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Clinical Correlation of Positive Lupus Anti-Coagulant Cases: A Cross-Sectional Study

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Abstract

Objective: To evaluate the clinical profile of lupus anticoagulant–positive patients and to determine the association between LA ratio levels and clinical manifestations.

Methodology: This cross-sectional descriptive study was conducted between September 2025 and January 2026 at Chughtai Institute of Pathology, Lahore. A total of 138 patients aged 8–90 years undergoing LA testing were included. Lupus anticoagulant was detected using a two-step dilute Russell viper venom time (DRVVT)–based screening and confirmatory assay. Results were interpreted using LA1/LA2 ratios and categorized as strongly positive (>2.0), moderately positive (1.5–2.0), weakly positive (1.2–1.5), or borderline (1.0–1.2). Clinical data were extracted from patient records.

Results: Of the 138 LA-positive cases, 59% were female. Strongly positive LA ratios were observed in 26 cases, moderately positive in 28, and weakly positive in 82 cases. Venous thrombosis was the most frequent clinical manifestation, particularly among strongly positive cases (50%). Recurrent miscarriages and arterial events, including stroke and ischemic heart disease, were also noted. Among weakly positive cases, 31% were asymptomatic.

Conclusion: LA positivity is associated with a broad spectrum of clinical manifestations, with venous thrombosis being the most common. Weakly positive LA results may be clinically silent, emphasizing the importance of correlating laboratory findings with clinical context and follow-up to exclude transient or false positivity.

Key Words: Lupus Anticoagulants, Systemic Lupus Erythemotosis, Miscarriages, Venous Thrombosis

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Introduction

Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disease characterized by immune dysregulation, autoantibody production, and involvement of multiple organ systems. Among the immunologic abnormalities encountered in SLE, antiphospholipid antibodies (aPL) constitute a clinically significant subgroup due to their strong association with thrombotic and hematologic complications. Lupus anticoagulant (LA), one of the major aPL antibodies, plays a central role in the prothrombotic state observed in a subset of patients with SLE and related autoimmune disorders.[1,2]

Lupus anticoagulant represents a heterogeneous group of autoantibodies directed against phospholipid-binding plasma proteins, primarily β2-glycoprotein I and prothrombin. Despite its misleading nomenclature, LA is paradoxically associated with thrombosis rather than bleeding in vivo. Proposed mechanisms include endothelial activation, inhibition of natural anticoagulant pathways, platelet activation, and acquired resistance to activated protein C, collectively contributing to a hypercoagulable state.[4,6,11] Several studies have demonstrated that LA positivity confers a higher thrombotic risk compared to other antiphospholipid antibodies, even in the absence of overt antiphospholipid syndrome (APS).[1,5,11]

Clinically, LA positivity has been linked to a wide spectrum of manifestations, including venous and arterial thromboembolic events, obstetric complications, hematologic abnormalities such as thrombocytopenia and hemolytic anemia, and non-thrombotic cardiovascular involvement. [5,7,9] Multiple cohort studies have shown that SLE patients with LA positivity experience higher rates of thrombosis, greater disease severity, and poorer long-term outcomes compared to LA-negative individuals.[1,8,13] Furthermore, LA has emerged as an independent predictor of thrombosis in SLE, surpassing other aPL antibodies in prognostic value.[11]

Laboratory detection of LA remains challenging due to its functional nature and variable interaction with phospholipid-dependent coagulation assays. Diagnosis relies on a stepwise approach involving screening, mixing, and confirmatory tests, most commonly using

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lupus anticoagulant–sensitive activated partial thromboplastin time (APTT) and dilute Russell viper venom time (DRVVT) assays. These tests demonstrate phospholipid dependence of clotting time prolongation rather than direct antigen–antibody binding [4]. Results are often expressed as normalized ratios, which may reflect inhibitor strength and have potential clinical relevance.

Emerging data suggest that higher LA ratios are associated with increased thrombotic burden and more severe clinical manifestations. Persistent and strongly positive LA results have been linked to higher risks of thrombosis, hematologic complications, and adverse outcomes, whereas weakly positive or borderline results may reflect transient antibodies, assay variability, or false positivity related to inflammation, anticoagulant therapy, or intercurrent illness.[2,4,10] Differentiating clinically significant LA positivity from laboratory artifacts is therefore essential for appropriate risk stratification and patient management.

Despite growing recognition of LA's prognostic importance, data correlating the magnitude of LA positivity with specific clinical presentations remain limited, particularly in South Asian populations. Evaluating the relationship between LA ratios and clinical manifestations may improve individualized patient care and clinical decision-making.

This study aimed to assess the clinical profile of patients with positive lupus anticoagulant tests and to analyze the association between varying LA ratio levels and clinical manifestations, thereby contributing to a more refined understanding of the clinical significance of LA positivity.

Methodology

This cross-sectional descriptive study was carried out in the Hematology Department of the Chughtai Lab Head Office, Lahore, between September 2025 and January 2026, following approval from the Institutional Review Board (IRB). All samples submitted for LA screening based on clinicians' requests were included. A total of 138 cases, ranging in age from 8 to 90 years, were analyzed.

Inclusion Criteria

1. Patients of all genders aged 8–90 years who were referred for lupus anticoagulant (LA) testing at the Hematology Department of Chughtai Institute of Pathology, Lahore.
2. Patients whose samples underwent complete lupus anticoagulant testing using the DRVVT-based screening and confirmatory assay (LA1 and LA2).
3. Cases showing positive lupus anticoagulant results based on LA1/LA2 ratio ≥1.2, including weakly positive, moderately positive, and strongly positive results.
4. Patients with available clinical information or medical history allowing correlation of laboratory findings with clinical manifestations.

Exclusion Criteria

5. Samples with incomplete laboratory data, including cases where confirmatory LA2 testing was not performed after an abnormal screening test.
6. Hemolyzed, clotted, or insufficient plasma samples that could compromise the accuracy of coagulation testing.
7. Patients with missing or unavailable clinical records, preventing correlation between laboratory findings and clinical presentation.
8. Duplicate samples or repeat tests from the same patient during the study period, where only the first test result was considered for analysis.

Baseline APTT was performed for all samples. LA testing was conducted using an integrated two-step approach, comprising screening and confirmatory tests based on dilute Russell viper venom time (DRVVT). Samples were considered positive if prolonged clotting time was observed with screening reagents (LA1) and correction occurred with confirmatory reagents (LA2). The reference range for LA1 was 31–44 seconds. LA2 testing was performed in cases where LA1 values were ≥44 seconds. All analyses were performed on a Siemens Healthiness analyzer, and results were interpreted using the LA1/LA2 ratio.

Results

Positive LA results were categorized as strongly positive (LA1/LA2 ratio >2.0), moderately positive (1.5–2.0), or weakly positive (1.2–1.5). Borderline results were defined as ratios between 1.0 and 1.2. Clinical information was

obtained from patient histories corresponding to positive laboratory findings. The majority of patients (56%) were between 21 and 30 years of age, followed by 26% aged 31–40 years and 22% aged 41–50 years. (Table I).

Among the 138 LA-positive cases, 59% (82) were female and 41% (56) were male. Strongly positive LA ratios were observed in 26 cases, moderate positivity in 28 cases, and weak positivity in 82 cases. Borderline results were noted in only 2 cases. (Table II). Of the 26 strongly positive cases, majority (50%) were associated with venous thrombosis (Table III). Among the 28 moderately positive cases, 37% presented with venous thrombosis (Table IV). The majority of patients (59.4%) demonstrated weakly positive LA ratios. Within this group, 31% were asymptomatic, 28% had recurrent miscarriages, and 24% experienced venous thrombosis. (Table V)

Table I: Age-wise Distribution of Patients in the Study Population

Age Group (Years)	Number of Patients (n)
0–10	2
11–20	16
21–30	56
31–40	26
41–50	22
51–60	8
61–70	4
71–80	2
81–90	2
Total	138

Table II: Strength of Lupus Anticoagulant.

Strength of lupus anticoagulant	No of cases (%)
Strong positivity	26 (18.84)
Moderate positivity	28 (2028%)
Weak positivity	82 (61.65)
Broader positivity	2 (1.44)

Table III: Clinical presentation of strongly positive lupus cases

Clinical diagnosis	Percentage
Venous thrombosis	50%
Pulmonary embolism	26%
Joint pain	12%
Ischemic heart disease	12%

Table IV: Clinical presentation of moderately positive lupus cases.

Clinical diagnosis	Percentage
Venous thrombosis	37%
Recurrent miscarriages	25%
Stroke	13%
Asymptomatic	13%

Table V: Clinical presentation of weakly positive lupus cases.

Clinical diagnosis	Percentage
Asymptomatic	31%
Recurrent miscarriages	28%
Venous thrombosis	24%

In our study, the majority of patients who presented with a positive LA/LA2 ratio were female. Most cases with a strongly present LA 1/LA2 ratio were associated with venous thrombosis. In most of the positive 59% of showed a weakly present LA1/LA2 ratio. Out of which 31% asymptomatic with no significant clinical history. It is important to note that these patients were lost to follow-up and ruling out the transient and false LA positivity is integral in such cases

Discussion

This study evaluated the clinical spectrum associated with lupus anticoagulant positivity in 138 patients referred to a tertiary diagnostic center in Pakistan, with a female predominance of 59%. The primary objective was to correlate laboratory LA positivity, including weak and strong ratios, with clinical manifestations such as thrombosis, pregnancy loss, and cardiovascular events.

Venous thrombosis emerged as the most frequent clinical manifestation, consistent with international data identifying LA as a major risk factor for thromboembolic events. Singhal et al. reported a high prevalence of venous thromboembolism among LA-positive SLE patients in a nationwide US cohort, highlighting its contribution to morbidity and mortality.[16] Similarly, You et al. demonstrated that LA positivity independently predicts venous thromboembolism in SLE patients.[17]

Recurrent pregnancy loss was another prominent finding. The role of LA in obstetric complications is well established. Yap et al. reported strong associations between aPL antibodies and adverse pregnancy outcomes in patients with lupus nephritis [19], supporting our observations.

Ischemic heart disease, though less frequent, was also observed. Fischer et al. demonstrated increased cardiovascular risk in LA-positive SLE patients, emphasizing the need for cardiovascular surveillance in this population.[20]

Notably, 24% of weakly positive LA cases in our study were associated with SLE. Yucelnel et al. highlighted that

hematologic manifestations, including LA positivity, contribute to increased thrombotic risk in SLE patients.[14] Conversely, 31% of weakly positive cases were asymptomatic. Marco-Rico emphasized that weak or borderline LA positivity may represent transient antibodies or laboratory variability [18]. Alam et al. similarly reported asymptomatic LA positivity in a subset of Pakistani patients.[22] These findings underscore the importance of interpreting LA results within the clinical context.

Overall, the spectrum of clinical manifestations observed in this study reflects the heterogeneity of LA positivity. While venous thrombosis predominated, obstetric and arterial events were also observed, consistent with reports by Noordermeer et al. and Barcellona et al. [15,21]

Lupus anticoagulant (LA) is one of the most clinically significant antiphospholipid antibodies and is strongly associated with thrombotic events, pregnancy morbidity, and autoimmune disorders, particularly systemic lupus erythematosus. Despite its well-recognized clinical relevance, the interpretation of LA testing remains challenging in routine practice. Laboratory results are frequently reported as normalized LA ratios (LA1/LA2), which may reflect the strength of the inhibitor; however, the clinical implications of varying degrees of LA positivity are not always clearly defined. In particular, weakly positive or borderline results may represent transient antibodies, laboratory variability, or the influence of concurrent illnesses and medications, leading to uncertainty in clinical decision-making. Consequently, establishing a clear correlation between the magnitude of LA positivity and the spectrum of clinical manifestations is essential for improving diagnostic interpretation and risk stratification.

Furthermore, most available evidence regarding LA positivity and its clinical consequences originates from studies conducted in Western populations or in cohorts with established antiphospholipid syndrome or systemic lupus erythematosus. Data evaluating the clinical significance of different LA ratio levels in broader diagnostic populations remain limited, particularly in South Asian settings where regional clinical patterns may differ. In Pakistan, published studies correlating laboratory LA positivity with thrombotic, obstetric, and cardiovascular manifestations are scarce. Therefore, this study was undertaken to evaluate the clinical profile of patients with positive lupus anticoagulant tests and to analyze the association between varying LA1/LA2 ratio levels and their corresponding clinical presentations, with the aim of generating locally relevant evidence to support more accurate interpretation of LA testing and improved patient management.

Conclusion

1.This study demonstrates a wide spectrum of clinical manifestations associated with positive LA1/LA2 ratios in a cross-section of the Pakistani population.

2.Venous thrombosis was the most common clinical presentation.

3. A subset of individuals with weakly positive LA ratios remained asymptomatic, highlighting the necessity of excluding transient or false-positive LA results through clinical correlation and follow-up.

4.These findings reinforce the importance of individualized risk assessment and cautious interpretation of LA positivity in clinical practice.

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