AL-ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

Al-Zahraa Journal for Health and Medical Sciences 2026; 4:129-145 **Vol. 4, No.1, 2026**
www.zjhms.alzahraa.edu.iq

The biochemical structure, physiology and clinical significance of fibrinogen: a review

Haneen Abdulsalam Ali[1], Sadeq Mohammad Jaafar Almosawi [2], Amjed Salim Naser[3], Ali A. Al-fahham[4*]

[1] College of Medicine , Ibn Sina University of Medical and Pharmaceutical Sciences, Iraq.
[2] Department of Medical physiology, Faculty of Medicine , University of Kufa, Iraq.
[3] Department of Pharmacology and Toxicology, College of Pharmacy, University of Misan, Iraq.
[4] Corresponding Author, Faculty of nursing, University of Kufa, Iraq.
***** **aliaz.mahdi@uokufa.edu.iq**

Received: 27 February (2026), Accepted: 23 March 2026. Published: 31 March 2026

ABSTRACT

Fibrinogen is a plasma glycoprotein with a high-molecular weight, it plays a critical role in hemostasis and as a precursor to fibrin, which is the main clotting factor. Fibrinogen exerts several functions, not only blood coagulation, but also in tissue repair, vascular integrity, immune regulation, and inflammation. When exposed to thrombin, fibrinogen is converted into fibrin, which make a three-dimensional mesh to stabilize the platelet plug and stop bleeding. Fibrinogen also functions as a positive acute-phase reactant, so that it is highly released during inflammation, infection, and tissue injury. There is increasing evidence that fibrinogen plays a role in the pathophysiology of several clinical conditions such as malignancies, metabolic disorders, chronic inflammatory states, cardiovascular disease, thrombotic diseases, and congenital and acquired bleeding disorders are also characterized by perturbations in the fibrinogen system. At the clinical level, fibrinogen levels have been commonly estimated in order to diagnose and monitor coagulation disorders, perioperative bleeding, trauma, and critical illness, whereas increased fibrinogen has become an independent marker of cardiovascular and inflammatory risk. The D-dimer/fibrinogen ratio is a critical biomarker that reflects the equilibrium between blood coagulation and fibrinolysis, which aid in the assessment of thrombotic risk and disease severity. This review is designed to summarize the current knowledge about the biochemistry, physiology, and clinical relevance of fibrinogen, with a focus on recent discoveries and novel concepts about fibrinogen as a biomarker and the mechanism of action in health and disease.

Keywords: : Acute Phase Proteins, Fibrinogen, Blood Coagulation, Hepatocytes.

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

Introduction

Fibrinogen is a glycoprotein in blood plasma with a very large molecular mass which is the main component of the fibrin and a key player in hemostasis signaling [1]. Fibrinogen is synthesized primarily in the liver and is an important clotting factor, but it also plays an important role in mediating inflammation, wound healing, and cell–cell interactions [2]. Fibrinogen has attracted considerable interest in the biomedical sciences due to its multifaceted physiological roles, especially for cardiovascular disease, thrombotic disorders, and inflammatory disease. Fibrinogen is a symmetrical dimer consisting of three polypeptide chains (Aα, Bβ, and γ) homodimers connected by disulfide bonds, building a 340 kDa molecule [1,2]. Its elaborate domain structure allows for selective binding to thrombin, platelets, and cell surface integrin receptors that play an essential role in clotting and stability. Thrombin acts on fibrinogen, cleaving fibrinopeptides A and B to produce soluble fibrin monomers which polymerize into a three-dimensional network to stabilize the platelet plug upon vascular injury [1]. Novel imaging and structural biology studies have deepened our perspective on not only the full molecular conformation of fibrinogen but also the elastic properties of fibrin under both health and disease [3].Fibrinogen, besides having a unique biochemical structure, is widely engaged in the homeostasis of vascular integrity and inflammation. As an important determinant of both the thrombotic tendency of blood as well as the course of inflammatory disorders, elevated fibrinogen is associated with increased risk of cardiovascular disease including coronary artery disease and stroke [4,5] at levels well below the clinical cut-off range found in our study system. In multiple prospective cohort studies, higher levels of fibrinogen have been shown to be independently associated with increased risk of myocardial infarction and ischemic stroke, even after controlling for conventional risk factors including hypertension and hyperlipidemia. As a result, fibrinogen level is increasingly assessed as a biomarker and target for treatment of cardiovascular risk [4]. Apart from its cardiovascular implications, fibrinogen has been associated with various pathological conditions other than thrombosis. Fibrinogen (FIB), an acute-phase protein, is found elevated in inflammatory conditions like rheumatoid arthritis, systemic lupus erythematosus and chronic obstructive pulmonary disease [5]. As pertinent to immunobiology, fibrinogen binds to many immune cell receptors, particularly toll-like receptors and integrins, impacting leukocyte adhesion, migration, and cytokine production. Such

IRAQI Academic Scientific Journals

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

interactions emphasise fibrinogen as both a coagulation factor and an immune-modulatory protein, bridging the realm of hemostasis and inflammation, simultaneously [6]. In the registry of recent advances, the genetic and molecular control of fibrinogen production has been elucidated. The Aα, Bβ and γ chain genes (FGA, FGB and FGG) are located very close together on chromosome 4, and cytokines like interleukin-6 also affect the transcription of these genes during acute phase responses [6]. Common polymorphisms in these genes have been associated with plasma fibrinogen levels and different susceptibility to thrombotic and cardio-vascular diseases, supporting an important genetic contribution to fibrinogen-related profiles of risk [7]. They also defined the biochemical properties of fibrinogen which, in addition to post-translational modifications of glycosylation and oxidation, influence the functional properties of fibrinogen and subsequently influence the structure, stability and susceptibility to fibrinolysis of fibrin clots [2]. Fibrinogen also has clear clinical significance that goes on to affect therapeutic monitoring and management. Fibrinogen is being used more frequently as a target for hemostatic therapy [8] in surgical and trauma settings, fibrinogen has emerged as a key risk factor for bleeding and is routinely measured. Fibrinogen deficiency acquired from major bleeding, obstetric hemorrhage and cardiac surgery is often treated with fibrinogen concentrates and cryoprecipitate. Timing and dosing of these interventions remains an active area of clinical investigation, and results from recent randomized controlled trials have assessed their effect on bleeding and transfusion outcomes. While our knowledge of the functions of fibrinogen has improved enormously during the last century, major knowledge gaps still exist. Specifically, the definitive pathways through which fibrinogen mediates chronic inflammatory processes and the long-term consequences of genetic variants on disease progression remain undefined. Furthermore, although fibrinogen is well-established cardiovascular risk marker, less is known about modulating fibrinogen in clinical practice, and large-scale clinical evidence is needed to reveal its therapeutic potential [9]. This aims to summarize the current knowledge about the biochemistry, physiology, and clinical relevance of fibrinogen, with a focus on recent discoveries and novel concepts about fibrinogen as a biomarker and the mechanism of action in health and disease.

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

Biochemistry and Biosynthesis of Fibrinogen

Fibrinogen is a bio complex glycoprotein in plasma, which plays a central role in hemostasis, and acts as a precursor to fibrin and is a mediator for cellular interactions during clot formation [1]. Fibrinogen is a hexameric molecule formed by three pairs of non-identical polypeptide chains— Aα, Bβ, and γ—symmetrically covalently linked through disulfide bonds. Such a configuration is necessary for its role as a soluble thrombin substrate and as a cross-linking factor during clot formation [2]. The individual polypeptide chains provide specific domains that modulate fibrin polymerization, binding to cellular receptors, and susceptibility to enzymatic degradation.

Molecular Structure of Fibrinogen

Fibrinogen contains three chains (FGG, FGB and FGA), all of which are translated by distinct genes, which are tightly co-regulated on chromosome 4 in humans [10]. Under ultrastructural examination, the middle region of the molecule called the E-domain contains the N-terminus of all six chains and is where fibrinopeptides are cleaved by thrombin. In addition to this domain, the C-terminal halves of the Bβ and γ chains form two terminal D-domains which flank this domain and create polymerization interfaces during the formation of fibrin [1,2]. Glycosylation and other post-translational modifications are prevalent on the Aα and Bβ chains and are believed to regulate the circulatory half-life of fibrinogen and its interaction with cell surface receptors [6]. Fibrinogen three-dimensional structures, as shown by X-ray crystallography and electron microscopy, are flexible rod-shaped molecules approximately 45 nm in length [2]. Coiled-coil regions linking the central E-domain and the distal D-domains may allow necessary conformational changes for function. In particular, the γ chain has a polymerisation site which interacts with complementary sites, revealed by thrombin cleavage, to nucleate protofibrils [3]. Together, these structural characteristics highlight the need for fibrinogen to be both stable in circulation and able to undergo dynamic structural rearrangements during clot formation.

Biosynthesis and Regulation

The synthesis of fibrinogen occurs in hepatocytes. The three polypeptide chains of fibrinogen are translated in the rough endoplasmic reticulum and then undergo folding and assembly of the $(Aα, Bβ, γ)_2$ hexamer. Chaperone proteins and enzymatic catalysts in the endoplasmic reticulum (ER) cooperate to form disulfide bonds between the same chain (intrachain) and other chains

IRAQI Academic Scientific Journals

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 **Vol. 4, No.1, 2026**
www.zjhms.alzahraa.edu.iq

(interchain) (Figure 1). Misfolded chains are degraded to prevent secretion of nonfunctional molecules of fibrinogen [6].

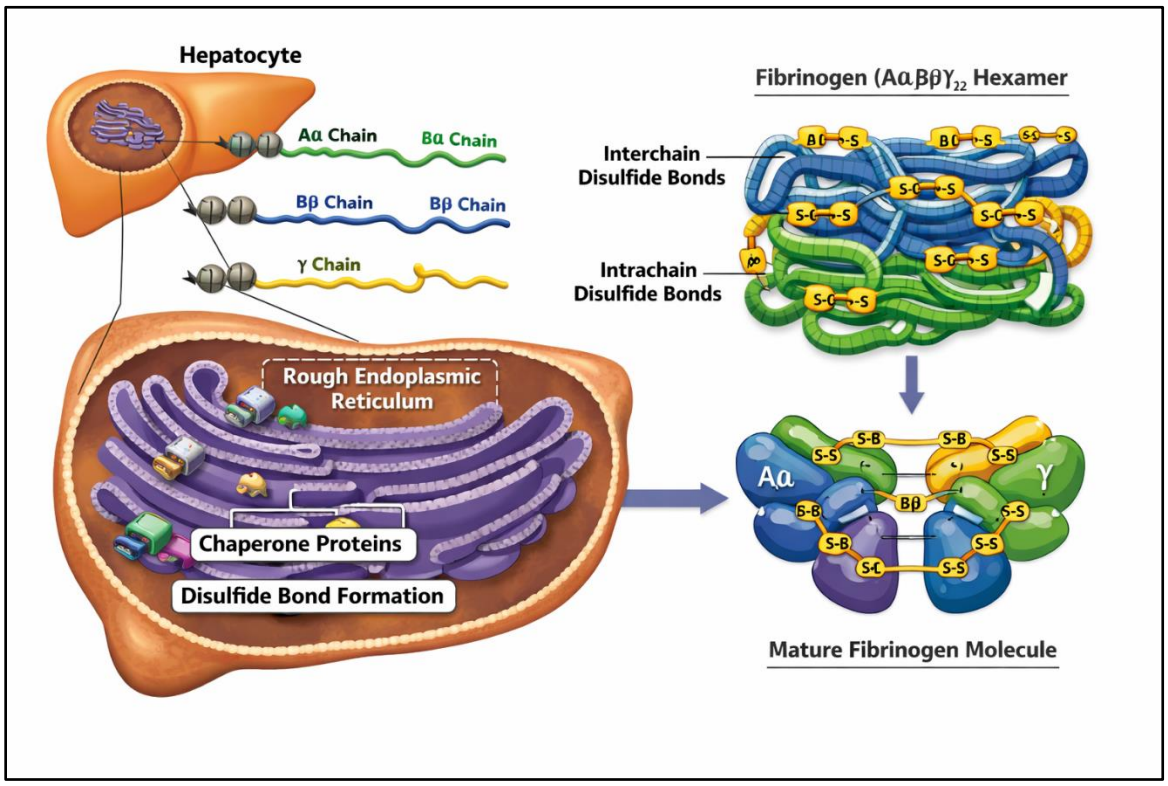

Figure 1. The biosynthesis of fibrinogen (adapted from [11])

Gene expression of fibrinogen is essentially controlled by transcription — and most specifically by inflammatory signals. Interleukin-6 (IL-6) is a strong stimulator for fibrinogen production, it triggers transcription of FGG, FGB and FGA by activation of C/EBP and STAT3 transcription factors in hepatocytes upon acute-phase response [6,12]. This mechanism connects the production of fibrinogen with systemic inflammation and accounts for the rapid increase in plasma fibrinogen during infection and trauma, as well as the increase in chronic inflammatory diseases. Genetic polymorphisms in the promoter regions of the fibrinogen genes have been linked to differences in baseline fibrinogen levels which greatly increase the risk of thrombotic disease among individuals [7]. On the other hand, fibrinogen is characterized by important post-translational modifications. A multitude of posttranslational modification occurs within and around the thrombin cleavage sites of the fibrinogen molecule [2]. N-linked glycosylation of the β and γ chains affects fibrinogen solubility and stability in the circulation, while O-linked

IRAQI Academic Scientific Journals

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

glycosylation of the Aα chain influences interactions with leukocytes and platelets. Furthermore, during oxidative stress (i.e. in atherosclerosis) fibrinogen becomes nitrated and oxidized, which can be accountable for changes in clot structure and function. Such alterations can increase resistance to fibrinolysis and thus may augment the prothrombotic setting in cardiovascular disease [13].

Functional Activation and Polymerization

The coagulation cascade finally leads to the formation of thrombin, which cleaves fibrinogen at two peptide bonds within the Aα and Bβ chains on vascular injury. Removal of fibrinopeptide A reveals polymerization sites that allow fibrin monomers to spontaneously bundle into half-staggered protofibrils, which finally aggregate laterally to yield a three-dimensional fibrin network [1]. D-domains play an especially critical role by complementary "knob-hole" interactions which stabilize protofibril formation, while thrombin-activated factor XIIIa catalyzes covalent cross-linking of γ chains, which increases clot stability and resistance to mechanical disruption [14]. These cascade chemical steps are summarized in this equation [2]:

$$\text{Fibrinogen} \xrightarrow{\text{Thrombin}} \text{Fibrin monomers} \rightarrow \text{Protofibrils} \rightarrow \text{Fibrin network} \xrightarrow{\text{Factor XIIIa}} \text{Stable clot}$$

Fibrin polymerization can also affect a number of biochemical events such as cell migration, angiogenesis, and wound healing. Fibrin mesh supports endothelial proliferation, and provide a provisional matrix for tissue repair. Fibrinogen and fibrin bind to integrin receptors expressed on platelets and immune cells, causing cellular adhesion and activating signaling pathways that regulate inflammation and tissue repair [1].

Plasma Levels and Clinical Correlates

Physiological plasma fibrinogen concentrations are 2–4 g/L but these levels can vary according to age, sex, smoking and systemic inflammation. High fibrinogen is a recognized cardiovascular risk factor, associated with increased myocardial infarction and stroke incidence independent of classical risk factors [4]. The association between fibrinogen and thrombosis is multifactorial: elevated fibrinogen contributes to increased blood viscosity, increased platelet aggregation, and the production of more compact and firmer fibrin clots resistant to fibrinolysis [11]. The importance of fibrinogen in hemostasis is illustrated by the rare congenital disorders, hypofibrinogenemia and afibrinogenemia. Patients with these disorders bleed spontaneously and

IRAQI Academic Scientific Journals

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

have poor wound healing because stable fibrin clots cannot form. In contrast, dysfibrinogenemia (where the amount of fibrinogen is normal but the structure or function is abnormal) can present with either bleeding or thrombotic tendencies, depending on the type of structural defect involved [6].

Connection between Biochemistry and Clinical Function

The biochemical complexity of fibrinogen is strongly correlated to its physiology and clinical importance. In addition to clot formation, fibrinogen modulates inflammation and binds cellular receptors on platelets, leukocytes, and endothelial cells, linking hemostatic and immune systems. Fibrinogen functions both as a structural protein and as a modulator of biological processes, which highlights its multifunctional nature [2].

Physiology of Fibrinogen

Fibrinogen is a multifunctional physiological protein that connects hemostasis, inflammation, tissue repair and vascular homeostasis. It circulates in plasma at unusually high concentrations, and act as a substrate within the coagulation cascade and an acute-phase reactant whose level increases and decreases with systemic physiological and pathological stimuli [15].

Role in Hemostasis and Coagulation

Fibrinogen is mainly associated with hemostasis [16]. Thrombin converts fibrinogen into insoluble fibrin upon vascular injury and provides the structural backbone of the hemostatic clot [2]. This conversion is the last step of the coagulation cascade and is critical to reducing blood loss after an injury. Furthermore, as a ligand for platelet integrin receptors glycoprotein IIb/IIIa, fibrinogen is an important mediator of platelet aggregation and stabilization of the platelet plug during primary hemostasis at sites of injury [6]. Physiologically, fibrinogen level is one of the determinants of clot structure and clot firmness. Increased concentrations of fibrinogen produce denser fibrin structures with reduced pore dimensions and hence clots that are less susceptible to fibrinolysis. On the other hand, decreased fibrinogen levels undermine clot traffic, and bleeding predisposing state. This implies that under “normal” physiological conditions the concentrations of fibrinogen must be kept at optimal levels so as to appropriately balance coagulation and fibrinolysis [17].

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

Regulation During the Acute-Phase Response

Fibrinogen is a positive acute-phase protein whose plasma concentration is raised in inflammation, infection, trauma and tissue injury. It is mainly mediated by pro-inflammatory cytokines, especially interleukin-6 (IL-6), which induces hepatic production of fibrinogen during the acute-phase reaction. However, from pathophysiological aspects, elevated fibrinogen during inflammation promotes clot formation at areas of tissue injury to prevent pathogen spreading and support tissue healing [18]. Nevertheless, abnormal high fibrinogen is a noxious factor in duration. Persistent high fibrinogen concentrations are observed in chronic inflammatory states like obesity, diabetes mellitus, and autoimmune disorders, thereby creating a prothrombotic state. This underlines the fact that fibrinogen has a dual role in physiology: a protective factor soon after acute injury, but a potential pathogenic factor in case of chronic high levels [4].

The main above-mentioned aspects of fibrinogen have been known to affect blood viscosity and erythrocyte aggregation, thus affecting microcirculatory flow. Consequently, physiological levels of fibrinogen induce reversible red blood cell aggregation, which modulates shear stress and oxygen delivery in the microcirculation. Fibrinogen is a plasma protein that is increased in the acute phase and raises plasma viscosity and erythrocyte aggregation and this can hinder tissue perfusion [5]. Fibrinogen has interactions with endothelial cells and plays a role in vascular integrity. It gets involved in processes such as endothelial cell adhesion and migration that are important for the maintenance of the endothelial barrier and the repair of injured blood vessels and, therefore, emphasize the role of fibrinogen in the maintenance of vascular homeostasis apart from coagulation [19].

Function in Inflammatory and Immune Events

Fibrinogen, critically acting as a link between coagulation and inflammation, It also interacts with particular receptors on immune cells such as integrins and toll-like receptors, modulating leukocyte activation, migration, and cytokine production. Biologically, this interaction has a role in the recruitment of immune cells to sites of tissue damage or infection, thereby aiding the host response [20]. Fibrin matrices, derived from initially circulating fibrinogen, provide provisional scaffolds during inflammation at the injury site by trapping pathogens and inflammatory cells, and therefore localizing immune responses. This is helpful in acute settings but film-based fibrin deposits may aggravate inflammation and cause tissue injury in chronic inflammatory and

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

fibrotic disease settings. Consequently, fibrinogen has an immunoregulatory function in immune physiology which is highly sensitive in both directions, with pathogenic consequences if not properly regulated [22].

Role in Wound Healing and Tissue Regeneration

Fibrinogen molecules also play an important role in normal wound healing, as are vital components of fibrinogen and its conversion to fibrin. Fibrin matrices at injured tissues act as provisional extracellular matrices perennial assisting cell adhesion, migration and proliferation. Fibrin scaffolds are used by fibroblasts, endothelial and epithelial cells to rebuild tissue architecture, and to ensure angiogenesis [2]. At the physiological level, fibrinogen degradation products produced during fibrinolysis contribute to the regulation of tissue remodeling and regeneration by modulating signaling pathways in cells responsible for these processes. Consequently, fibrin formation is coupled to a tightly regulated process of fibrinolysis, which is at least as important as the initial mending process to eventually replace provisional matrices by mature tissue structures [23].

Physiological Variability and Homeostasis

Plasma fibrinogen concentration differs by age, sex, hormonal status and lifestyle factor such as smoking and physical activity. Some of these changes include gradual increases in concentration of fibrinogen with aging, which may help to explain in part the increase in thrombotic risk with age. Estrogen status also affects fibrinogen levels, and fibrinogen is a major contributor to sex differences in physiology of coagulation [4]. In the state of homeostasis, the level of fibrinogen is a steady state due to the dynamic balance between hepatic synthesis, intravascular consumption and fibrinolytic degradation. Any disturbance of this equilibrium, whether it be genetic, inflammatory or metabolic pathologies, may tip the physiological processes to bleeding or thrombosis [23].

Physiological Relevance in Health and Disease

Fibrinogen is a platform molecular that plays diverse physiological effects crossing different biological systems and life process, from the homeostasis, immunity, vascular biology, and wound healing response. Acute-phase increase of C-reactive protein and its effect is protective, while chronic regulation leads to a significant role in the pathophysiology of cardiovascular disease, chronic inflammation and thrombotic diseases [11]. Fibrinogen thus provides a

IRAQI
Academic Scientific Journals

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

physiological measure of commonality in systemic health as well as an accessible functional protein. Fibrinogen is an acute phase reactant, whose concentration evolves in parallel with inflammatory parameters and lymphocyte subtypes, when induced, though the physiological roles of fibrinogen help explain its integration into clinical medicine and the consequences exerted in exerted human health from altered fibrinogen concentration, function or both [23]. The presence of hyperfibrinogenemia is common in metabolic disorders like obesity, type 2 diabetes mellitus and the metabolic syndrome. In these disorders, high fibrinogen indicates the presence of low-grade chronic inflammation, promoting the high thrombotic risk specific to these patients. Measurement of fibrinogen could play a role in clinical use for cardiovascular risk stratification in subjects with metabolic disease [4].

Clinical Significance of Fibrinogen

Fibrinogen is clinically important as it plays a pivotal role in coagulation, inflammation, and vascular biology. Changes in fibrinogen level or activity are related to different clinical diseases, from bleeding state to thrombotic and cardiovascular disorders. As a coagulation factor and a component of the acute-phase reaction, fibrinogen has clinical significance not only in hemostasis but also in states of systemic inflammation/metabolism [1].

Fibrinogen in Bleeding Disorders

The essential role of fibrinogen in normal hemostasis is underscored by congenital and acquired deficiencies of fibrinogen. Mutations in the fibrinogen chain genes (FGG, FGB, and FGA) can lead to congenital fibrinogen disorders including afibrinogenemia, hypofibrinogenemia, and dysfibrinogenemia. Afibrinogenemia is a condition in which fibrinogen is entirely lacking, the resultant clinical manifestations are severe bleeding manifestations from birth, including umbilical stump bleeding, mucosal hemorrhage, and spontaneous intracranial. Hypofibrinogenemia which is characterized by the reduced fibrinogen plasma levels, can generally lead to mild bleeding symptoms while dysfibrinogenemia presents with structurally abnormal fibrinogen which can lead to bleeding, thrombosis, or both bleeding [6]. Acquired fibrinogen deficiency is a frequently encountered clinical diagnosis such as in massive hemorrhage, liver disease, disseminated intravascular coagulation (DIC), and trauma. Under these scenarios, fibrinogen is typically one of the first coagulation factors to drop to critically low concentrations and therefore is a particular sensitive indicator of coagulopathy. As a result,

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

measuring fibrinogen is routinely performed to direct transfusion therapy for surgical and trauma victims [8].

Fibrinogen Replacement Therapy

In practice, fibrinogen deficiency is often treated with replacement therapy with either cryoprecipitate or fibrinogen concentrate. Fibrinogen concentrate has become increasingly desirable because of established dosing, viral inactivation, and the ability to rapidly administer. International studies have undertaken clinical trials showing that fibrinogen supplementation improves clot firmness and reduces bleeding in major surgery, obstetric hemorrhage and trauma cohort patients [8].

Cardiovascular Risk Factor

Plasma fibrinogen is a major independent risk factor for cardiovascular disease. High fibrinogen levels have been associated with increased risk of myocardial infarction, ischemic stroke, and peripheral arterial disease in large studies and meta-analyses [4]. Clinically, hyperfibrinogenemia favors thrombosis by several mechanisms, including platelet activation, increased blood viscosity, and the production of fibrin clots with high density and low susceptibility to fibrinolysis. Fibrinogen involvement and role in atherogenesis It builds into atheromatous plaques and facilitates inflammatory cell attraction, smooth muscle cell proliferation, and endothelial dysfunction. The advancement and instability of plaque promoted by these processes further increase the risk of thromboembolic events. Thus, fibrinogen has found a new role as a cardiovascular biomarker and mediator of pathology [5].

Inflammation, Infection, and Systemic Disease

Fibrinogen plasma levels increase during the acute phase in response to inflammatory cytokines such as interleukin-6, making it a positive acute-phase protein. High plasma fibrinogen levels are frequently seen in other chronic inflammatory diseases like rheumatoid arthritis, COPD, and inflammatory bowel diseases that involve continuous activation of the immune system [6].

A feature of infectious disease is that the hallmark increase in plasma fibrinogen can serve to localize pathogens within abundant fibrin matrices, limit spread, and support the recruitment of effector immune cells related to host defense. Nonetheless, abundant fibrin accumulation can worsen tissue damage and microvascular thrombin, as evident in some severe infections and sepsis. Clinically, increased fibrinogen in these situations frequently ties with severity of disease

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

and prognosis [24]. Fibrinogen has been reported as a prognostic biomarker in some malignancies in oncology. Pre-treatment fibrinogen led to overall survival in lung, colorectal and gastric cancer. Mechanistically, fibrinogen drives tumor progression through the promotion of angiogenesis, adherence of tumor cells and the protection of circulating tumor cells from immune clearance. The clinical importance of such findings furthers fibrinogen behaviour beyond coagulation [25].

A Diagnostic and Prognostic Marker

Clinically, fibrinogen values are readily available and frequently measured in diagnostic laboratories. Traditionally, it is measured by functional assays like the Clauss method, which reflects the capacity of fibrinogen to be converted into fibrin by thrombin [26]. In the clinic fibrosis is used to diagnose coagulation disorders, monitor inflammatory activity and promote thrombotic risk, levels can cause deficiency or excess thrombosis, presenting as death or bleeding respectively (Table 1).

Table 1. Clinical measurement and significance of fibrinogen levels (summarized from [26]).

Aspect	Description
Routine measurement	Fibrinogen is routinely measured in diagnostic laboratories as part of coagulation testing
Clinical applications	coagulation disorders, monitoring of inflammatory activity, and assessment of thrombotic risk
Low fibrinogen levels	bleeding tendencies and fibrinogen deficiency states
High fibrinogen levels	hypercoagulability and increased risk of thrombosis

More recently, fibrinogen has attracted interest in terms of "multimarker" approaches for disease prediction and prognosis. Although its independent association with cardiovascular disease, sepsis, and trauma is well established, the ability to integrate Carotid Intima–Media Thickness (cIMT) with other models and inflammatory and coagulation markers serves to augment risk stratification [27].

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

Clinical Implications and Future Perspectives

Fibrinogen is an abundant mediatory with a functional role at the crossroads of coagulation, inflammation and vascular biology with an intrinsic clinical significance. Fibrinogen deficiency and excess predispose to life-threatening bleeding disorders and thrombotic and inflammatory complications, respectively; thus fibrinogen levels have major clinical impact. Current and future studies are developing therapies targeting fibrinogen, improving replacement strategies, and investigating the role of fibrinogen as a therapeutic target in cardiovascular and inflammatory diseases. Such information makes it obvious that a full understanding of the clinical importance of fibrinogen is required for clinicians practicing in many different fields: hematology, cardiology, critical care, and surgery [28].

Conclusion

Fibrinogen is an essential plasma glycoprotein that performs multiple biological processes. Basically, it serves as a central substrate in fibrin clot formation, which is critical for effective hemostasis and vascular integrity. The bioconversion of fibrinogen with thrombin, platelets, endothelial cells and immune components place it as a link between coagulation, inflammation, and tissue repair. Therefore, it plays a key role in regulating cellular responses engaged during vascular injury and wound healing. Additionally, Fibrinogen is an important acute-phase protein which modulates both inflammatory status and systemic stress. In acute injury or infection, transient elevations in fibrinogen provide primary protection, while chronic dysregulation of fibrinogen is associated with unfavorable clinical outcomes. Clinically, fibrinogen is involved both quantitatively and qualitatively in hundreds of clinical disorders, including congenital and acquired bleeding states, thrombotic events, cardiovascular disease, chronic inflammatory states, metabolic disorders, and malignancies. Recent advances using molecular biology, structural analysis and hemostatic testing approaches have provided considerable insight into the biosynthesis of fibrinogen, genetic regulation of circulating fibrinogen concentration. Together these updates improved the diagnostic accuracy for fibrinogen related disorders and enabled the increasing application of fibrinogen measurement and replacement therapy in peri-operative, trauma and critical care settings. In addition, more evidence indicates that fibrinogen has predictive value for cardiovascular and inflammatory diseases, and all together, these reinforce its clinical relevance for the risk stratification. While these advances demonstrate that fibrinogen

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

likely plays many important roles in disease progression and/or therapeutic response, important gaps remain in fully understanding its complex mechanisms.

Acknowledgement

The authors would like to express their heartfelt gratitude to the staff of Central Library – University of Kufa, for their unwavering support and assistance. Their patience and willingness to enlighten helped make this research completion possible. We are extremely grateful for their time and collaboration during the study.

Reference

1. Mosesson, M.W. (2005) 'Fibrinogen and fibrin structure and functions', *Journal of Thrombosis and Haemostasis*, 3(8), pp. 1894–1904. https://doi.org/10.1111/j.1538-7836.2005.01365.x
2. Weisel, J.W. and Litvinov, R.I. (2017) 'Fibrin formation, structure and properties', *Sub-Cellular Biochemistry*, 82, pp. 405–456. https://doi.org/10.1007/978-94-024-1257-0_13
3. Litvinov, R.I. and Weisel, J.W. (2016) 'What is the best description of fibrin network structure?', *Blood Reviews*, 30(6), pp. 191–199. https://doi.org/10.1016/j.blre.2016.06.003
4. Danesh, J., Lewington, S., Thompson, S. G., Lowe, G. D., Collins, R., Kostis, J. B., Wilson, A. C., Folsom, A. R., Wu, K., Benderly, M., Goldbourt, U., Willeit, J., Kiechl, S., Yarnell, J. W., Sweetnam, P. M., Elwood, P. C., Cushman, M., Psaty, B. M., Tracy, R. P., … Wood, A. (2005) 'Plasma fibrinogen level and the risk of major cardiovascular diseases and non-vascular mortality: an individual participant meta-analysis', *JAMA*, 294(14), pp. 1799–1809. https://doi.org/10.1001/jama.294.14.1799
5. Ernst, E. and Resch, K.L. (1993) 'Fibrinogen as a cardiovascular risk factor: a meta-analysis and review of the literature', *Annals of Internal Medicine*, 118(12), pp. 956–963. https://doi.org/10.7326/0003-4819-118-12-956
6. de Moerloose, P. and Boehlen, F. (2013) 'Fibrinogen and fibrinogen disorders: a delicate balance between haemorrhage and thrombosis', *Best Practice & Research Clinical Haematology*, 26(2), pp. 125–137. https://doi.org/10.1016/j.beha.2013.06.002
7. Dehghan, A., Yang, Q., Peters, A., Basu, S., Bis, J.C., Rudnicka, A.R., Kavousi, M., Chen, M.H., Baumert, J., Lowe, G.D., McKnight, B., Tang, W., de Maat, M., Larson, M.G., Eyhermendy, S., McArdle, W.L., Lumley, T., Pankow, J.S., Hofman, A., Massaro, J.M. *et al.*

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 **Vol. 4, No.1, 2026**
www.zjhms.alzahraa.edu.iq

(2009) 'Association of novel genetic loci with circulating fibrinogen levels: a genome-wide association study in 6 population-based cohorts', *Circulation: Cardiovascular Genetics*, 2(2), pp. 125–133. https://doi.org/10.1161/CIRCGENETICS.108.825224

8. Wikkelsø, A., Lunde, J., Johansen, M., Stensballe, J., Wetterslev, J., Møller, A.M. and Afshari, A., (2013) 'Fibrinogen concentrate in bleeding patients', *Cochrane Database of Systematic Reviews*, 8, CD008864. https://doi.org/10.1002/14651858.CD008864.pub2

9. Luyendyk, J.P., Schoenecker, J.G. and Flick, M.J. (2019) 'The multifaceted role of fibrinogen in tissue injury and inflammation', *Blood*, 133(6), pp. 511–520. https://doi.org/10.1182/blood-2018-07-818211

10.] Fish, R.J. and Neerman-Arbez, M. (2012) 'Fibrinogen gene regulation', *Thrombosis and Haemostasis*, 108(3), pp. 419–426. https://doi.org/10.1160/TH12-04-0273

11. Kattula, S., Byrnes, J.R. and Wolberg, A.S. (2017) 'Fibrinogen and fibrin in hemostasis and thrombosis', *Arteriosclerosis, Thrombosis, and Vascular Biology*, 37(3), pp. e13–e21. https://doi.org/10.1161/ATVBAHA.117.308564

12. Fuller, G.M. and Zhang, Z. (2001) 'Transcriptional control mechanism of fibrinogen gene expression', *Annals of the New York Academy of Sciences*, 936, pp. 469–479. https://doi.org/10.1111/j.1749-6632.2001.tb03534.x

13. Borghi, S., Nencini, F., Giurranna, E., Barbaro, I., Taddei, N., Fiorillo, C. and Becatti, M. (2025) 'Fibrinogen glycosylation and glycation: molecular insights into thrombosis and vascular disease', *Frontiers in Molecular Biosciences*, 12, 1680332. https://doi.org/10.3389/fmolb.2025.1680332

14. Nencini, F., Borghi, S., Giurranna, E., Barbaro, I., Taddei, N., Fiorillo, C. and Becatti, M. (2025) 'Reactive nitrogen species and fibrinogen: exploring the effects of nitration on blood clots', *Antioxidants*, 14(7), 825. https://doi.org/10.3390/antiox14070825

15. Vilar, R., Fish, R.J., Casini, A. and Neerman-Arbez, M. (2020) 'Fibrin(ogen) in human disease: both friend and foe', Haematologica, 105(2), February 2020. https://doi.org/10.3324/haematol.2019.236901

16. Chang, Y., Lu, J. and Chen, C. (2025) 'Biomarkers in venous thrombosis: diagnostic potential and limitations', *Biology*, 14(7), 800. https://doi.org/10.3390/biology14070800

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 **Vol. 4, No.1, 2026**
www.zjhms.alzahraa.edu.iq

17. Risman, R.A., Belcher, H.A., Ramanujam, R.K., Weisel, J.W., Hudson, N.E. and Tutwiler, V. (2024) 'Comprehensive analysis of the role of fibrinogen and thrombin in clot formation and structure for plasma and purified fibrinogen', *Biomolecules*, 14(2), 230. https://doi.org/10.3390/biom14020230

18. Jensen, T., Kierulf, P., Sandset, P.M., Klingenberg, O., Joø, G.B., Godal, H.C. and Skjønsberg, O.H. (2007) 'Fibrinogen and fibrin induce synthesis of proinflammatory cytokines from isolated peripheral blood mononuclear cells', *Thrombosis and Haemostasis*, 97(5), pp. 822–829. https://doi.org/10.1160/th07-01-0039

19. Tyagi, N., Roberts, A.M., Dean, W.L., Tyagi, S.C. and Lominadze, D. (2008) 'Fibrinogen induces endothelial cell permeability', *Molecular and Cellular Biochemistry*, 307(1–2), pp. 13–22. https://doi.org/10.1007/s11010-007-9579-2

20. Costantini, T.W., Kornblith, L.Z., Pritts, T. and Coimbra, R. (2024) 'The intersection of coagulation activation and inflammation after injury: what you need to know', *The Journal of Trauma and Acute Care Surgery*, 96(3), pp. 347–356. https://doi.org/10.1097/TA.0000000000004190

21. Bayer, I.S. (2022) 'Advances in fibrin-based materials in wound repair: a review', *Molecules*, 27(14), 4504. https://doi.org/10.3390/molecules27144504

22. Chapin, J.C. and Hajjar, K.A. (2015) 'Fibrinolysis and the control of blood coagulation', *Blood Reviews*, 29(1), pp. 17–24. https://doi.org/10.1016/j.blre.2014.09.003

23. Pieters, M. and Wolberg, A.S. (2019) 'Fibrinogen and fibrin: an illustrated review', *Research and Practice in Thrombosis and Haemostasis*, 3(2), pp. 161–172. https://doi.org/10.1002/rth2.12191

24. Ko, Y.P. and Flick, M.J. (2016) 'Fibrinogen is at the interface of host defense and pathogen virulence in Staphylococcus aureus infection', Seminars in Thrombosis and Hemostasis, 42(4), pp. 408–421. https://doi.org/10.1055/s-0036-1579635

25. Li, M., Wu, Y., Zhang, J., Huang, L., Wu, X. and Yuan, Y. (2019) 'Prognostic value of pretreatment plasma fibrinogen in patients with colorectal cancer: a systematic review and meta-analysis', *Medicine*, 98(37), e16974. https://doi.org/10.1097/MD.0000000000016974

AL ZAHRAA UNIVERSITY JOURNAL
Health and Medical Science

*Al-Zahraa Journal for Health and Medical Sciences 2026; 4:*129-145 Vol. 4, No.1, 2026
www.zjhms.alzahraa.edu.iq

26. Tiscia, G.L. and Margaglione, M. (2018) 'Human fibrinogen: molecular and genetic aspects of congenital disorders', *International Journal of Molecular Sciences*, 19(6), 1597. https://doi.org/10.3390/ijms19061597

27. Abebe, E. C., Dejenie, T. A., Anley, D. T., Mengstie, M. A., Gebeyehu, N. A., Adella, G. A., Kassie, G. A., Tesfa, N. A., Gesese, M. M., Feleke, S. F., Zemene, M. A., Dessie, A. M., Bayih, W. A., Solomon Kebede, Y., Bantie, B., Seid, M. A., Enyew, E. F., Dessie, G., Adugna, D. G., Ayele, T. M., … Admasu, F. T. (2024) 'Diagnostic performance of plasma D-dimer, fibrinogen, and D-dimer to fibrinogen ratio as potential biomarkers to predict hypertension-associated acute ischemic stroke', Heliyon, 10(5), e27192. https://doi.org/10.1016/j.heliyon.2024.e27192

28. Ameera, K., Choraria, G., Basha, S. and Mahato, K.K. (2025) 'Emerging insights of fibrinogen glycation in cardiovascular disorders: A review', International Journal of Biological Macromolecules, 331(Pt 2), 148461. https://doi.org/10.1016/j.ijbiomac.2025.148461