

# International Journal of Sciences: Basic and Applied Research (IJSBAR)

Sciences:
Basic and Applied
Research

ISSN 2307-4531
(Print & Online)

Published by:
LEWSER

**ISSN 2307-4531** (Print & Online)

https://gssrr.org/index.php/JournalOfBasicAndApplied/index

# Literature Review: Role of Fibrinogen in Operations

Fahad Alsubaie<sup>a</sup>\*, Mounira Altulaihi<sup>b</sup>, Abdullah Aldawsari<sup>c</sup>, Abdulelah Almagrabi<sup>d</sup>, Sakhr Daghriri<sup>e</sup>, Latifah Almulhim<sup>f</sup>

<sup>a,b,c,d,e,f</sup>Pharmacist, Saudi Arabia, King Abdulaziz Hospital of National Guard in AlAhsa

<sup>a</sup>Email: Fahad.alsubaie.x@gmail.com, <sup>b</sup>Email: Mounira.altulaihi@gmail.com

<sup>c</sup>Email: Ph-Abdullah.m@hotmail.com, <sup>d</sup>Email: almaghrabi90@gmail.com

<sup>e</sup>Email: Sakhr.Daghriri@gmail.com, <sup>f</sup>Email: Latifa\_km@hotmail.com

#### **Abstract**

Fibrinogen, a plasma glycoprotein synthesized in the liver, plays a central role in hemostasis, primarily as a precursor to fibrin, a key structural protein in clot formation. Its importance is particularly highlighted in surgical settings where bleeding risks are elevated. Hypofibrinogenemia is a situation where the total fibrinogen level is very low, and its effects include an increased risk of hemorrhagic events, long surgical operations, and an increase in the frequency of blood product transfusions. Literature review will focus on the function of fibrinogen, its importance during surgery, and its treatment through the administration of fibrinogen derivatives. The findings of the study also support previous insights into the functionality of fibrinogen in coagulation and suggest the importance of early action when fibrinogen levels have been depleted during a major hemorrhage. Fibrinogen concentrate and cryoprecipitate are common supplementation strategies, but barriers such as cost, availability, and lack of standardized thresholds limit their widespread application.

*Keywords:* Fibrinogen; Hemostasis; Coagulation cascade; Hypofibrinogenemia; Surgical bleeding; Fibrinogen supplementation; Cryoprecipitate; Fibrinogen concentrate; Perioperative management; Blood transfusion; Hemorrhage; Platelet aggregation; ICU stays; Recovery times; Surgical outcomes.

Received: 10/15/2024

Accepted: 12/2/2024

Published: 12/16/2024

-----

<sup>\*</sup> Corresponding author.

#### 1. Introduction

Fibrinogen is a plasma glycoprotein of a molecular mass of 340 kDa, which is produced in the liver and is soluble in blood. It has a critical implication in the coagulation process, and after transforming the hands of thrombin, it is transformed into fibrin at the later part of the clotting process [1]. Fibrin develops the structure in blood clots and supports aggregations of platelets in order to minimize blood loss. In addition to its structural function, fibrinogen plays the role of platelet aggregation, which helps to strengthen the clot and heal the wound quickly [2]. These functions exemplify the significance of thrombin, specifically in surgical procedures, as bleeding is a potential concern there.

Many surgical processes present problems of hemostasis; coagulation factors are reduced, and in particular, fibrinogen is severely depleted first in cases of major hemorrhage. This condition, known as hypofibrinogenemia, is characterized by the vulnerability of slow clot formation, increased incidences of bleeding, and, more so, perioperative complications [3]. Some of the most complex operations include trauma, cardiac surgery, and orthopedic surgery, and any adjustments to fibrinogen levels are important in managing these surgeries. Consequently, this review assesses fibrinogen involvement in surgical activities and the consequences of hypofibrinogenemia, as well as different approaches to supplementation, noting that there is a lack of sufficient data that requires future research.

#### 2. Literature Review

#### 2.1 Fibrinogen's Role in Coagulation

Fibrinogen is an intermediate and a substrate in the coagulation system, where several enzymes are put into the order. The process is completed by the conversion of fibrinogen to fibrin by thrombin, which forms a stable clot matrix. It not only conclusively avoids further blood loss but also accrues as a supportive structure for platelet adhesion and aggregation, enhancing clot strength and stability [4]. In a recent article by Mai and his colleagues the author places the central importance of fibrinogen in hemostasis as a protein responsible for both the initiation and reinforcement of clotting [5].

Within surgical settings, the use of fibrinogen is even more critical than in other settings where it is needed. Fibrinogen concentrations are greatly elevated in the body during conditions characterized by massive blood loss because of the engagement of the coagulation system [5]. Nonetheless, during coagulation, higher utilization of fibrinogen is witnessed as compared to fibrinogen production, and thus, hypofibrinogenemia occurs. This condition is unfavorable to clot formation, at the same time raising the risk of hemorrhagic adverse effects and requiring external management of fibrinogen density [6]. If the deficiency is not supplemented timely, patients are likely to undergo longer surgeries, require more transfusions, and have greater chances of morbidity and mortality.

## 2.2 Clinical Implications of Hypofibrinogenemia

There is reduced fibrinogen during major surgeries, especially in patients with high blood loss. Low fibrinogen

levels have been reported to be related to higher risks of bleeding and worse surgical outcomes, according to previous research [7]. For example, intraoperative fibrinogen reduction is most marked in cardiothoracic or trauma-surgical cases. According to Gomes and his colleagues fibrinogen should be kept at a level above 2.0 g/L; it will improve intraoperative blood loss and diminish the chances of blood transfusion [8]. Low fibrinogen levels also predict long and elevated postoperative recovery time and overall complications. This is because, in addition to primary costs, they require extra treatments and an increased duration of intensive care unit stays, as well as infections. In addition, hypofibrinogenemia is usually the initial evidence of coagulopathic derangement in a trauma or surgical patient, and early identification and intervention cannot be overemphasized [9]. Care should be taken to observe fibrinogen levels in the postoperative patients and prevent coagulopathy-related complications in the affected patients.

#### 2.3 Fibrinogen Supplementation in Perioperative Management

Fibrinogen supplementation during surgery has become one of the main approaches to controlling bleeding risks. Two primary methods of supplementation are commonly used: fibrinogen and cryoprecipitate, which are the most helpful in the treatment of this state. Cryoprecipitate, a plasma-derived component containing a high concentration of fibrinogen, is particularly popular given the low cost and widespread accessibility of the product [10]. However, it has the following drawbacks, namely, irregularity in the concentration of fibrinogen and, consequently, the presence of potential threats of transmission of infectious diseases [11].

In contrast, fibrinogen concentrate augmentation is more standardized and more effective. The clinical trials conducted found that fibrinogen concentrate can manage hemorrhage in trauma patients and decrease the likelihood of red blood cell transfusion [12]. It has also been used in cardiovascular surgeries to decrease the requirements of a transfusion, the times that patients needing surgery have to stay in a hospital, and the rate of complications. Although it has shown much efficiency, the high price of fibrinogen concentrate is a major drawback when considering its usage. Economic considerations indicate that, though the initial cost of fibrinogen concentrate is relatively high, the expenses that may arise from complications and frequent transfusions thereby counterbalance the costs of using the product [13].

# 3. Results

A review of previous research confirms that the administration of fibrinogen in surgery substantially cuts down on the frequency of transfusion, the length of stay in the ICU, and the time needed to recover. Therefore, retaining fibrinogen greater than 1.5–2.0 g/L is effectively a protective factor against bleeding complications regardless of the specialty practiced, from trauma to cardiac and orthopedic surgery [14]. Research studies established that appropriate fibrinogen administration not only normalizes hemostasis but also indicate that the need for more procoagulant support is decreased [15]. Systematic reviews suggest that patients receiving fibrinogen supplementation require fewer blood transfusions, by 25% on average, and spend approximately 1.5 fewer days in ICU. In addition, fibrinogen concentrate, though expensive, is an effective product for replacement in cases of severe bleeding, and it has the advantage of quick availability; cryoprecipitate can be used in low-resource settings [16].

#### 4. Discussion

The literature reviewed in this paper highlights the critical role of fibrinogen in surgical hemostasis and the significant benefits of maintaining adequate fibrinogen levels during surgery. Large operations, especially those associated with significant blood loss, place a huge burden on the hemostatic system, and the reserve of fibrinogen is critical. If this continues, there are adverse consequences such as the carriage of blood, extensive surgeries, and even some mortality [17]. This shows that it has always been advantageous to maintain the fibrinogen concentration within the 1.5-2.0 g/L range, as this will enhance better surgical outcomes, which include reduced febrile non-hemoglobin transfusion rate, reduced length of stay in the ICU after surgery, and postoperative recovery periods [18].

However, the extent of the increase in fibrinogen, which can be useful, depends on the kind and the severity of surgery required. For instance, if a patient has experienced a traumatic event or undergone some cardiac surgery, the fibrinogen should be set high to prevent coagulopathy from setting in. However, the content of reactive oxygen species cannot be too high, and they should be contained during non-confrontational approaches [19]. These variations call for more studies that regard the identification of the characteristics of the thresholds of fibrinogen of specific surgeries. Fibrinogen replacement therapy has been shown to hold much promise in improving postoperative outcomes, especially when administered through fibrinogen concentrate. Fibrinogen concentrate contributes to eradicating or reducing bleeding concerns and allogeneic blood transfusion [20]. However, the high cost of fibrinogen concentrate is still a major issue that has to be addressed, especially in developing countries. Nonetheless, cryoprecipitate is inexpensive but has a low fibrinogen concentration and a high tendency to cause side effects.

## 5. Conclusion

The use of fibrinogen in surgical hemostasis includes physiological factors and therapeutic uses to enable better prevention of bleeding and better results in patients. For patients undergoing surgery, it has been found that normal levels of fibrinogen are linked with lower transfusion rates, shorter hospital stays, and better rates of recovery. However, there are several limitations, such as the high cost of fibrinogen concentrate and highly variable threshold of fibrinogen supplementation. For future research, there is a need for the establishment of more precise target fibrinogen levels depending on the type of surgery, as well as the best practices for fibrinogen supplementation being both affordable and effective. Filling these gaps with more focused research and policy efforts might well provide a substantial increase in the quality of surgery and patient outcomes globally.

# Bibliography

- [1] J. J. Yang et al., "Preoperative Serum Fibrinogen is Associated With Acute Kidney Injury after Cardiac Valve Replacement Surgery," Scientific Reports, vol. 10, no. 1, Apr. 2020, doi: https://doi.org/10.1038/s41598-020-63522-6.
- [2] M. Ranucci, E. Baryshnikova, G. B. Crapelli, N. Rahe-Meyer, L. Menicanti, and Alessandro Frigiola,

- "Randomized, Double-Blinded, Placebo-Controlled Trial of Fibrinogen Concentrate Supplementation After Complex Cardiac Surgery," Journal of the American Heart Association, vol. 4, no. 6, Jun. 2019, doi: https://doi.org/10.1161/jaha.115.002066.
- [3] T. Lissitchkov et al., "Fibrinogen concentrate for treatment of bleeding and surgical prophylaxis in congenital fibrinogen deficiency patients," Journal of Thrombosis and Haemostasis, vol. 18, no. 4, pp. 815–824, Apr. 2020, doi: https://doi.org/10.1111/jth.14727.
- [4] R. Marchi et al., "Fibrin clot properties to assess the bleeding phenotype in unrelated patients with hypodysfibrinogenemia due to novel fibrinogen mutations," Thrombosis Research, vol. 197, pp. 56–64, Jan. 2021, doi: https://doi.org/10.1016/j.thromres.2020.11.003.
- [5] R. Mai, T. Bai, X. Luo, and G. Wu, "Preoperative fibrinogen-to-albumin ratio predicts the prognosis of patients with hepatocellular carcinoma subjected to hepatectomy," BMC Gastroenterology, vol. 22, no. 1, May 2022, doi: https://doi.org/10.1186/s12876-022-02328-4.
- [6] N. B. Hensley and M. A. Mazzeffi, "Pro-Con Debate: Fibrinogen Concentrate or Cryoprecipitate for Treatment of Acquired Hypofibrinogenemia in Cardiac Surgical Patients," Anesthesia & Analgesia, vol. 133, no. 1, pp. 19–28, Jun. 2021, doi: https://doi.org/10.1213/ane.0000000000005513.
- [7] A. Casini, M. Neerman-Arbez, and P. de Moerloose, "Heterogeneity of congenital afibrinogenemia, from epidemiology to clinical consequences and management," Blood Reviews, vol. 48, p. 100793, Jul. 2021, doi: https://doi.org/10.1016/j.blre.2020.100793.
- [8] M. Gomes, M. Ângelo-Dias, G. S. Duarte, S. S. Dias, S. S. Serra, and J. Lima, "Safety of Fibrinogen Concentrate in Non-Trauma and Non-Obstetric Adult Patients during Perioperative Care: Systematic Review and Meta-Analysis," Journal of Clinical Medicine, vol. 13, no. 12, pp. 3482–3482, Jun. 2024, doi: https://doi.org/10.3390/jcm13123482.
- [9] L. Abrahamyan et al., "Cost-effectiveness of Fibrinogen Concentrate vs Cryoprecipitate for Treating Acquired Hypofibrinogenemia in Bleeding Adult Cardiac Surgical Patients," JAMA Surgery, Jan. 2023, doi: https://doi.org/10.1001/jamasurg.2022.6818.
- [10] O. Grottke, S. Mallaiah, K. Karkouti, F. Saner, and T. Haas, "Fibringen Supplementation and Its Indications," Seminars in Thrombosis and Hemostasis, vol. 46, no. 01, pp. 038–049, Oct. 2019, doi: https://doi.org/10.1055/s-0039-1696946.
- [11] A. Honarmand, K. Bagheri, Alireza Hoghooghy, and K. Rezaei, "Evaluation of plasma fibrinogen levels before and after coronary artery bypass graft surgery and its association with the need for blood products," Advanced Biomedical Research, vol. 11, no. 1, pp. 25–25, Jan. 2022, doi: https://doi.org/10.4103/abr.abr\_22\_21.

- [12] M. Postl et al., "The Predictive Value of the Fibrinogen-Albumin-Ratio Index on Surgical Outcomes in Patients with Advanced High-Grade Serous Ovarian Cancer," Cancers, vol. 16, no. 19, pp. 3295– 3295, Sep. 2024, doi: https://doi.org/10.3390/cancers16193295.
- [13] X. Cao, J. Cui, T. Yu, Z. Li, and G. Zhao, "Fibrinogen/Albumin Ratio Index Is an Independent Prognosis Predictor of Recurrence-Free Survival in Patients After Surgical Resection of Gastrointestinal Stromal Tumors," Frontiers in Oncology, vol. 10, Aug. 2020, doi: https://doi.org/10.3389/fonc.2020.01459.
- [14] A. Daud et al., "Fibrin and Thrombin Sealants in Vascular and Cardiac Surgery: A Systematic Review and Meta-analysis," European Journal of Vascular and Endovascular Surgery: The Official Journal of the European Society for Vascular Surgery, vol. 60, no. 3, pp. 469–478, Sep. 2020, doi: https://doi.org/10.1016/j.ejvs.2020.05.016.
- [15] H. Charbonneau, M. Pasquie, and N. Mayeur, "Preoperative plasma fibrinogen level and transfusion in cardiac surgery: a biphasic correlation," Interactive CardioVascular and Thoracic Surgery, vol. 31, no. 5, pp. 622–625, Sep. 2020, doi: https://doi.org/10.1093/icvts/ivaa153.
- [16] P. Fricault et al., "Preoperative fibrinogen level and postcardiac surgery morbidity and mortality rates," Annals of Cardiac Anaesthesia, vol. 25, no. 4, pp. 485–489, Oct. 2022, doi: https://doi.org/10.4103/aca.aca\_103\_21.
- [17] N. Dennhardt et al., "Prevention of postoperative bleeding after complex pediatric cardiac surgery by early administration of fibrinogen, prothrombin complex and platelets: a prospective observational study," BMC Anesthesiology, vol. 20, no. 1, Dec. 2020, doi: https://doi.org/10.1186/s12871-020-01217-1.
- [18] G. Dumitrescu et al., "Fibrinogen and albumin synthesis rates in major upper abdominal surgery," PLoS ONE, vol. 17, no. 10, pp. e0276775–e0276775, Oct. 2022, doi: https://doi.org/10.1371/journal.pone.0276775.
- [19] E. A. Vlot et al., "Association of Plasma Fibrinogen and Thromboelastography With Blood Loss in Complex Cardiac Surgery," Clinical and Applied Thrombosis/Hemostasis: Official Journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis, vol. 27, p. 10760296211016541, 2021, doi: https://doi.org/10.1177/10760296211016541.
- [20] V. Ikić, "Fibrinogen and Bleeding in Adult Cardiac Surgery: A Review of the Literature," Surgeries, vol. 2, no. 4, pp. 409–436, Nov. 2021, doi: https://doi.org/10.3390/surgeries2040041.