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Serum Thrombospondin-1 as a Biomarker of Vaso-occlusive Crises in Adults with Sickle Cell Anaemia: Associations with Platelet Indices and Inflammation

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Abstract

Background: Thrombospondin-1 (TSP-1), a platelet-derived adhesive glycoprotein, contributes to vaso-occlusive crises (VOC) in sickle cell anaemia (SCA). Although elevated TSP-1 levels have been reported in paediatric and high-income settings, its relationship with platelet indices in African adults with SCA remains poorly defined. This study aimed to evaluate serum TSP-1 concentrations in adult Nigerian patients with SCA during VOC and steady state, and to explore associations with platelet indices and haematological parameters.

Materials and Methods: We conducted a cross-sectional comparative study at Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria. Participants comprised 40 SCA patients in VOC, 40 in steady state, and 40 age- and sex-matched HbAA controls. Clinical data were obtained using a structured questionnaire. Complete blood counts and platelet indices were analysed using an automated haematology analyser, and serum TSP-1 was quantified by enzyme-linked immunosorbent assay (ELISA). Group comparisons were performed using ANOVA, correlations were assessed with Pearson's or Spearman's tests as appropriate, and predictors of TSP-1 were identified by multivariable linear regression.

Results: A total of 120 participants were enrolled (median age 26 years, 67·5% female). Mean TSP-1 levels were significantly higher in VOC (406·0 ng/mL, SD 164·6) than steady state (312·4 ng/mL, SD 145·6) and controls (192·3 ng/mL, SD 121·2; $p < 0·001$). In steady state, TSP-1 correlated positively with haemoglobin ($r = 0·42$, $p = 0·01$) and haematocrit ($r = 0·49$, $p = 0·01$), but inversely with mean platelet volume ($r = –0·38$, $p = 0·02$) and platelet large cell ratio ($r = –0·36$, $p = 0·02$). During VOC, TSP-1 showed a modest inverse correlation with numeric pain scores ($r_s = –0·41$, $p = 0·01$). In multivariable regression, white blood cell count independently predicted TSP-1 levels ($\beta = 7.309$, $t = 2.285$, $p = 0.024$).

Conclusion: TSP-1 levels were markedly elevated during VOC in adult Nigerian patients with SCA and were independently associated with leukocytosis. Platelet indices are significantly altered but added limited predictive value for TSP-1 variance, supporting their role as complementary rather than substitute biomarkers.

Keywords: Sickle cell anaemia; Thrombospondin-1; Vaso-occlusive crisis; Platelet indices; Biomarkers

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Introduction

Sickle cell anaemia (SCA) is the most common and severe form of sickle cell disease (SCD), representing about 70% of all cases worldwide.[1,2] It is a major global health problem, with an estimated 300,000 affected newborns annually, and more than 80% of these births occuring in sub-Saharan Africa, particularly in Nigeria and the Democratic Republic of Congo.[2,3,4] In Nigeria alone, over 150,000 babies are born with SCA each year, with 10–30% of the population carrying the sickle cell trait and approximately 2–3% affected by the disease.[2,5] Despite significant advances in newborn screening and early interventions in high-income countries—where up to 94% of children now survive to adulthood—mortality rates remains high in sub-Saharan Africa.[6] It is estimated that 50–90% of affected infants in low-resource settings die before their first birthday, largely due to late diagnosis, poor access to care, and under-recognition of disease complications.[6]

The hallmark clinical feature of SCA is the vaso-occlusive crisis (VOC), a

painful and often debilitating complication that results from microvascular obstruction.[7,8,9] VOC is driven by complex interactions between sickled erythrocytes, leukocytes, platelets, and plasma proteins.[10,11,12]

Recurrent pain episodes are the leading cause of hospital admissions among SCA patients, contributing to a marked reduction in quality of life (QoL).[13] In the United States alone, direct annual healthcare costs for SCA-related pain crises exceed US$1.1 billion.[14,15] Hospitalizations for pain are also a strong predictor of early mortality, and in Nigeria, approximately 20.7% of affected families experience catastrophic health expenditures related to disease complications.[15,16,17] The frequency of hospital attendance due to VOC varies widely, with 0.5–27.9% of patients seeking care annually and 0.3–5% requiring emergency intervention.[18]

Platelets play an important role in the pathophysiology of VOC. They contribute to vascular occlusion by releasing adhesive proteins, including thrombospondin-1 (TSP-1), stored in their alpha granules.[19,20] TSP-1 is a multifunctional glycoprotein that not only enhances cellular adhesion but also inhibits nitric oxide (NO) signalling and promotes anti-angiogenic activity.[20,21] Although platelets are a major source of TSP-1, other cell types can release it in response to injury or inflammatory stimuli. Upon platelet activation, alpha granules release TSP-1, which can bind to platelet surfaces, stabilize aggregates through crosslinking fibrinogen–GpIIb/IIIa complexes, and promote adhesion to vascular endothelium via GpIb receptors.[22,23,24] These processes contribute to the formation and persistence of microvascular occlusions in SCA.

Several studies have shown that plasma TSP-1 levels are elevated during VOC compared with steady-state SCA and healthy controls.[25,26] High TSP-1 concentrations have been linked to increased sickle erythrocyte adherence to the vascular endothelium, acting as a molecular bridge between receptors on erythrocytes and endothelial cells.[27] Elevated TSP-1 has also been associated with a history of acute chest syndrome, pulmonary embolism, more frequent VOC episodes, lower haemoglobin levels, and higher markers of haemolysis, such as lactate dehydrogenase, aspartate aminotransferase, and bilirubin.[19] In steady state, TSP-1 levels correlate with platelet count; however, this relationship is often lost during acute VOC.[19]

Platelet activation can be assessed indirectly through platelet indices (PIs), which are routinely available as part of automated blood counts. Commonly reported indices include mean platelet volume (MPV), platelet distribution width (PDW), platelet–large cell ratio (P-LCR), platelet–large cell concentration (P-LCC), and plateletcrit (PCT). These parameters reflect platelet size, morphology, and activity, and abnormalities have been observed in both acute and chronic diseases, including SCA.[28]

In SCA, increased MPV has been linked to greater disease severity and frequency of VOC.[28] Studies have demonstrated positive correlations between MPV and pain scores during VOC, as well as with annual crisis frequency and cerebrovascular events.[29,30,31] Similar associations have been reported for PDW, which tends to be higher in VOC compared with steady state.[32] Although MPV and PDW often rise together following platelet activation, PDW may be a more specific marker, and their combined measurement may improve predictive accuracy for coagulation activation.[33] Other indices, such as P-LCR and PCT, have shown inconsistent associations with SCA complications, though some studies suggest they may also increase with VOC frequency.[31,34]

These findings underscore the potential of platelet indices as inexpensive, rapid, and widely accessible biomarkers of disease activity and prognosis.

Despite extensive research on platelet biology in SCA, relatively few studies have examined the relationship between TSP-1 and platelet indices, particularly in adults. Most available data come from paediatric populations or from high-income settings. This knowledge gap is important because, in Nigeria and similar low-resource settings, increasing numbers of SCA patients are surviving into adulthood. Furthermore, VOC-related complications tend to increase with age, underscoring the need for improved risk stratification in this population. Since TSP-1 assays are not routinely available and have long turnaround times, identifying surrogate markers based on readily available platelet indices could have substantial clinical utility.

The current study therefore aimed to evaluate serum TSP-1 levels in adult SCA patients, both in steady state and during VOC, and to explore their relationship with various platelet indices and other haematological parameters. By identifying correlations between TSP-1 and simple, inexpensive laboratory measures such as MPV, PDW, PCT, and platelet counts, it may be possible to develop practical tools for predicting VOC risk and guiding early intervention. Such an approach could be particularly valuable in resource-limited settings, where access to advanced laboratory assays is restricted, but automated blood counts are increasingly available.

Given the established role of TSP-1 in mediating sickle erythrocyte adhesion and stabilizing thrombi, and the

documented abnormalities in platelet indices in SCA, understanding their interrelationship could shed light on the mechanisms underlying VOC and other complications. Moreover, this knowledge could contribute to the development of cost-effective biomarker strategies that improve patient outcomes while minimizing costs.

Materials and Methods

Study Design and Population

This was a cross-sectional comparative study conducted at the Department of Haematology, Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria.

Participants comprised three groups: adults with SCA (HbSS on haemoglobin electrophoresis) either experiencing vaso-occlusive episode (VOC) or in steady state, and age- and sex-matched healthy controls (HbAA on haemoglobin electrophoresis). Eligible SCA patients were aged 18 years or older and were either in steady state or presenting with VOC. Steady state was defined as the absence of acute painful crisis, hospital or emergency department visits for VOC in the preceding four weeks, no blood transfusion in the preceding four months, no intercurrent illness (including infection) in the preceding four weeks, and no antibiotic use within the preceding three weeks.[35] Exclusion criteria for SCA participants included current hydroxyurea therapy, receipt of a blood transfusion within the past three months, pregnancy, or use of antiplatelet agents within the preceding 10 days. HbAA controls aged ≥18 years were recruited from hospital staff and relatives of the participants. Individuals with HbAS or other haemoglobin variants on Hb electrophoresis, a history of blood transfusion within the past three months, pregnancy, or antiplatelet use within 10 days were excluded.

Sample size and sampling

The minimum required sample size per group was calculated using the formula for comparison of means between two groups,[36] with an effect size of 0.74 derived from previously reported mean serum thrombospondin-1 (TSP-1) levels in SCA (148.4 ng/mL, SD 82.7) and Hb AA controls (99.9 ng/mL, SD 41.3).[37] With $\alpha = 0.05$ and 90% power, 40 participants were required per group with a total of 120 across the three groups. Participants and controls were recruited consecutively as they presented to the haematology day-care or sickle cell clinic.

Data collection

Data were obtained using a structured, interviewer-administered questionnaire capturing sociodemographic characteristics, clinical history, and findings from general physical and systemic examination. Laboratory data included complete blood count (CBC) parameters and serum TSP-1 concentrations.

Laboratory investigations

Venous blood (8 mL) was drawn from the antecubital vein under aseptic conditions. Three milliliters were placed in a K_3-EDTA anticoagulated tube, gently mixed to prevent clotting, and analysed within 6 hours for CBC using an automated haematology analyser (Dymind DH36, China). Parameters measured included red cell count, haematocrit, red cell indices (mean corpuscular volume [MCV], mean corpuscular haemoglobin [MCH], mean corpuscular haemoglobin concentration [MCHC], red cell distribution width [RDW-SD, RDW-CV]), total and differential white cell counts, platelet count, and platelet indices - MPV, PCT, PDW, P-LCR, P-LCC.

The remaining 5 mL of blood was placed in a plain tube, allowed to clot, and centrifuged to obtain serum, which was stored at –20 °C until analysis. Serum TSP-1 was quantified using a commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions.

Statistical analysis

Data were analysed using SPSS version 28 (IBM Corp., Armonk, NY, USA). Categorical variables were summarised as frequencies and percentages, with associations between categorical variables assessed using Chi-square χ^2 tests. The distribution of continuous variables was tested using the Shapiro–Wilk test. Normally distributed variables were reported as mean (SD), and non-normally distributed variables as median (IQR). Group comparisons were made using independent t tests for haematological parameters and Mann–Whitney U tests for non-normally distributed clinical variables

Correlations of serum TSP-1 levels with platelet indices and other haematological parameters were assessed using Pearson's correlation, while correlations with non-normally distributed clinical variables was determined using Spearman's rank correlation coefficients. Multiple linear regression analysis was performed to determine independent predictors of TSP-1 variance. A p- value ≤ 0.05 was considered statistically significant.

Ethical considerations

The study was approved by the Health Research Ethics Committee of ABUTH, Zaria, Nigeria. Written informed consent was obtained from all participants before enrolment, after providing detailed information about study objectives and procedures. All data were kept confidential and anonymised during analysis.

Results

Participant characteristics

A total of 120 individuals were enrolled in the study, comprising 40 patients with sickle cell anaemia (SCA) in vaso-occlusive crisis (VOC), 40 patients in steady state (SS), and 40 age- and sex-matched healthy Hb AA controls. The median age of the entire cohort was 26 years (IQR 22–29), with little variation across groups. Age distribution was similar, with 45% of participants aged 18–24 years and 32·5% aged 25–29 years. Overall, 39 (32·5%) were male and 81 (67·5%) were female, with sex proportions balanced across groups. The majority of participants were single (70·8%), particularly among SCA patients, while a higher proportion of controls were married (35·0%). Students formed the largest occupational group (59·2%), and educational attainment differed significantly: 97·5% of HbAA controls had tertiary education compared with 65·0% of VOC patients and 32·5% of those in steady state.

Clinical profile of SCA patients

Among SCA participants, 75·0% of those in VOC and 87·5% of those in steady state had a history of blood transfusion in their lifetime. Hospital admissions in the preceding year were significantly more common in VOC patients (72.5%) than in steady state (42.5%) (OR = 3.57, p = 0.007). Febrile episodes were also more frequent in VOC (20·0% vs 5·0%; OR = 4·75, p = 0·043). Splenomegaly (17·5% vs 12·5%) and hepatomegaly (10·0% vs 5·0%) were observed but did not differ significantly between the two groups (p > 0.05). Table 1 presents the clinical characteristics of SCA participants.

Haematological parameters

Marked differences in haematological indices were observed across the three study groups (Table 2). Both VOC and steady-state patients had significantly lower mean haemoglobin (Hb) levels (8.0 ± 1.3 g/dL and 7.7 ± 1.6 g/dL, respectively) and haematocrit (Hct) (23.1% and 23.0%) compared with HbAA controls (12.5 ± 1.6 g/dL, 41.1%; p < 0.001 for both). White cell counts were elevated in SCA, particularly during VOC (16.2 × 10^9/L vs 11.5 × 10^9/L in steady state and 5.2 × 10^9/L in controls; p < 0.001). Platelet counts were also significantly higher in SCA patients than controls (377.7 × 10^9/L) than in controls (284.2 × 10^9/L, p < 0.001). Platelet indices demonstrated group-specific variations (Table 2). Mean platelet volume (MPV) was lowest in steady state (8·9 fL) compared with Hb AA (9·5 fL, p = 0·004), while plateletcrit (PCT), was higher in SCA than Hb AA (0·34% vs 0·27%, p<0·001). Platelet distribution width (PDW) was significantly increased in both SCA groups compared with controls (p < 0·001), and was higher in VOC than steady state (15·9 vs 15·5, p = 0·002). The platelet large cell ratio (P-LCR) was reduced in steady state relative to HbAA (19·6% vs 24·0%, p = 0·009). These findings underscore the haematological activation and dysregulation characteristic of SCA, with further derangement during VOC.

Serum thrombospondin-1 and correlations

Serum thrombospondin-1 (TSP-1) levels differed markedly between groups (Figure 1). VOC patients had

Table 1: Clinical Characteristics of SCA Participants

Clinical Variable	Clinical Status		X^2	Odds Ratio (OR)	*P*
	VOC (n = 40) Count (%)	SS (n = 40) Count (%)			
Transfused in the past					
Yes	30 (75.0)	35 (87.5)	2.05	0.43	0.152
No	10 (25.0)	5 (12.5)			
Admitted in the last 1 year					
Yes	29 (72.5)	17 (42.5)	7.37	3.57	**0.007***
No	11 (27.5)	23 (57.5)			
Febrile					
Yes	8 (20.0)	2 (5.0)	4.11	4.75	**0.043***
No	32 (80.0)	38 (95.0)			
Splenomegaly					
Yes	7 (17.5)	5 (12.5)	0.39	1.49	0.531
No	33 (82.5)	35 (87.5)			
Hepatomegaly					
Yes	4 (10.0)	2 (5.0)	0.72	2.11	0.396
No	36 (90.0)	38 (95.0)			

*=significant, VOC = vaso-occlusive crisis, SS= steady state

Table 2: Haematological parameters of study participants

Haematological Parameter	VOC (n =40) Mean±SD	SS (n =40) Mean±SD	HbAA (n =40) Mean±SD	*P*
Hct (%)	23.06±4.20	23.04±5.15	41.07±4.66	**<0.001***
Hb (g/dL)	8.00±1.34	7.73±1.56	12.52±1.56	**<0.001***
WBC count (x 10^9/L)	16.16±4.76	11.51±3.72	5.21±1.15	**<0.001***
Platelet count (x10^9/L)	362.75±135.01	392.56±153.27	284.15±65.50	**<0.001***
MPV (fL)	9.05±0.90	8.94±0.71	9.48±0.94	**0.014***
PDW	15.89±0.69	15.48±0.36	15.90±0.29	**<0.001***
PCT (%)	0.33±0.11	0.35±0.14	0.27±0.05	**<0.002***
P-LCR (%)	22.25±7.09	19.61±5.05	23.98±6.50	**0.009***
P-LCC (x 10^9/L)	74.45±27.76	74.88±29.58	65.98±18.47	0.223

*=significant, VOC = vaso-occlusive crisis, SS= steady state, Hb AA=haemoglobin AA phenotype

Table 3: Correlation of TSP-1 with haematological indices and clinical parameters

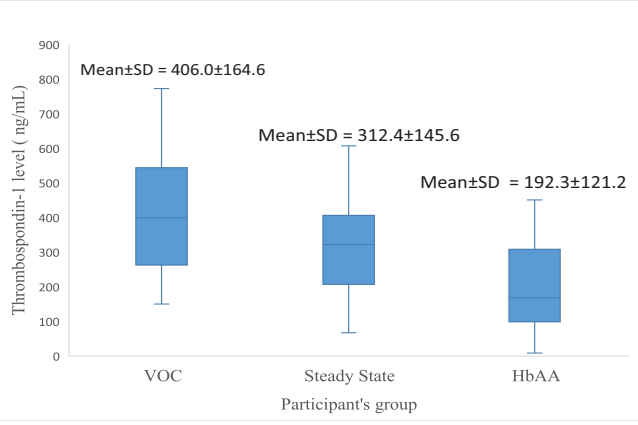
	TSP-1 Levels					
Haematological Variable	**VOC (n = 40)**		**SS (n = 40)**		**HbAA (n = 40)**	
	r	***P – Value***	**r**	***P - Value***	**R**	***P - Value***
Hct (%)	-0.26	0.11	0.49	**0.01***	-0.13	0.42
Hb (g/dL)	-0.27	0.09	0.42	**0.01***	-0.07	0.67
WBC count (x 10^9/L)	-0.09	0.59	0.06	0.71	-0.15	0.37
Platelet count (x10^9/L)	0.27	0.09	0.02	0.91	-0.29	0.07
MPV (fL)	0.12	0.45	-0.38	**0.02***	0.14	0.39
PDW	0.03	0.88	-0.07	0.67	0.18	0.27
PCT (%)	0.27	0.09	0.13	0.44	-0.21	0.19
P-LCR (%)	0.01	0.96	-0.36	**0.02***	0.15	0.36
P-LCC (x 10^9/L)	0.26	0.10	-0.03	0.85	-0.11	0.49
Age	-0.03 ^{rs}	0.85	-0.27	0.09	-	-
No of Bone Pains/year	0.03 ^{rs}	0.87	0.25	0.12	-	-
No of transfusions/years	0.17 ^{rs}	0.29	-0.01	0.98	-	-
No of admissions/years	0.14 ^{rs}	0.39	-0.16	0.33	-	-
NPS	-0.41^{rs}	**0.01***	-	-		

*=significant, VOC = vaso-occlusive crisis, SS= steady state , HbAA=haemoglobin AA, TSP-1 = thrombospondin-1, NPS = Numeric Pain Score, rs= spearmans correlation coefficient

the highest concentrations (mean 406·0 ng/mL, SD 164·6), followed by steady state (312·4 ng/mL, SD 145·6) and HbAA (192·3 ng/mL, SD 121·2). ANOVA confirmed significant group differences ($F=21·86$, $p < 0·001$). Post hoc testing showed that TSP-1 was significantly higher in VOC than steady state ($p = 0·013$) and HbAA ($p < 0·001$), and in steady state compared with HbAA ($p = 0·001$).

Correlations of TSP-1 with clinical and haematological variables revealed state-specific associations (Table 3). In VOC, TSP-1 was moderately and inversely correlated with numeric pain score ($r_s = –0·41$, $p = 0·01$). No other clinical variables correlated significantly with TSP-1 during VOC. In steady state, TSP-1 correlated positively with haemoglobin ($r = 0·42$, $p = 0·01$) and haematocrit ($r = 0·49$, $p = 0·01$), but negatively with MPV ($r = –0·38$, $p = 0·02$) and P-LCR ($r = –0·36$, $p = 0·02$) (Table 3).

Multiple regression analysis confirmed white blood



VOC= vaso-occlusive crisis, HbAA=haemoglobin AA, SD= standard deviation

Figure 1: Box plots showing the Mean TSP-1 levels across the study groups.

cell count as the only independent predictor of TSP-1 levels, with each unit increase in WBC associated with a mean 7·3 ng/mL rise in TSP-1 ($p = 0·024$). Haemoglobin, platelet count, and plateletcrit did not contribute independently to variance in TSP-1 (Table

Table 4: Multiple linear regression analysis of predictors of thrombospondin-1 (TSP-1) variance among study participants

Predictor Variable	R^2	Adj R^2	F	P	Constant	Gradient(β)	*t-test*	*p*
Model	0.196	0.168	7.004	<0.001	263.926			
Hb(g/dL)						-11.151	-1.613	0.110
WBC (x10^9/L)						7.309	2.285	**0.024***
Platelet (X10^9/L)						-0.078	-0.365	0.716
Plateletcrit (%)						290.241	1.168	0.245

*=significant

4).

Discussion

This study provides evidence on the relationship between TSP-1 levels and platelet indices in adults with sickle cell anaemia (SCA) during vaso-occlusive crises (VOC) and in the steady state. Consistent with previous reports, we found that serum TSP-1 concentrations were significantly higher during VOC compared with the steady state and healthy HbAA controls.[19,25,26] These findings reinforce the central role of TSP-1 in mediating sickle erythrocyte adhesion and vascular occlusion,[7,27] supporting its potential use as a biomarker of acute disease activity.

The elevated TSP-1 levels observed in this Nigerian adult cohort are consistent with prior observations from paediatric populations and studies conducted in high-income settings.[19,25,26] Importantly, our study demonstrates that TSP-1 elevation persists beyond childhood, indicating it is a consistent feature of VOC even in adulthood. This is particularly relevant in sub-Saharan Africa, where increasing numbers of SCA patients are surviving into adulthood but continue to experience substantial morbidity from recurrent crises.[2,4,6]

We also explored the associations between TSP-1 and platelet indices (PIs) which are inexpensive surrogate markers of platelet activation. Platelets are increasingly recognised as active participants in SCA pathophysiology,[10,12] contributing adhesive proteins and procoagulant activity that amplify vaso-occlusion. In our study, platelet counts were significantly elevated in SCA compared with controls, while indices such as platelet distribution width (PDW) and plateletcrit (PCT) were also higher. These findings are consistent with earlier reports showing abnormal platelet morphology and function in SCA.[28,31,32]

Interestingly, correlations between TSP-1 and platelet indices differed between steady state and VOC. In steady state, TSP-1 correlated positively with haemoglobin and haematocrit, but inversely with mean platelet volume (MPV) and platelet large cell ratio (P-LCR). These findings suggest that, in quiescent disease, TSP-1 levels may be influenced by baseline haematological status and subclinical platelet activation. By contrast, during VOC, no significant positive correlations between TSP-1 and platelet indices were observed, except for a modest inverse association with pain scores. This loss of correlation echoes earlier observations that while platelet count and TSP-1 track together at baseline, their relationship is dissociated during acute crises when multiple cell types, including endothelial and inflammatory cells, contribute to TSP-1 release.[19,22,23]

Our regression modelling identified white blood cell (WBC) count as the only independent predictor of TSP-1 levels. Elevated leukocytes are well-established contributors to VOC pathophysiology, promoting adhesion, inflammation, and endothelial injury.[12,29] The association between WBC and TSP-1 underscores the intertwined roles of inflammation and platelet activation in sickle cell pathobiology. This supports Sundd et al.'s model, which positions neutrophils, platelets, and sickled erythrocytes at the centre of the vaso-occlusive process.[8,12]

Clinical correlates of TSP-1 in our study were limited. The inverse association between TSP-1 and numeric pain scores during VOC is counterintuitive, given that higher TSP-1 might be expected to worsen vascular obstruction and pain. This paradox may reflect complex temporal dynamics: TSP-1 may peak early during VOC as platelets and endothelial cells are activated, but decline as crises progress, pain intensifies, and interventions such as hydration and analgesia are

initiated. Alternatively, pain intensity scores may reflect subjective perception rather than biochemical severity, limiting their correlation with laboratory markers.[15]

Our findings also highlight the limitations of relying solely on platelet indices as predictors of VOC severity. While MPV and PDW were significantly altered in SCA, they did not independently predict TSP-1 variance in regression analysis. This suggests that, although platelet indices are accessible and useful adjuncts, they cannot fully substitute for direct biomarkers such as TSP-1. Nevertheless, their combined measurement could help stratify clinical risk in low-resource settings where TSP-1 assays are unavailable.[28,33]

This study has several strengths. It recruited well-characterized adult SCA patients in both steady state and VOC, with age- and sex-matched controls, and employed rigorous laboratory methods for TSP-1 quantification. It also provides much-needed data from sub-Saharan Africa, where the burden of SCA is highest.[2,5] However, several limitations must be acknowledged. The cross-sectional design precludes evaluation of temporal changes in TSP-1 during VOC progression. The modest sample size may limit statistical power for detecting weaker correlations. Additionally, the absence of longitudinal follow-up prevents assessment of whether TSP-1 predicts recurrent crises or chronic complications.

Future studies should therefore adopt longitudinal designs, capturing serial measurements of TSP-1 and platelet indices before, during, and after VOC, to clarify their temporal dynamics. Incorporation of additional markers of endothelial activation (e.g., von Willebrand factor, soluble P-selectin, and VCAM-1) may also help distinguish platelet-derived vs endothelial-derived TSP-1 sources.[11,27] Ultimately, integration of TSP-1 with other inexpensive indices could enable development of practical, locally feasible biomarker panels to improve risk stratification and guide interventions in resource-limited settings.

In conclusion, this study confirms that TSP-1 is elevated during VOC in adult SCA patients and is closely associated with inflammatory burden as reflected by WBC count. While platelet indices are significantly altered in SCA, their independent contribution to TSP-1 variance is limited, suggesting they may serve as complementary rather than substitute biomarkers. These findings deepen our understanding of platelet-mediated vascular pathology in SCA, support the role of TSP-1 as a biomarker of acute disease activity, and highlight the potential for inexpensive haematological indices to inform care where advanced assays are unavailable.

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