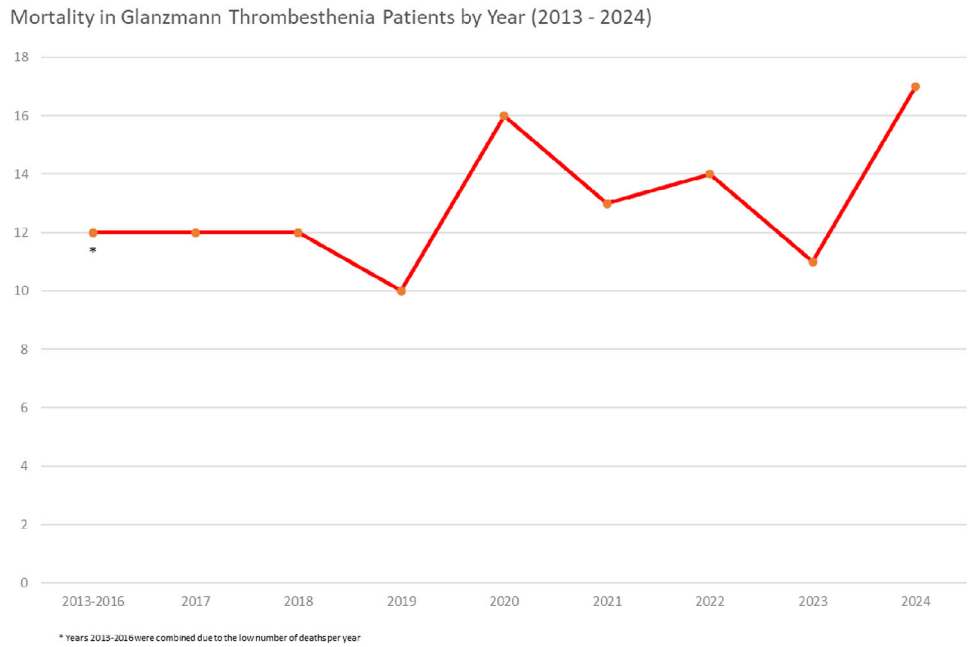


FIGURE 3 | Mortality by year (2013–2024).

data on prevalence, clinical burden and outcomes to the limited literature on this rare disorder.

4.1 | Prevalence of GT

The prevalence of GT is often cited as approximately 1 in 1,000,000, though estimates vary widely across regions [3, 10, 11]. In regions with high consanguinity, such as Saudi Arabia and other GCC countries, prevalence ranges from 1 in 10,000 to 1 in 400,000 [12, 13]. In the United Kingdom, 143 cases were reported between April 2023 and March 2024, and with a total population of 60.9 million, the estimated prevalence is 1 in 425,874 [14, 15]. In the United States, the CDC HTC Population Profile (2012–2024) documented 373 GT cases, translating to ~1 in 911,000 [16]. Prevalence estimates for GT can be calculated using data from the 2024 World Federation of Haemophilia (WFH) report [17] and several other countries having higher prevalence rates. In contrast, our study identified 1059 US GT cases from 2013 to 2024 out of 265,456,285 US patients in EPIC Cosmos database, corresponding to a prevalence of 1 in 250,636. This higher estimate may reflect underreporting in HTC-based data, as not all GT patients receive care at HTCs; one study found that 3 of 8 US GT participants were managed outside the HTC network [18]. Conversely, our prevalence estimate may itself be conservative, as it only includes individuals from institutions using the Epic EMR system.

4.2 | Demographics

When compared to the CDC's HTC population profile [16], our cohort had fewer children: 0–12 years made up 7.4% (vs. 17% ages 2–10 in CDC) and 11–19 years were 10.7% versus 28%. This may reflect underdiagnosis, delayed recognition or limited pediatric EMR data. Adults 45–64 years (21.9% vs. 13%) and 65+ (33.9%) were more represented, possibly due to higher healthcare utilisation. Racial distributions were similar for White (71.7% vs. 65%) and Black individuals (14.7% vs. 16%). Asian/Pacific Islanders were underrepresented (5.4% vs. 10%). Hispanic ethnicity was equal (11.9%). 'Other' race categories (AIAN, multiracial) were more common in our data (13.6% vs. 9%). Racial distributions were similar for White (71.7% vs. 65%) and Black individuals (14.7% vs. 16%). Asian/Pacific Islanders were underrepresented (5.4% vs. 10%). Hispanic ethnicity was equal (11.9%). 'Other' race categories (AIAN, multiracial) were more common in our data (13.6% vs. 9%). These findings suggest EMR-based datasets may capture broader diversity in certain racial categories but may miss others, particularly in pediatric or non-EPIC settings.

4.3 | Bleeding Symptoms

The International GT Registry reported higher rates overall, with epistaxis in 38%–42% and gastrointestinal bleeding in 19% [6]. Similarly, the Paris cohort reported purpura as a frequent finding, epistaxis in 60%–80%, gum bleeding in 20%–60%, gastrointestinal bleeding in 10%–20% and intracranial haemorrhage in 1%–2% of patients [19]. Our cohort demonstrated lower rates of bleeding compared to these. These discrepancies likely reflect differences in study design, patient population or methods of data capture, genotype, but consistently underscore the high frequency of mucocutaneous bleeding in GT.

In our cohort, AUB was reported in 29.7% of females aged 11–45 years, which is higher than the prevalence described in International GT registry (10%–12%) but lower than other reports, like the Paris cohort (60%) [6, 19]. In addition, the hidden nature of AUB and cultural taboos surrounding menstruation may contribute to under-reporting, suggesting that the true prevalence of AUB in this population is likely underestimated.

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When compared to VWD, the overall mucosal bleeding burden in GT appears greater than that typically seen in type 1 VWD, but lower than the severe, systemic bleeding phenotype observed in type 3 VWD, where life-threatening events such as intracranial haemorrhage and deep hematomas occur at rates at least five-fold higher than in type 1 [20, 21]. Thus, the bleeding phenotype in GT most closely parallels VWD, with mucocutaneous bleeding consistently prominent but intracranial haemorrhage remaining relatively uncommon (1%–2% in the Paris cohort).

4.4 | Anaemia and Clinical Burden

Anaemia was the most prevalent comorbidity in GT, affecting 37.7% of patients overall, with iron deficiency anaemia (IDA) documented in 31.0%. Both conditions were far more common than in the general population, highlighting the chronic impact of recurrent bleeding. While unspecified anaemia occurred at similar rates in males and females (36.0% vs. 34.9%, $p = 0.724$), IDA was significantly more frequent in females (33.9% vs. 26.7%, $p = 0.012$), consistent with the added contribution of gynecologic blood loss. Nonetheless, males with recurrent epistaxis, GI bleeding or hematuria also remain at high risk. Anaemia contributes substantially to morbidity, leading to fatigue, reduced physical and cognitive function and increased risk of long-term complications [22, 23]. Insights from the GT 360 Study by Khair et al. further illustrate this burden [23, 24]. The study highlighted how chronic anaemia, resulting from frequent and often daily mucosal bleeding, severely impacted the quality of life for GT patients.

4.5 | Medications

In our study, the use of hemostatic medications in managing bleeding episodes among patients with GT demonstrated distinct patterns based on medication type and sex. Compared to the International GT Registry (GTR), which reported antifibrinolytics alone in 27.9% of moderate and 22.2% of severe bleeds, and platelets (with/without antifibrinolytics) as the most common strategy (34.8% moderate, 45.8% severe), our study found lower overall use of Factor VII products. The GTR reported rFVIIa (alone or with antifibrinolytics) in up to 17.2% of severe bleeds [6], whereas our cohort showed less frequent use, even among males. These differences may reflect institutional protocols, clinical practice variations or regional preferences in managing GT-related bleeding.

4.6 | Mortality

In our study, the average crude mortality rate in GT was approximately 0.94% annually, equating to 944 deaths per 100,000 GT patients. A transient increase in deaths observed in 2020 may reflect broader public health factors, such as the COVID-19 pandemic, rather than GT-specific risk. For context, this crude death rate in GT (≈944 per 100,000 per year) is about **26% higher** than the **age-adjusted** all-cause mortality in the general US population in 2023 (750 per 100,000); however, this comparison should be interpreted cautiously because our estimate is **not age-standardised** and reflects a disease cohort rather than the general population [28]. The only large cohort reporting GT-related mortality was from Japan (1976–1991), where rates ranged from 490 to 680 per 100,000 [27]; mortality in our cohort exceeded these estimates, which may reflect differences in healthcare access, treatment practices or data capture methodologies. While large-scale cohorts reporting cause-specific mortality in GT remain scarce, available literature consistently highlights bleeding—particularly intracranial haemorrhage—as the major driver of GT-related mortality. Case reports and small series describe fatal haemorrhages in both patients and affected relatives [26]. Early data from the Paris cohort (1956–1989) reported four deaths among 64 patients, two directly attributable to haemorrhage (intrahepatic and unspecified) and two from unrelated causes (car accidents) [19]. Together, these findings underscore that haemorrhage remains the central contributor to excess mortality in GT and support our observation of increased overall mortality risk in this population.

4.7 | Limitations and Strengths

This study has several important limitations. The EPIC Cosmos database underrepresents patients from non-EPIC systems, particularly in community practices and the Western United States, and the geographical distribution of our cohort was skewed toward the east and west coasts. This may influence the sociodemographic profile of the study population and limit generalizability. Data completeness also depends on clinical workflows—diagnoses not consistently added to problem lists or inconsistently documented procedures may have been missed. Surgical interventions were particularly difficult to isolate because of broad categorisation and the inclusion of non-procedural data.

A further limitation is the reliance on a single coded encounter to identify GT patients, which introduces a small risk of diagnostic misclassification. However, given the rarity and specificity of GT, the likelihood of miscoding is expected to be low. Our cohort also contained relatively fewer children compared to adults, which may understate the incidence of pediatric-predominant bleeding symptoms (e.g., recurrent childhood epistaxis) and contribute to an apparently higher mortality rate, since a greater proportion of older adults were represented. Importantly, our mortality estimate represents a crude all-cause death rate and was not age-adjusted, limiting direct comparison with US population mortality rates. Additionally, outcomes such as quality of life, school or work absenteeism and functional impact—which would provide important context for disease burden—were not available in this dataset. Future studies should address these patient-centred outcomes to better characterise the real-world impact of GT. Finally, assessing anaemia was complicated by inconsistent ICD coding, as multiple overlapping codes were used to capture related conditions, further underscoring the need for improved diagnostic clarity.

Despite these limitations, this study also offers notable strengths. Restricting the study period to 2013–2023 improved data quality, coinciding with the broad adoption of EHR systems following the HITECH Act. Cosmos allows identification using ICD-10, SNOMED codes, and raw text entries, which is critical for rare conditions like GT, where ICD-10 codes lack specificity. The

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SNOMED code 32942005 enabled precise GT identification, while automated record matching across institutions minimised duplication and misclassification. Together, these features strengthened case capture accuracy and highlighted the importance of developing a unique ICD code for GT to further enhance research and clinical care in this rare disorder.

5 | Conclusion

In conclusion, this national database study provides one of the most comprehensive characterisations of Glanzmann Thrombasthenia in the United States, demonstrating a higher prevalence than previously reported and confirming the substantial clinical burden associated with recurrent bleeding, anaemia and transfusion dependency. These findings highlight the need for earlier recognition, consistent anaemia screening and evidence-based management strategies to reduce morbidity and improve long-term outcomes in this rare disorder.

Author Contributions

D.C. conceptualised and designed the study. D.L. accessed the database and performed the data analysis. Both authors contributed to drafting the manuscript and completed all subsequent revisions.

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The authors have nothing to report.

Ethics Statement

This study used de-identified data from the EPIC Cosmos dataset and did not involve human subjects research; therefore, institutional review board approval was not required. The study complied with Wiley's policies on human studies, biosecurity and research reporting guidelines.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

De-identified data are available through Epic Cosmos with appropriate institutional agreements. Due to security requirements, all analyses were performed within Epic's hosted Data Science platform virtual environment, with only aggregate results or figures exported. If you are interested in reproducing/collaborating and have Cosmos access, please contact the corresponding author, and we can add you to the project.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Table 3: List of ICD-10 codes used for analysis.

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