

Original article

The Role of D-Dimer as a Diagnostic Biomarker of Thrombotic Events in Libyan Patients at EL-Beyda City

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Abstract

Stroke and thromboembolic events represent a global health issue of long-term disability and mortality. While neuroimaging is foundational for initial diagnosis, it has limitations in detecting subtle microvascular changes, making the integration of quantifiable blood-based biomarkers, such as D-dimer, critical for early diagnosis and prognostic evaluation. This study aims to evaluate the diagnostic utility of plasma D-dimer levels in patients with thrombosis by assessing its effectiveness as a clinical biomarker compared to healthy controls. This case-control study evaluated 120 participants aged ≥ 40 years, divided equally into 60 newly diagnosed thrombosis patients and 60 healthy controls at Al-Tarahum and Al-Thiqah Laboratories. Patients with chronic kidney disease, active malignancy, inflammatory disorders, or those on long-term anticoagulant therapy were excluded. Venous blood samples were collected in 3.2% sodium citrate, centrifuged, and stored at -80°C . Quantitative measurements of D-dimer were performed using the Fluorescence Immunoassay (FIA) technique via the ichroma™ system with a diagnostic cut-off value of $0.5\mu\text{g/mL}$. Statistical analysis was conducted using SPSS version 26.0, applying independent-samples t-tests and Pearson correlation analysis. The cohort was well-balanced, consisting of 52.5% females and 47.5% males, with the majority of participants (63.3%) falling within the 40 to 60 years age group. A statistically significant positive correlation was identified between age and plasma D-dimer levels ($r = 0.567$, $p = 0.001$). Furthermore, thrombosis patients demonstrated a substantial and clinically significant elevation in mean D-dimer concentrations ($1.500 \pm 0.32\mu\text{g/mL}$) compared to the healthy control group ($0.350 \pm 0.12\mu\text{g/mL}$, $p < 0.001$). Plasma D-dimer levels serve as a vital biomarker with high diagnostic and predictive value in thrombotic conditions, exhibiting a strong, statistically significant elevation in patients and a positive correlation with advancing age.

Introduction

Stroke stands as a massive global health challenge, representing a primary driver of long-term disability and mortality worldwide [1,2]. Approximately 80% of all cerebrovascular incidents are classified as acute ischemic stroke (AIS), which primarily stems from thromboembolic occlusions of cerebral arteries [3]. The physiological consequence is an immediate disruption of localised blood supply, triggering rapid ischemic cascades and irreversible neuronal damage if not managed promptly [4]. While neuroimaging modalities like non-contrast computed tomography (CT) and magnetic resonance imaging (MRI) remain foundational for baseline diagnosis, they exhibit limitations in predicting dynamic clinical subtle microvascular changes [1]. Consequently, the integration of quantifiable blood-based biomarkers has become critical to enhancing early diagnosis and predicting post-stroke complications [5]. During an acute ischemic event, the concurrent activation of the coagulation cascade and the fibrinolytic system leads to intravascular fibrin turnover [5]. As plasmin cleaves cross-linked fibrin to dissolve the obstructive thrombus, D-dimer—the smallest identifiable fibrin degradation product is released into the systemic circulation [6]. Therefore, circulating plasma D-dimer concentrations serve as an indirect marker of active thrombin generation and subsequent clot degradation [7]. Experimentally, clinical tracking demonstrates that D-dimer levels are significantly elevated in stroke patients within 6 to 24 hours of symptom onset compared to individuals presenting with stroke-mimicking conditions, confirming its diagnostic utility during initial emergency triage [3]. Beyond its diagnostic capacity, early plasma D-dimer serves as a powerful prognostic indicator. Elevated baseline levels within 24 hours of admission are strongly associated with early neurological deterioration (END), poor functional outcomes at 3 months, and increased short-term mortality rates [8,6]. Moreover, higher concentrations are heavily correlated with specific stroke etiologies, particularly cardioembolic subtypes and embolic strokes of undetermined source (ESUS), often highlighting occult paroxysmal atrial fibrillation or hidden systemic malignancies [7]. Recent prospective studies have also shown that elevated D-dimer levels in stroke-free populations can independently predict the long-term incidence of ischemic stroke, confirming its role as a marker for systemic hypercoagulability [2,9]. Furthermore, monitoring longitudinal D-dimer kinetics during the acute hospitalisation period provides critical clinical insights. While initial levels reflect baseline clot burden, continuous or secondary rises in D-dimer on the 7th day or at

discharge are indicative of hidden malignancy and the development of deep vein thrombosis (DVT) or pulmonary embolism [5]. Patients presenting with a history of malignancy experience a severe reciprocal interaction, where cancer increases stroke risk, and the ischemic event accelerates hypercoagulable states [10,11]. Therefore, a comprehensive synthesis of D-dimer configurations is essential to guide tailored anticoagulant strategies, prevent recurrent thromboembolic events, and lower the overall global stroke burden. D-dimer has increasingly been examined as a clinically relevant biomarker in stroke research because it reflects activation of coagulation and fibrinolysis. Earlier evidence suggested that elevated D-dimer may help distinguish stroke cases from stroke mimics during the early hours of presentation. In a meta-analysis of studies assessing D-dimer within 24 hours [1], found that patients with stroke had substantially higher D-dimer levels than stroke mimics or controls. Beyond diagnosis, D-dimer has also been studied as a long-term vascular risk marker [2]. Furthermore, epidemiological evidence from the Atherosclerosis Risk in Communities (ARIC) study demonstrated that elevated baseline plasma D-dimer concentrations are independently associated with an increased long-term risk of incident ischemic stroke [2]. Notably, this positive correlation was most pronounced in cardioembolic stroke subtypes, whereas the association with coronary heart disease was comparatively modest [2]. These observations highlight that D-dimer functions not only as an acute-phase diagnostic biomarker for ongoing thrombus formation, but also as a meaningful long-term predictor of subclinical cerebrovascular and thromboembolic risk in acute ischemic stroke, has also been supported by evidence synthesis [7]. Investigated patients with embolic stroke of undetermined source and found that higher baseline D-dimer levels were associated with a significantly increased risk of recurrent stroke; more recent evidence has extended the role of D-dimer from baseline assessment to serial measurement during hospitalisation. [5] showed that both initial and follow-up D-dimer levels were significantly associated with early neurological deterioration in patients with acute ischemic stroke. Notably, follow-up D-dimer levels were also linked to underlying cancer and venous thromboembolism, suggesting that repeated D-dimer testing may provide additional clinical value beyond admission measurement alone. Thus, the study aimed to evaluate the diagnostic utility of plasma D-dimer levels in patients with thrombosis by assessing its effectiveness as a clinical biomarker in early detection.

Materials and Methods

Study Design and Selection Criteria

This case-control study was conducted at AL-Tarahum and AL-Thiqah Medical Laboratories and included 120 Libyan participants at EL-Beyda city aged ≥ 40 years, divided into two equal groups (60 patients and 60 healthy controls) in the period between March and August 2026.

Inclusion Criteria

Individuals aged ≥ 40 years; patients with a newly confirmed clinical and radiological diagnosis of thrombosis at the initiation of anticoagulant therapy; and healthy volunteers with no history of thromboembolic diseases or vascular disorders.

Exclusion Criteria

Patients with chronic kidney disease, active malignancy, inflammatory disorders, or those currently on long-term anticoagulant therapy, as these conditions significantly alter baseline D-dimer levels.

Sample Collection

Venous blood samples were collected under aseptic conditions into vacuum tubes containing 3.2% sodium citrate (9:1 blood-to-additive ratio). Samples were immediately centrifuged at 3000 rpm for 15 minutes to obtain clear plasma, then aliquoted and stored at -80°C until analysis.

Laboratory Investigation

Quantitative measurement of D-dimer was performed using the Fluorescence Immunoassay (FIA) technique via the ichroma™ automated system (Boditech Med Inc., South Korea). All procedures were conducted according to the manufacturer's instructions. The diagnostic cut-off value was set at $0.5 \mu\text{g/mL}$.

Statistical Analysis

Data were analysed using SPSS (version 26.0). Continuous variables were expressed as Mean $\pm$ SD, and categorical variables as frequencies. An independent-samples t-test was used to compare means between groups. Diagnostic performance was evaluated through sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Statistical significance was defined as $P < 0.05$.

Results

The study analysed data from 120 participants to evaluate the diagnostic utility of D-dimer in thrombotic conditions.

Table 1. Frequency distribution of gender, age, and D-dimer status (N=120)

Variable	Category	Frequency	Percentage (%)
Gender	Female	63	52.5
	Male	57	47.5
Age	40-60 years	76	63.3
	61-80 years	32	26.7
	81+ years	12	10.0
D-dimer	Healthy	60	50.0
	Thrombosis Patient	60	50.0

The demographic distribution indicates that the study cohort was well-balanced, with a 50/50 split between thrombosis patients and healthy controls. The concentration of participants within the 40–60 years bracket (63.3%) is consistent with the epidemiological profile of populations prone to thrombotic events. This segmentation ensures that the comparative analysis between diseased and healthy states is robust and representative.

Table 2. Pearson Correlation between Age and D-dimer levels (N=120)

Variable	Pearson Correlation (r)	Sig. (2-tailed)
Age & D-dimer	0.567	0.001

The correlation analysis reveals a statistically significant positive relationship between age and plasma D-dimer concentrations ($r = 0.567$, $p = 0.001$). The p-value of 0.001, being below the alpha threshold of 0.05, confirms that the observed correlation is statistically significant rather than a result of random variation.

Table 3. Comparison of Plasma D-dimer Levels in Thrombosis Patients vs. Healthy Controls

Variable	Thrombosis Patient Group (N=60)	Healthy Control Group (N=60)	P-value
D-dimer level (µg/mL)	1.500 ± 0.32	0.350 ± 0.12	$< 0.001^*$

The table above presents a statistical comparison of plasma D-dimer levels between the thrombosis patient group and the healthy control group. The Independent-Samples T-test demonstrated a statistically significant elevation in the mean plasma of the D-dimer concentration among thrombosis patients (1.500 ± 0.32 µg/mL) as it compared to the healthy control group (0.350 ± 0.12 µg/mL), moreover, the P-value was ($P < 0.001$) confirming the high diagnostic sensitivity of D-dimer in identifying acute thrombosis events.

Discussion

This study investigated the diagnostic efficacy of plasma D-dimer levels in a cohort of 120 individuals using advanced Fluorescence Immunoassay (FIA) technology via the ichroma™ system. Our findings demonstrate a clear clinical distinction between healthy controls and patients with thrombosis, characterised by a statistically significant elevation in D-dimer concentrations within the patient group. This observation is consistent with the previous literature, which demonstrates that D-dimer serves as a rapid and reliable biomarker for active thrombin generation and fibrinolysis [4]. These data provide empirical support for integrating D-dimer measurement as a fundamental component of emergency diagnostic triage for thromboembolic conditions [6]. The most significant finding in this study showed a positive correlation between age and plasma D-dimer levels ($r=0.567$, $p=0.001$). This correlation represents major clinical importance, as the homeostatic balance between coagulation and fibrinolysis gradually shifts toward a state of mild pro-coagulant activity with advancing age [12,13]. Age-related vascular alterations often lead to the formation of microscopic fibrin deposits; in response, the body maintains vascular patency by upregulating the fibrinolytic system, which consequently increases fibrin degradation products, specifically D-dimer [12]. Furthermore, the chronic low-grade systemic inflammation frequently observed in the elderly may stimulate endothelial cells to release pro-coagulant factors [13], thereby elevating basal D-dimer levels in older individuals compared to younger individuals. Comparing our results with the meta-analysis conducted by [1], the diagnostic utility of D-dimer remains consistent across diverse clinical settings. While neuroimaging remains the gold standard for stroke diagnosis, our data confirms that D-dimer acts as predictor tool for early diagnosis, particularly in resource-limited environments where access to computed tomography (CT) or magnetic resonance imaging (MRI) may be delayed. Furthermore, our outcomes are in agreement with a study conducted by [5], who emphasised that initial D-dimer measurement is essential not only for preliminary diagnosis but also for stratifying patients at risk of early neurological

deterioration (END) and poor functional outcomes [14,15]. The significance of our research extends to the management of "Embolus Stroke of Undetermined Source" (ESUS). By identifying elevated D-dimer levels in our patient cohort, we provide evidence supporting targeted anticoagulation strategies, which are vital for reducing the risk of stroke recurrence [16]. The statistical power achieved in our case-control model underscores the reliability of the FIA technique. Nevertheless, D-dimer levels should always be interpreted within the context of a patient's age and overall clinical history.

Conclusion

Plasma D-dimer levels serve as a vital biomarker with high diagnostic and predictive value in thrombotic conditions and demonstrate a significant correlation between elevated D-dimer concentrations and advancing age.

Recommendation

We recommend the integration of D-dimer testing as a routine screening tool in emergency departments to facilitate rapid clinical decision-making. Ultimately contributing to the reduction of mortality and minimising the adverse outcomes associated with delayed diagnosis in thromboembolic cases.

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Conflicts of Interest

There are no financial, personal or professional conflicts of interest to declare.

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