Study of bleeding disorders in pediatric patients presented with bleeding at Qena University Hospital

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Abstract

Background: Hemophilia A and B cause musculoskeletal bleeding, but mucocutaneous inherited bleeding disorders are more common and underrecognized. These include VWD, platelet disorders, and connective tissue disorders, many remaining undiagnosed despite significant mucocutaneous bleeding.

Objectives: To characterize the spectrum of inherited mucocutaneous bleeding disorders in pediatric patients presenting with recurrent mucocutaneous bleeding.

Patients and methods: This prospective observational study included 51 children with recurrent mucocutaneous bleeding at Qena University Hospital. Comprehensive clinical evaluation and stepwise laboratory testing, including coagulation studies, platelet function assays, VWF analysis, factor XIII testing, and flow cytometry, were performed to diagnose inherited bleeding disorders.

Results: The study included 51 children (mean age 7.6 ± 3.1 years), predominantly males (58.8%), mostly from urban areas (80.4%). Mean age of onset was 28.6 months, and epistaxis was the commonest presentation (45.1%). Pallor was frequent (92.2%). Laboratory findings showed mild anemia (Hb 10.4 ± 1.24 g/dL), normal platelet counts (277 ± 79 $\times 10^3/\mu L$), prolonged aPTT (37.8 ± 19.4 s), and reduced platelet aggregation in 54.9%. Low factor XIII levels were found in 19.6%. Final diagnoses were Glanzmann thrombasthenia (49.0%), von Willebrand disease (33.3%), factor XIII deficiency (13.7%), and rare factor V or fibrinogen deficiencies (1.96% each).

Conclusion: At Qena University Hospital, Glanzmann thrombasthenia was the commonest cause of pediatric mucocutaneous bleeding, presenting early with epistaxis and anemia, highlighting the importance of advanced platelet function and flow cytometric testing.

Keywords: Pediatric bleeding disorders; Glanzmann Thrombasthenia; Von Willebrand Disease; Rare coagulation disorders

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Introduction

Hemophilia A and B, caused by deficiencies of clotting factors VIII and IX respectively, are the most well-known inherited bleeding disorders and are classically associated with musculoskeletal bleeding and long-term complications. In contrast, mucocutaneous bleeding (MCB) and mucocutaneous inherited bleeding disorders (MCIBD) are more prevalent, affecting up to ≤1:33 individuals, yet they are comparatively less recognized **(Sidonio et al., 2023)**.

Building on this, MCIBD encompass a broad and heterogeneous group of conditions, including inherited platelet disorders (IPD), hereditary hemorrhagic telangiectasia (HHT), hypermobility spectrum disorders (HSD), Ehlers–Danlos syndromes (EDS), and the most common inherited bleeding disorder, von Willebrand disease (VWD). Despite this range, many people with mucocutaneous bleeding are ultimately diagnosed with a bleeding disorder of unknown cause (BDUC) or remain without a definitive diagnosis **(Baker & O'Donnell, 2021)**.

Among these disorders, von Willebrand disease is the most prevalent and results from quantitative or qualitative defects in the von Willebrand factor (VWF) plasma protein. Nevertheless, VWD is frequently underdiagnosed in symptomatic individuals due to limited disease awareness and the complexity of both clinical evaluation and laboratory testing **(Sidonio Jr et al., 2020)**.

Similarly, Glanzmann thrombasthenia (GT) represents a rare but severe inherited platelet disorder caused by autosomal recessive mutations in *ITGA2B* and/or *ITGB3*, leading to defective or absent αIIbβ3 integrin and impaired fibrinogen-mediated platelet aggregation. Affected patients typically present in early childhood with easy bruising and prominent mucocutaneous bleeding, further highlighting the clinical burden of MCIBD **(Mathews et al., 2021)**.

The aim of the study is to characterize the spectrum of inherited mucocutaneous bleeding disorders in pediatric patients presenting with recurrent mucocutaneous bleeding.

Patients and methods

This prospective observational study was conducted in the Pediatric Department of Qena University Hospital. It included children who presented with recurrent or severe mucocutaneous bleeding and were admitted to the pediatric wards or evaluated in the emergency room or outpatient clinics. Mucocutaneous bleeding was defined as epistaxis, gum bleeding, easy bruising, petechiae, purpura, or menorrhagia **(Neunert et al., 2019).** Recurrent bleeding was defined as ≥2 spontaneous bleeding episodes or bleeding disproportionate to trauma **(Rodeghiero et al., 2010).**

Bleeding severity was objectively assessed using the International Society on Thrombosis and Haemostasis Bleeding Assessment Tool (ISTH-BAT), a validated standardized instrument for evaluating bleeding symptoms in both adults and children**.** The ISTH-BAT score was calculated for each patient at enrollment and bleeding of ISTH-BAT score ≥ 6–7 was considered severe **(Rodeghiero et al., 2010; Bowman et al., 2008)**.

Children were excluded if bleeding was secondary to identifiable non-primary hemostatic causes, including thrombocytopenia, hematologic malignancies (e.g., leukemia), aplastic anemia, disseminated intravascular coagulation, severe liver disease, renal failure, trauma, recent surgery, or current use of anticoagulant or antiplatelet medications. Patients with isolated local causes of bleeding were also excluded. These criteria were applied to ensure inclusion of patients with suspected inherited or primary hemostatic mucocutaneous bleeding disorders.

The sample size was calculated for this study using the single population proportion formula based on the prevalence reported by **Sen et al. (2020).** Assuming a 95% confidence level (Z = 1.96) and a 5% margin of error, the required sample size was computed using $n = Z^2 P (1 - P) / d^2$ with Epi Info software. The minimum sample size obtained was 51 participants.

All patients included in the study underwent a structured and comprehensive clinical assessment. This began with detailed history taking focused on the onset, frequency, severity, and pattern of mucocutaneous bleeding, followed by a full general and systemic examination. Special emphasis was placed on mucocutaneous assessment, where the skin was carefully examined for spontaneous bruising and petechiae, particularly in areas not

usually exposed to trauma. The oral cavity was inspected for spontaneous or excessive gingival bleeding during routine oral hygiene, and the eyes were examined for subconjunctival hemorrhage as an indicator of underlying bleeding tendency. In patients presenting with epistaxis, a complete nasal and local examination was performed using a nasal speculum or otoscope to assess the nasal cavity for evidence of trauma, infection, crusting, or scarring suggestive of recurrent bleeding episodes or prior interventions.

Laboratory Investigations

All participants underwent standardized laboratory evaluation. Six milliliters of aseptic venous blood were collected from each patient; two milliliters were placed in 3.2% sodium citrate tubes for coagulation studies, maintaining a 9:1 blood-to-anticoagulant ratio, and two milliliters were collected in K2-EDTA tubes for hematological analysis. Complete blood count parameters, including hemoglobin concentration, red blood cell count, white blood cell count, and platelet count, were measured using an automated analyzer (XN-1000, Sysmex, Japan). Peripheral blood smears stained with Leishman stain were examined to assess platelet size, morphology, and differential leukocyte count. Baseline coagulation testing included prothrombin time and activated partial thromboplastin time, allowing assessment of both primary and secondary hemostasis.

Advanced Hemostatic Assessment

Further diagnostic evaluation focused on specialized hemostatic testing. Von Willebrand factor antigen levels were quantitatively measured using enzyme-linked immunosorbent assay (ELISA), following strict adherence to manufacturer protocols, and results were interpreted using a standard calibration curve. Functional activity of VWF was assessed through ristocetin cofactor testing, which measured platelet agglutination via changes in optical density over a defined time interval. Platelet function was further evaluated using light transmission aggregometry. Platelet-rich plasma was prepared by sequential centrifugation, adjusted to a standardized platelet count between 200 and 400 × 10^9/L, and tested against a panel of agonists including ADP, collagen, epinephrine, arachidonic acid, ristocetin, thrombin receptor–activating peptide, and thrombin. Aggregation responses were measured two hours after blood collection using a turbidimetric method.

Factor XIII and Flow Cytometric Analysis

Factor XIII activity was assessed using ELISA-based methods, with results derived from a standard curve constructed from serial dilutions of known concentrations. This allowed identification of both severe and mild deficiencies. In addition, flow cytometric analysis of platelet surface glycoproteins was performed to evaluate CD41, CD61, CD42a, and CD42b expression. Platelet-rich plasma samples were incubated with fluorochrome-conjugated monoclonal antibodies and analyzed using FACS Calibur flow cytometry. Platelet populations were identified using forward and side scatter characteristics, and glycoprotein expression levels were quantitatively assessed using specialized software.

Diagnostic Interpretation

The diagnosis of von Willebrand disease (VWD) was established using repeated laboratory assessments, including von Willebrand factor antigen (VWF:Ag), von Willebrand factor activity (VWF:RCo), and factor VIII (FVIII) coagulant activity. Tests were performed using the ACL TOP 700 CTS coagulation analyzer (Instrumentation Laboratory, Werfen, Italy). The VWF activity-to-antigen ratio was used to distinguish type 1 from type 2 VWD. All assays were performed at least twice on separate occasions to confirm abnormal results. The intra- and inter-assay coefficient of variation (CV) for VWF:Ag and VWF:RCo were approximately 5–8% and 7–10%, respectively, with assay sensitivity around 1 IU/dL and an analytical error margin of ±5%. Severe VWD was defined by markedly reduced VWF levels and activity, typically below 30 IU/dL, accompanied by low FVIII activity **(Rodeghiero et al., 2010; Federici et al., 2002).**

Glanzmann thrombasthenia was suggested by absent platelet aggregation in response to ADP, collagen, and epinephrine, with preserved response to ristocetin, measured using the Chrono-Log 700 platelet aggregometer (Chrono-Log Corp., USA). Subtyping into type I, II, or III was performed based on CD41 and CD61 expression by flow cytometry using BD FACSCanto II (BD Biosciences, USA).

Factor XIII deficiency was diagnosed using the FXIII activity assay (Berichrom FXIII, Siemens Healthcare, Germany) and the clot solubility test. Severe deficiency was defined by FXIII activity below 5% **(Karimi et al., 2009; Karimi et al., 2018).** Assays had intra- and inter-assay CVs of 4–7%, sensitivity of 1–2 IU/dL, and an error margin of ±5%.

Ethical consideration

Written informed consent was obtained from the patients prior to enrollment and study was conducted in accordance with the ethical standards of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of the Faculty of Medicine, Qena University with ethical approval code: SVU-MED-PED025-1-24-11-991.

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Statistical analysis

Data were entered and analyzed using SPSS version 26. Qualitative variables are presented as numbers and percentages, while quantitative variables are expressed as mean ± standard deviation (SD). The mean was used to describe the central tendency, and SD measured the variability around the mean. Data normality was assessed with Shapiro Wilk test. ANOVA and post hoc was used for comparison between three or more groups with continuous data and chi square test for categorical data.

Results

The study included 51 children with a mean age of 7.59 ± 3.09 years. Males were more common than females, accounting for 58.82% of cases, while females represented 41.18%**.** Most participants were from urban areas (80.39%), with a smaller proportion residing in rural regions (19.61%). Regarding clinical background, a past surgical history was reported in 13.73% of cases, while 9.8% had a past medical history. Fever was documented in 15.69% of patients, and a positive family history of bleeding disorders was present in 13.73% of the study population.

The mean age of onset was 28.64 ± 32.77 months, with a median of 24 months (range: 0.23–144 months). The most frequent presenting complaint was epistaxis, reported in 23 cases (45.1%) **(Fig 1)**. Among the 51 studied cases, Glanzmann thrombasthenia was the most frequent diagnosis, identified in 25 patients (49.02%). Von Willebrand disease followed, occurring in 17 cases (33.33%). Factor XIII deficiency was detected in 7 patients (13.73%), while Factor V deficiency and fibrinogen deficiency were rare findings, each reported in 1 case (1.96%) **(Fig 2).**

The mean systolic blood pressure was 102.49 ± 4.84 mmHg, while the mean diastolic blood pressure was 61.2 ± 4.58 mmHg. The mean heart rate was 103.04 ± 6.83 beats/min. Body temperature averaged 37.12 ± 0.08 °C, and the mean respiratory rate was 26.2 ± 1.89 breaths/min. There was no significant difference between different diseases regarding vital signs **(Table 1).**

Among the 51 patients, pallor was the most common finding (92.16%) across all diagnoses, followed by nasal bleeding (33.33%) and bruises (23.53%). No significant differences were observed among the three diagnoses ($p > 0.05$). **(Table 2).**

Findings showed mild anemia with near-normal WBC and platelet counts. PT and aPTT were mildly prolonged. VWF antigen and activity were moderately reduced. Over half of patients had decreased platelet aggregation, and about one-fifth had low Factor XIII levels. Flow cytometry showed moderate CD41/CD61 expression and higher CD42a/CD42b expression. There was no significant differences in CBC parameters or aPTT among VWD, Glanzmann thrombasthenia, and Factor XIII deficiency ($P>0.05$), while PT was significantly different ($P=0.009$). VWF antigen and activity were markedly lower in VWD ($P=0.0016$ and $P=0.0009$). Platelet aggregation was significantly reduced in Glanzmann thrombasthenia ($P<0.0001$), and Factor XIII levels were significantly low only in Factor XIII deficiency ($P<0.0001$). CD41 and CD61 expression were significantly decreased in Glanzmann thrombasthenia ($P<0.0001$), whereas CD42a and CD42b showed no significant differences. **(Table 3).**

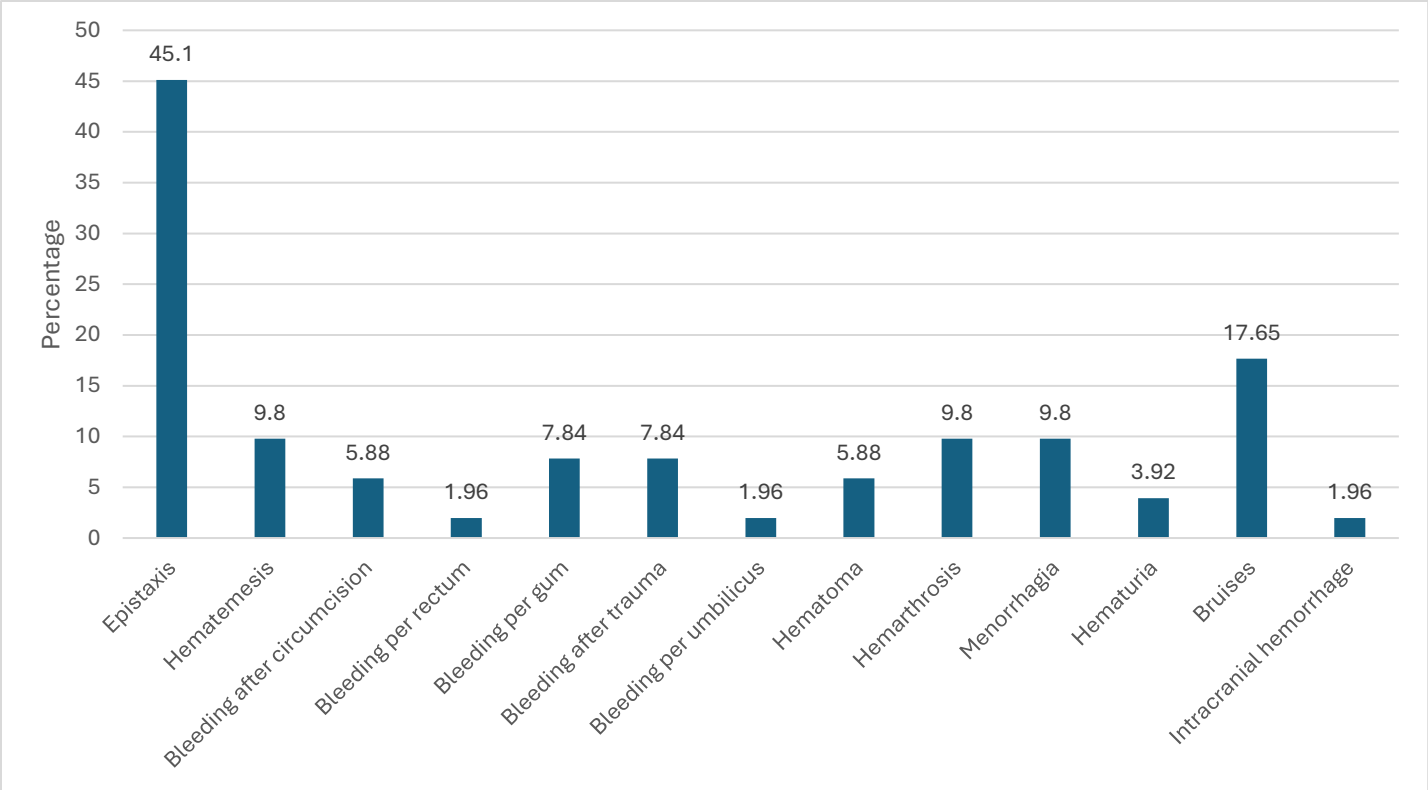


Fig 1. Main Complaint among the included cases.

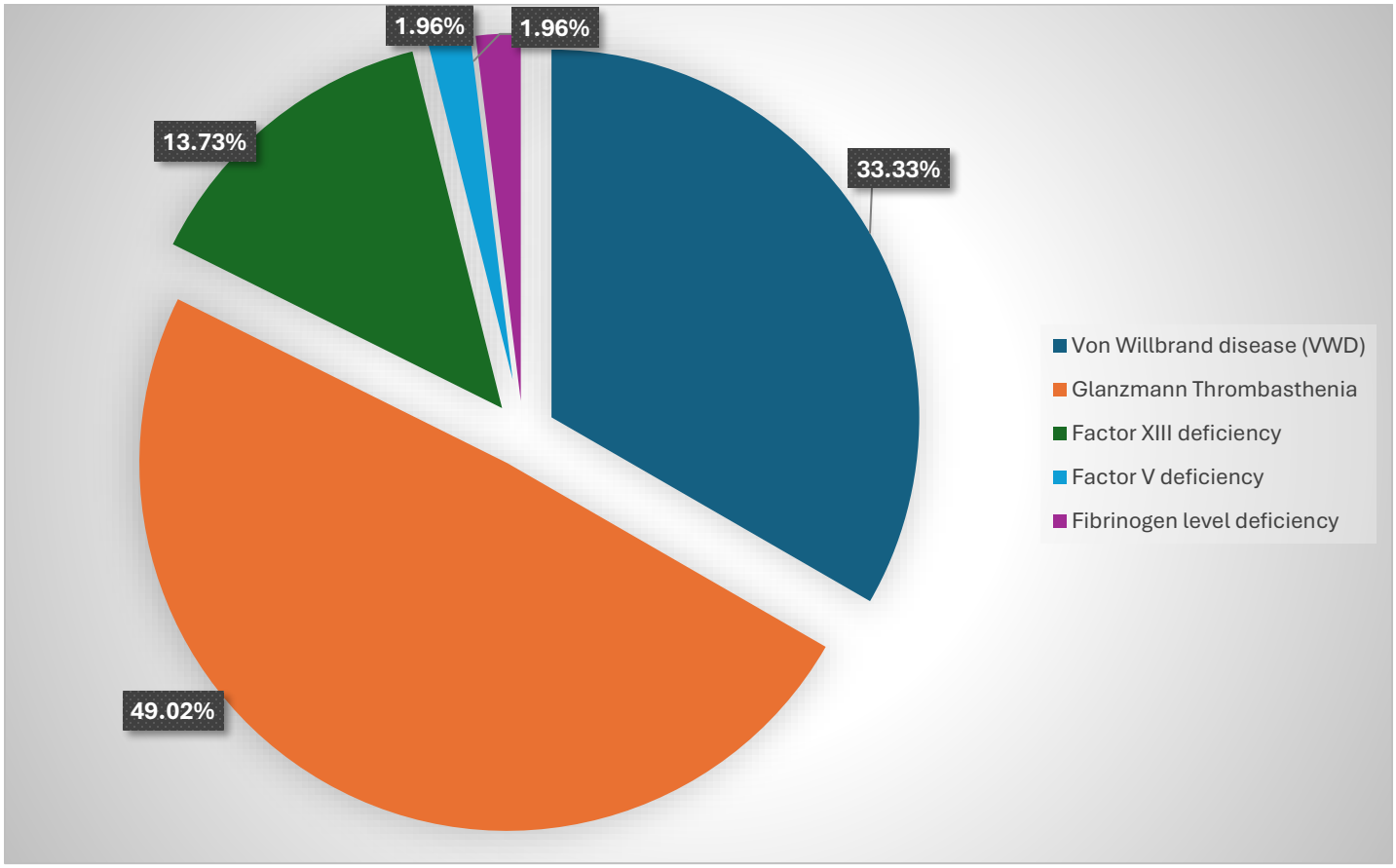


Fig 2. Diseases distribution among included subjects

Table (1). Vital signs distribution among most common diagnoses

Variables	All Cases (N = 51)	VWD (N = 17)	Glanzmann Thrombasthenia (N = 25)	Factor XIII deficiency (N = 7)	P. Value[F]
Systolic blood pressure (mmHg)	102.49 ± 4.84	101.06 ± 5.89	103.72 ± 3.78	102 ± 3.16	0.197897
		P1=0.1805, P2=0.8964, P3=0.6705			
Diastolic blood pressure (mmHg)	61.2 ± 4.58	60.94 ± 5.36	61.8 ± 4.24	60 ± 3.74	0.642749
		P1=0.8339, P2=0.8984, P3=0.6514			
Heart rate (Beat/min)	103.04 ± 6.83	104.82 ± 7.26	101.72 ± 5.63	101.57 ± 5.07	0.270235
		P1=0.2778, P2=0.4968, P3=0.9984			
Temperature (° C)	37.12 ± 0.08	37.12 ± 0.06	37.12 ± 0.08	37.09 ± 0.08	0.519219
		P1=0.9636, P2=0.6348, P3=0.4888			
Respiratory rate (Breath/min)	26.2 ± 1.89	26.76 ± 1.55	25.84 ± 1.35	25.71 ± 1.75	0.12628
		P1=0.1442, P2=0.2876, P3=0.9799			

P1: Comparison between VWD and Glanzmann Thrombasthenia, P2: Comparison between VWD and Factor XIII deficiency, P3: Comparison between Factor XIII deficiency and Glanzmann Thrombasthenia. F: ANOVA

Table (2): Clinical findings distribution among most common diagnoses

Variables	All Cases (N = 51)	VWD (N = 17)	Glanzmann Thrombasthenia (N = 25)	Factor XIII deficiency (N = 7)	P. Value[X]
Pallor	47 (92.16%)	16 (94.12%)	23 (92%)	6 (85.71%)	0.791
Jaundice	4 (7.84%)	1 (5.88%)	2 (8%)	1 (14.29%)	0.791
Bruises	12 (23.53%)	5 (29.41%)	7 (28%)	0 (0%)	0.2645
Petechiae	1 (1.96%)	0 (0%)	1 (4%)	0 (0%)	0.6126
Gums bleeding	3 (5.88%)	3 (17.65%)	0 (0%)	0 (0%)	0.051
Nasal bleeding	17 (33.33%)	7 (41.18%)	6 (24%)	3 (42.86%)	0.4181
Subconjunctival hemorrhage	4 (7.84%)	3 (17.65%)	0 (0%)	1 (14.29%)	0.0997

X: Chi Square Test

Table (3). Findings of laboratory investigations among most common diagnoses

Variables	All cases (N = 51)	VWD (N = 17)	Glanzmann Thrombasthenia (N = 25)	Factor XIII deficiency (N = 7)	P. Value[F]
Complete blood count					
RBCs (×10^6 / µL)	3.98 ± 0.28	3.98 ± 0.28	4 ± 0.27	3.94 ± 0.32	0.9139
		P1=0.988, P2=0.9516, P3=0.9059			
Hb (g/dL)	10.4 ± 1.24	10.25 ± 1.04	10.35 ± 1.19	10.81 ± 1.55	0.5898
		P1=0.9608, P2=0.5686, P3=0.6602			
WBCs (×10^3 / µL)	6.35 ± 1.81	6.42 ± 1.82	5.92 ± 1.39	7.16 ± 2.33	0.2445
		P1=0.6393, P2=0.6213, P3=0.2363			
PLTs (×10^3 / µL)	277.49 ± 79.49	282.35 ± 71.64	258.44 ± 82.38	337.57 ± 58.52	0.0685
		P1=0.5972, P2=0.2672, P3=0.0565			
Coagulation profile					
PT (Sec)	13.07 ± 6.72	11.42 ± 0.83	11.61 ± 0.98	12.93 ± 1.57	0.009*
		P1=0.8338, P2=0.0083*, P3=0.0169*			

aPTT (Sec)	37.8 ± 19.42	35.95 ± 19.63	34.14 ± 6.15	38.84 ± 25.74	0.7862
		P1=0.9332, P2=0.9172, P3=0.7782			
VWF antigen (IU/dL)	85.37 ± 45.41	52.99 ± 45.94	101.57 ± 34.75	96.54 ± 40.64	0.0016*
		P1=0.0014*, P2=0.0575, P3=0.9559			
VWF activity (%)	81.51 ± 49.39	45.86 ± 51.38	101.99 ± 38.53	85.51 ± 33.75	0.0009*
		23 (45.1%)	P1=0.0006*, P2=0.1245, P3=0.661		
Positive platelet aggregation					
Normal	23 (45.1%)	15 (88.24%)	1 (4%)	7 (100%)	<0.0001*(X)
Low	28 (54.9%)	2 (11.76%)	24 (96%)	0 (0%)	
Factor XIII (%)					
Normal	41 (80.39%)	14 (82.35%)	25 (100%)	0 (0%)	<0.0001*(X)
Low	10 (19.61%)	3 (17.65%)	0 (0%)	7 (100%)	
Immunohistochemical staining					
CD 41 (%)	55.67 ± 42.6	93.47 ± 3.11	19.8 ± 29.07	94.71 ± 3.06	<0.0001*
		P1<0.0001*, P2=0.9909, P3<0.0001*			
CD 61 (%)	55.47 ± 42.2	93.18 ± 3.09	20 ± 28.86	93.57 ± 4.34	<0.0001*
		P1<0.0001*, P2=0.9991, P3<0.0001*			
CD 42a (%)	93.76 ± 13.53	94.84 ± 4.08	92.21 ± 18.86	95.94 ± 2.26	0.7568
		P1=0.8265, P2=0.9834, P3=0.812			
CD 42b (%)	94.17 ± 13.52	95.63 ± 3.27	92.49 ± 18.92	96.3 ± 2.73	0.7082
		P1=0.7599, P2=0.9939, P3=0.8039			

P1: Comparison between VWD and Glanzmann Thrombasthenia, P2: Comparison between VWD and Factor XIII deficiency, P3: Comparison between Factor XIII deficiency and Glanzmann Thrombasthenia. F: ANOVA, (X): Compared with Chi Square test, *Significant P. Value < 0.05. CBC: Complete blood count; RBCs: Red blood cells; Hb: Hemoglobin; WBCs: White blood cells; PLTs: Platelets; PT: Prothrombin time; aPTT: Activated partial thromboplastin time; VWF Ag: Von Willebrand factor antigen; VWF Act: Von Willebrand factor activity; FXIII: Factor XIII; IHC: Immunohistochemical staining; CD: Cluster of differentiation.

Discussion

Our study included a cohort of pediatric patients with rare bleeding disorders presenting with mucocutaneous bleeding, primarily school-aged children. This aligns with a pediatric cohort in Egypt, where the mean age was 7.65 ± 4.07 years (**Hassab et al., 2024**), showing a similar age distribution. In contrast, a national referral center study in Iraq reported a younger mean age of 5.3 ± 3 years (**Abdulsalam et al., 2021**), significantly lower than our cohort, possibly due to referral patterns and earlier presentation of severe phenotypes.

Regarding sex distribution, our cohort showed male predominance, consistent with the Iraqi study reporting a male:female ratio of approximately 1.3:1 (~56.5% males) (**Abdulsalam et al., 2021**). Conversely, a multicenter study on Glanzmann thrombasthenia (GT) in Egyptian children found female predominance (61 females vs 26 males) with a median age of 8 years (**Sherief et al., 2025**), suggesting sample selection bias toward GT cases, whereas our study included a broader range of rare bleeding disorders.

Family history was positive in a low proportion of our patients, markedly lower than the 44.9% reported in Iraq (**Abdulsalam et al., 2021**) and 86% in Saudi Arabia (**Tarawah et al., 2023**), likely reflecting higher consanguinity rates and autosomal recessive inheritance in those populations.

Epistaxis was the most frequent presenting symptom in our cohort, followed by bruising, hematemesis, and menorrhagia, consistent with findings from a clinic-based cohort (**Yıldız et al., 2015**) where epistaxis, easy bruising, menorrhagia, and gingival bleeding were common. In contrast, severe presentations such as intracranial hemorrhage (ICH) were rare in our study, whereas **Sharma et al. (2012**) reported ICH in up to 20% of factor X deficiency cases, reflecting differences in disorder severity, genetics, and referral patterns.

Umbilical bleeding and post-circumcision bleeding occurred in 5.88% each in our cohort. This contrasts with Egyptian data reporting umbilical stump bleeding in ~20% and post-circumcision bleeding in ~3.1% (**Hassab et al., 2024**), likely due to higher proportions of factor XIII or fibrinogen deficiencies in their cohort. The median age at symptom onset in our study was 24 months, comparable to 1 year 6 months (range 3 days to 13 years) reported in Pakistan (**Mahmood et al., 2020**), indicating early pediatric onset with variability due to heterogeneous disorders.

The low rate of ICH in our cohort contrasts with 31% ICH in Egyptian children with congenital afibrinogenemia (**Abdelwahab et al., 2023**), reflecting differences in disorder severity. Mean systolic and diastolic blood pressures were 102.49 ± 4.84 mmHg and 61.2 ± 4.58 mmHg, respectively, within normal ranges for school-age children (90–120 mmHg systolic, 60–75 mmHg diastolic) (**Flynn et al., 2017; Lee et al., 2020**). Mean heart rate (103.04 ± 6.83 bpm) and respiratory rate (26.2 ± 1.89 breaths/min) were also consistent with normal pediatric centiles (**Fleming et al., 2011**), and mean temperature (37.12 ± 0.08 °C) aligned with typical pediatric values (36.5–37.5 °C) (**Dang et al., 2023; Leduc et al., 2000**).

The relatively high frequency of Glanzmann thrombasthenia (49%) and Factor XIII deficiency observed in this study likely reflects referral, as Qena University Hospital is a tertiary care center receiving complicated and recurrent bleeding cases from surrounding districts. The high rate of consanguinity in Upper Egypt may also contribute to increased prevalence of autosomal recessive bleeding disorders in this population **(Temtamy & Aglan, 2012; Mansouritorghabeh, 2021).** Additionally, the study specifically included children presenting with significant mucocutaneous bleeding, which may have enriched the sample for platelet function defects.

In the present study, comparisons between von Willebrand disease (VWD), Glanzmann thrombasthenia (GT), and factor XIII deficiency revealed no significant differences in vital signs. The absence of significant vital sign differences underscores the mucocutaneous nature of bleeding in these pediatric disorders, which typically does not lead to immediate hemodynamic instability, highlighting the importance of clinical history over routine vitals for early detection in resource-limited settings **(Nichols et al., 2008).**

Consistent with our findings of stable vital signs across VWD, GT, and factor XIII deficiency, a multicenter study on pediatric upper Egypt reported no vital sign abnormalities in 131 children, despite frequent mucocutaneous bleeding, suggesting that these disorders rarely cause acute hemodynamic compromise unless complicated by massive hemorrhage **(Khalifa et al., 2025).** Similarly, a review of factor XIII deficiency in children noted that while intracranial hemorrhage can occur, baseline vital signs remain normal in the absence of active bleeding, aligning with our lack of intergroup differences **(Pelcovits et al., 2021).** In contrast to our results, a case series on severe pediatric VWD described occasional tachycardia in patients with chronic anemia from recurrent epistaxis, with mean heart rates exceeding 110 beats/min in 20% of cases, possibly due to compensatory mechanisms not observed here **(Breakey & Carcao, 2017).** This discrepancy may be explained by variations in bleeding severity; our cohort had milder presentations without significant anemia impacting vitals, whereas the contrasting study included patients with type 3 VWD and more profound blood loss.

Pallor was the most prominent physical finding among our cases, reflecting anemia associated with mucocutaneous bleeding, consistent with literature (**Yurdakök et al., 2008**). Epistaxis occurred in one-third of patients, agreeing with multiple studies (**Alhuniti & Sharathkumar, 2024; ElAlfy et al., 2022**). Bruising was also common, as reported in reviews of primary hemostatic defects (**van Ommen & Peters, 2012**). Jaundice and subconjunctival hemorrhage were less frequent, aligning with literature indicating these signs are uncommon unless systemic involvement occurs (**Gallagher, 2022; van Ommen & Peters, 2012**). Gingival bleeding was observed and supported by pediatric bleeding disorder literature (**Acharya et al., 2018; Edme et al., 2024**). Petechiae were uncommon, likely due to predominance of coagulation factor deficiencies rather than platelet disorders (**NESMA et al., 2024; van Ommen & Peters, 2012**).

In our study also comparisons between von Willebrand disease (VWD), Glanzmann thrombasthenia (GT), and factor XIII deficiency revealed no significant differences in clinical findings. This suggests overlapping mucocutaneous manifestations without distinct patterns separating the groups. These clinical overlaps emphasize the need for targeted laboratory confirmation beyond symptoms, as mucocutaneous patterns in pediatric VWD, GT, and factor XIII deficiency stem from distinct mechanisms—platelet-vessel interactions in VWD and GT versus secondary hemostasis in factor XIII deficiency—yet present similarly in early childhood **(Sarnaik et al., 2010; Dunn et al., 2020).**

Laboratory evaluation showed mild anemia with normal white blood cell and platelet counts. Coagulation tests (PT, aPTT) were generally normal, and von Willebrand factor levels were mostly normal, while platelet aggregation was reduced in over half the patients. Factor XIII deficiency was present in 19.61%, and flow cytometry showed moderate expression of CD41 and CD61 with higher CD42a and CD42b. Mild-to-moderate anemia aligns with findings from Tunisia, where 87% of GT patients had anemia due to recurrent bleeding (**Elmahmoudi et al., 2017**). Normal platelet counts rule out thrombocytopenic disorders, consistent with GT registry data (**Ali & Schved, 2012**). Reduced platelet aggregation indicates a high prevalence of GT, as seen in regions with consanguinity (**Zolaly et al., 2021**).

The 19.61% prevalence of Factor XIII deficiency aligns with regional studies in Iran (**Dorgalaleh et al., 2015**) but contrasts with its ultra-rare global prevalence (1 in 2 million). This highlights the importance of including specific FXIII assays in workup (**Palla et al., 2015**). Flow cytometry averages may mask differences between Type I GT (<5% expression) and FXIII deficiency (**Mutreja et al., 2017**), while normal CD42a and CD42b excludes Bernard-Soulier Syndrome (**Keller Cecconello et al., 2024**).

GT was the most frequent disorder in our cohort, consistent with high consanguinity populations (**Khalifa et al., 2025; Tarawah et al., 2023**). In contrast, broader registries report VWD as more common (**Abdulsalam et al., 2021; El Demerdash et al., 2024**). Regional variability also shows lower GT prevalence in India (2.85%) and higher hemophilia rates (**Ahmad et al., 2022**). Epistaxis was common across both VWD and GT (**Hafez et al., 2023**), supporting its role as a consistent mucocutaneous manifestation.

Consistent with our normal CBC across groups, a diagnostic review of pediatric inherited platelet disorders reported preserved hemoglobin, WBCs, and platelet counts in GT and VWD, with mild anemia only in chronic bleeders, mirroring our non-significant comparisons **(Kim, 2022).** The significant PT prolongation in factor XIII deficiency versus others aligns with an overview, noting occasional mild PT elevation in severe cases due to secondary consumptive effects, though typically normal **(Jacobs et al., 2026).** For VWF parameters, our lower levels in VWD match a Haematologica guideline on VWD diagnosis, where antigen <50 IU/dL and activity <45% distinguish it from GT and factor XIII deficiency **(Tosetto & Eikenboom, 2026).** Reduced platelet aggregation in GT concurs with a JTH study on IPDs, showing absent responses to agonists in 95% of GT children, unlike normal in VWD and factor XIII deficiency **(Kim, 2022).** Flow cytometry findings of low CD41/CD61 in GT are supported by a StatPearls entry on GT, emphasizing GPIIb/IIIa deficiency detection via reduced expression, with preserved CD42a/CD42b as in our non-significant results **(Cecconello et al., 2024; Hassan et al., 2016).** In contrast to our PT differences, a pediatric thrombosis handbook reported uniformly normal PT/aPTT in factor XIII deficiency, possibly due to our cohort's inclusion of patients with concurrent mild liver involvement or methodological variations in assay sensitivity **(Breakey & Carcao, 2017).** This unexpected PT finding may biologically stem from fibrin instability indirectly affecting extrinsic pathway measurements, or methodologically from sample handling differences.

This study is limited by its small sample size (N=51) and single-center design, which may reduce generalizability. Focusing on pediatric patients at a tertiary referral hospital may overrepresent severe cases, such as Glanzmann Thrombasthenia, while missing milder, undiagnosed cases. Additionally, the lack of molecular genetic testing prevents definitive genotype-phenotype correlations.

Conclusion

This study at Qena University Hospital found Glanzmann Thrombasthenia (GT) to be the leading cause of mucocutaneous bleeding in children, followed by Von Willebrand Disease and Factor XIII deficiency. Patients often present in early childhood with epistaxis and pallor, frequently accompanied by microcytic anemia despite normal platelet counts. The high prevalence of autosomal recessive disorders in the region emphasizes the need for specific diagnostic tests—such as platelet aggregation and flow cytometry for CD41/CD61—beyond routine coagulation screens for accurate diagnosis and management.

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