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Computational Analysis of the Risk of Blood Clot Formation in Diabetes: A Mathematical Modeling-Based Approach

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Abstract

Our study delves into the heightened risk of blood clot formation in individuals with diabetes, a condition known for its potential to increase clotting tendencies, leading to severe complications like heart attacks and strokes. Utilizing a multidisciplinary approach, we integrate physiological data, principles of hemodynamic, and mathematical models to simulate the intricate dynamics of blood flow and clot formation within the vasculature of diabetic individuals. By considering critical factors such as altered blood viscosity, resistance to flow, endothelial dysfunction, and platelet aggregation, we gain valuable insights into the complex interactions between diabetes-related factors and the propensity for clotting. Factors like elevated levels of fibrinogen and other clotting factors contribute to blood thickening, increased resistance to flow, and heightened viscosity, exacerbating the clotting risk. As clots grow within blood vessels, they impede blood flow, elevating resistance and making blood movement more challenging. Moreover, the size of clots influences local blood viscosity, further complicating circulation. Through computational simulations, we explore diverse scenarios to evaluate how different parameters affect the risk of clot formation, providing crucial insights for developing preventive measures and targeted interventions tailored to diabetic patients' needs.

Keywords: Diabetes; Blood Clot Formation; Hemodynamics; Mathematical Modeling; Blood Viscosity; Resistance to Flow; Endothelial Dysfunction; Platelet Aggregation; Clot Size; Cardiovascular Health; Preventive Strategies; Targeted Interventions; Computational Simulations.

Introduction

Serious issues like heart attacks and strokes are more likely to occur in diabetics because their blood clots more easily. This risk may be reduced with effective diabetes treatment. The vast scale of the epidemic is underscored by recent statistics from the International Diabetes Federation (IDF). In 2021, 537 million adults aged 21-80 were affected, and this number is projected to increase to 784 million by 2045, according to various sources (Chaturvedi and Shah, 2023; Lenin and Shah, 2024; Sadique and Shah, 2022; Shah, 2013; Shah and Kumar, 2017). In 2021 alone, 6.9 million people died from the illness, which is the equivalent of one death every two seconds (Kasturia et al., 2024; Shah and Kumar, 2018; Stiehl et al., 2024). Furthermore, diabetes is the third most prevalent comorbidity in COVID-19 patients, leading to more severe disease and unfavorable outcomes, such as admission to the intensive care unit and death. This hidden pandemic is causing major problems for public health throughout the globe and is growing at a steady rate. Evidence from studies conducted by Geeta et al. (2013), Islam et al. (2023), Kumar and Shah (2022), and Sadique and Shah (2023) highlights the critical need of swift and efficient action to combat the diabetes pandemic and its consequences. Choturvedi et al. (2021), Kumar and Shah (2024), Shah (2012), Shah (2011), and Siddiqui and Shah (2016) all point to the increased risk of cardiovascular disease as one of the many problems associated with diabetes (see Fig. 1). The increased risk of thrombotic events, such as heart attacks and strokes, due to the development of blood clots inside the blood arteries, is a significant cardiovascular complication linked with diabetes. The exact mechanisms underlying the increased risk of clot formation in diabetic individuals have not been fully elucidated, despite considerable progress in comprehending the pathophysiology of vascular complications in diabetes (Kumar and Shah, 2017; Shah, 2021; Siddiqui and Shah, 2016; Tasneem et al., 2024). The complex hemodynamic and biochemical mechanisms of clot formation may be better understood via the use of mathematical models and computer simulations, which can provide light on the interplay between diabetes-related variables and thrombosis susceptibility. Type 1 and Type 2 diabetes are the most frequent forms of the disease. A lack of insulin production by the pancreas causes Type 1 diabetes, whereas insulin resistance or inadequate insulin production by the body causes Type 2 diabetes, which is more common (Akbar and Shah, 2024; Akinsola and Temitayo, 2019; Geeta et al., 2015; Shah, 2011; Shah and Kumar, 2020). Excessive thirst, hunger, lethargy, unexplained weight loss, frequent urination, infection risk, impaired eyesight, and sluggish wound healing are some of the symptoms that may be associated with diabetes. The risk of blood clot formation may be increased by both forms of diabetes, however the specific pathways may differ (Akinsola and Temitayo, 2014; Shah, 2013; Shah, 2017; Singh et al., 2016; Singh and Shah, 2010). Hyperglycemia (high blood sugar levels) and other complications of Type 1 diabetes, which is marked by insufficient insulin production, may damage blood vessels and reduce blood flow, raising the likelihood of blood clot formation. Additionally, increased blood clotting factor levels are one of the extra risk factors that may be present in individuals with type 1 diabetes. The risk of blood clots may be higher in type 2 diabetes, which is characterized by insulin resistance or reduced insulin production. This is because of factors such as inflammation, obesity, and metabolic abnormalities associated with insulin resistance (Gupta, 2024; Malik, 2020; Shah, 2013; Siddiqui and Shah, 2016). Changes in blood vessel function and an increased tendency for clot formation may be caused by

these factors. Anamika (2017), Geeta (2014), Chaturvedi and Shah (2024), and Kumar and Shah (2022) all state that people with type 1 and type 2 diabetes are at increased risk of blood clots, but they also suggest that the specific processes and risk factors may vary.

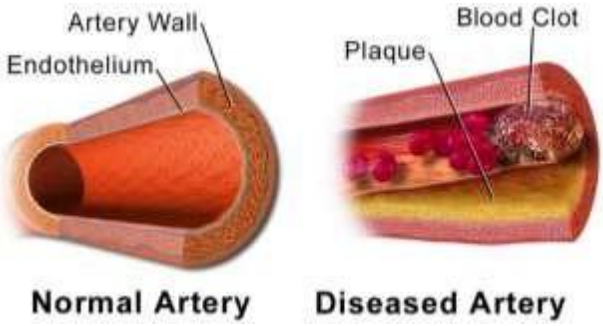


Fig.1: Normal artery with diseased artery with a blood clot

Addressing these risk factors through lifestyle changes and targeted interventions is vital in tackling the diabetes epidemic and alleviating its impact on both individuals and healthcare systems (Majhi et al., 2024; Shah, 2011; Shah ,2014). Diabetes can lead to severe complications affecting various organs, including the heart, blood vessels, eyes, teeth, kidneys, and nerves, and can ultimately result in death. Complications from diabetes often necessitate amputations, resulting in permanent disability. Individuals with diabetes face a higher risk of blockages and heart attacks compared to the general population. Diabetic neuropathy, a form of nerve damage caused by high blood sugar levels, is another common complication, particularly affecting the feet and increasing the risk of foot ulcers, infections, and subsequent limb amputations, especially when combined with poor blood circulation (Geeta and Shah, 2015; Geeta et al., 2016; Jaiswal et al., 2024; Kumar and Shah, 2017; Singh, 2011). Diabetic retinopathy, characterized by damage to the small blood vessels in the retina, is a leading cause of blindness worldwide, affecting nearly one million individuals. Additionally, diabetic nephropathy, which damages the small blood vessels in the kidneys, leads to kidney disease and can eventually cause kidney failure, representing one of the most prevalent causes of kidney failure (Sadique and Shah, 2022; Shah, 2011; Shah 2014; Singh, 2011). In this study, we conducted a computational analysis of clot formation risk in diabetes using mathematical modeling. Our research aims to uncover the complex mechanisms contributing to the increased risk of blood clotting in diabetic patients (Shah, 2010; Shah, 2013; Siddiqui and Shah, 2015; Singh, 2010). By utilizing mathematical models and computational simulations, we explored various scenarios to investigate the impact of diabetes-related factors, such as changes in blood rheology, endothelial dysfunction, and platelet hyperactivity, on the dynamics of clot formation. Through comprehensive analyses of hemodynamic parameters, clot formation

kinetics, and biochemical pathways, our goal is to elucidate the underlying mechanisms driving clot formation in diabetic individuals (Shah, 2013; Shah, 2022; Singh, 2011). The significance of clot formation risk in diabetes stems from its potential to trigger severe and life-threatening complications. Diabetes is characterized by an increased tendency for blood clot formation, a condition termed hypercoagulability. Moreover, individuals with diabetes are more prone to developing blood clots in smaller blood vessels, which can lead to conditions like deep vein thrombosis (DVT) and pulmonary embolism (PE). Therefore, comprehending and mitigating the risk of clot formation in diabetes is essential for averting adverse cardiovascular events and enhancing patient outcomes. Through our computational approach, we can integrate various physiological and pathological factors into a unified framework, offering a comprehensive understanding of the intricate relationship between diabetes and thrombotic risk. By identifying the key factors influencing clot formation in diabetes, our study aims to pinpoint potential therapeutic targets and interventions to mitigate the heightened thrombotic risk associated with this prevalent metabolic of the blockage is shown by L_0, and d indicates where along the artery it's positioned. The parameter m describes the shape of the blockage, with m=2 indicating an evenly shaped blockage. Lastly, there's another parameter, A, which is determined by the specific values of these variables and parameters (Anamika et al., 2017; Kasturia et al., 2024; Shah and Kumar, 2018; Siddiqui and Shah; 2016).

$$A = \delta_m \frac{m^{m/(m-1)}}{(m-1)} \sqrt{R_0 L_0}$$

This equation helps us find the maximum height of the blockage in the artery, indicated by the symbol δ. It is determined by factors such as the location of the blockage along the artery (z), its length (L_0), and the shape parameter (m). The expression also involves a fractional calculation, with the result being the maximum height of the blockage.by the blood flow, making it harder for blood to pass through the clot. Larger clots result in greater resistance to blood flow. This

elevated resistance can elevate pressure upstream of the clot and decrease pressure downstream, altering blood flow patterns and potentially leading to

complications such as tissue damage or ischemia. Hence, as clot size increases, so does the resistance to blood flow, which can significantly impact cardiovascular health and function (Shah, 2011; Shah, 2017). Fig. 3, illustrates the impact of increasing clot size within the blood vessels on blood viscosity, which refers to the thickness or stickiness of blood. This rise in viscosity stems from several factors. Initially, the clot traps various blood components such as red blood cells and platelets, leading to a concentration of these constituents around the clot. Additionally, the formation of fibrin, a crucial protein in clot structure, creates a dense meshwork that impedes blood flow. As more platelets aggregate at the clot site, they further contribute to the viscosity of the surrounding blood. The obstruction caused by a larger clot alters the flow dynamics within the blood vessel, affecting shear forces and pressure gradients,

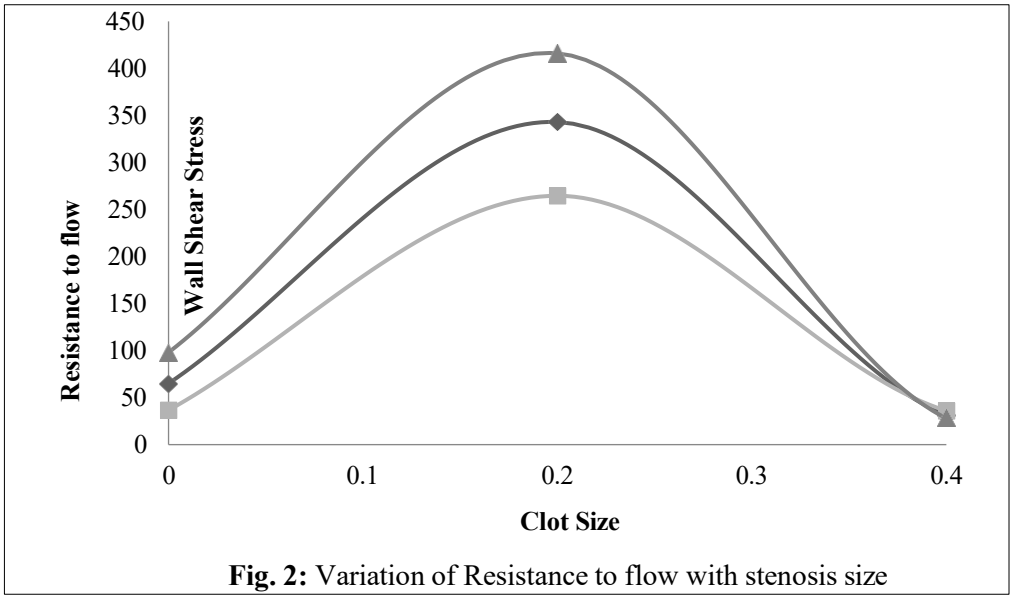


Fig. 2: Variation of Resistance to flow with stenosis size

which subsequently impact viscosity (Gupta, 2024; Siddiqui and Shah, 2016). Consequently, the growth of blood clots results in heightened local blood viscosity, influencing blood flow dynamics and potentially worsening thrombotic events. Our computational approach provides valuable insights into the intricate relationship between diabetes-related factors and the propensity for clot formation, offering a foundation for identifying new therapeutic targets and optimizing treatment approaches for diabetic individuals at an increased risk of thrombotic events. By elucidating the mechanisms underlying clot formation in diabetes, our research aims to pave the way for tailored interventions aimed at mitigating the heightened thrombotic risk associated with this prevalent metabolic disorder.

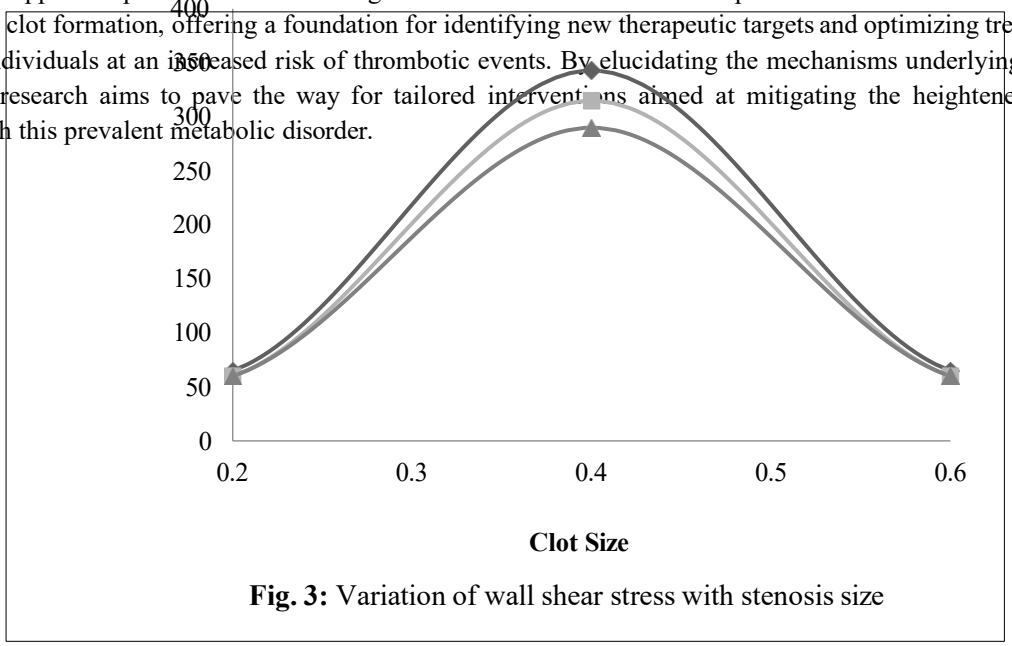


Fig. 3: Variation of wall shear stress with stenosis size

Conclusion

The complex link between diabetes and thrombosis may be better understood with the use of mathematical models and computer analysis, as shown by our study. We discovered possible treatment targets for people with diabetes who are prone to thrombotic problems by combining physiological data with computer models, which helped us understand the mechanics behind clot formation in diabetes. Our study's computational framework is useful for assessing the likelihood of clot formation, improving treatment strategies, and guiding clinical decision-making for patients with diabetes. When blood clots grow in the blood arteries, they block the flow of blood. It becomes increasingly difficult for blood to move through the clot because of this blockage, which increases the resistance to blood flow. In addition, the blood's viscosity might be affected by the size of the clot. The blood's viscosity may increase in the area around the clot as more blood cells and clotting components gather there. Ischemia and tissue injury are possible outcomes of both elevated flow resistances and increased viscosity, which further restrict blood circulation. Therefore, the clot's negative impact on blood circulation and general cardiovascular health is likely to get worse as the clot grows in size due to increased viscosity and resistance to flow.

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