Pregnancy and Von Willebrand Disease: A Modern Approach to Risk, Monitoring, and Prognosis

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Abstract

Von Willebrand disease (VWD), recognized as the most prevalent hereditary bleeding disorder, poses substantial challenges in the management of pregnancy for both the patient and the medical team. As gestation advances, physiological alterations in coagulation factors modify the hemostatic equilibrium; nevertheless, this intrinsic adaptation does not invariably confer sufficient safeguarding against hemorrhagic threats, particularly during the postpartum period. This article delineates the fundamental tenets of customized management, from biological surveillance to therapeutic decision-making, emphasizing the critical significance of multidisciplinary collaboration. The objective is to guarantee secure and personalized care for affected women, predicated on their hematological profile and obstetric circumstances.

Introduction:

Pregnancy represents a multifaceted physiological process characterized by substantial adaptations across numerous bodily systems, with alterations in blood coagulation being of paramount importance. These physiological modifications are designed to safeguard the pregnant woman from the risk of excessive hemorrhage during parturition. Nevertheless, in individuals with hereditary bleeding disorders, such as von Willebrand disease (VWD), the inherent physiological adjustments that occur during pregnancy may prove inadequate for ensuring hemostatic stability. The management of pregnancy within this specific context necessitates a meticulous equilibrium between maternal safety and fetal wellbeing, which is best achieved through a collaborative multidisciplinary team approach coupled with rigorous clinical oversight [1,2].

Physiological Changes in Coagulation During Pregnancy:

Pregnancy naturally induces a prothrombotic state to minimize bleeding risks during labor and postpartum. This is characterized by a gradual rise in plasma levels of von Willebrand factor (VWF), factor VIII, and fibrinogen, along with a decrease in fibrinolytic activity. These changes help prepare the body for the hemostatic challenges of childbirth [1]. However, in women with moderate to severe forms of VWD, this physiological boost is often inadequate to compensate for the underlying clotting defect, leaving them at risk for peripartum and postpartum hemorrhage [2].

Von Willebrand Disease: General Overview:

Von Willebrand disease (VWD) is the most common inherited bleeding disorder, affecting approximately 1% of the general population, although only a portion of individuals experience significant clinical symptoms [3]. It results from either a quantitative deficiency (types 1 and 3) or a qualitative defect (type 2) in von Willebrand factor (VWF), a multimeric glycoprotein that plays a key role in primary hemostasis by mediating platelet adhesion and stabilizing coagulation factor VIII [4].

Type 1 VWD, the most frequent form, is characterized by a partial quantitative reduction in VWF levels. Bleeding symptoms are generally mild and may include menorrhagia, easy bruising, or prolonged bleeding following trauma or surgery [3].

Type 2 VWD involves structurally abnormal VWF with impaired function. It is subdivided into several variants (2A, 2B, 2M, and 2N), each defined by a distinct molecular defect affecting VWF interaction with platelets or factor VIII. These qualitative forms are often associated with more pronounced bleeding than type 1 [6].

Type 3 VWD is rare but severe, with virtually undetectable levels of VWF and markedly reduced factor VIII, leading to a clinical picture resembling hemophilia, including spontaneous joint and deep tissue bleeding [5].

The diagnosis of VWD requires a combination of laboratory investigations, including VWF antigen (VWF:Ag), VWF activity tests (VWF:RCo or VWF:GPIbM), factor VIII activity (FVIII:C), multimer analysis, and sometimes VWF collagen binding or propeptide levels. These help classify the type of VWD and guide management decisions [4,7].

Identifying the specific VWD subtype is crucial for appropriate care, especially in pregnancy or surgery, where bleeding risk must be addressed. In some cases, particularly when family history is suggestive, genetic testing may assist with confirmation and counseling [4,6].

Pregnancy and von Willebrand Disease: Constant Vigilance Required:

Managing pregnancy in a patient with VWD requires a meticulous medical strategy based on anticipating bleeding risk, close biological monitoring, and therapeutic decisions tailored to the VWD subtype.

From early pregnancy, quarterly monitoring of plasma VWF and FVIII levels is essential. In type 1 VWD, a spontaneous physiological rise in these factors usually occurs during the third trimester, often reaching a safe threshold (>50 IU/dL), allowing some patients to avoid treatment. However, in types 2 and 3, where this increase is insufficient or absent, prophylactic substitution with VWF/FVIII concentrates (e.g., Wilate) is required during the peripartum period [3,4,5].

Desmopressin (DDAVP) can be used effectively in type 1 and selected type 2 patients, provided a prior challenge test shows good response. It is contraindicated in preeclampsia, eclampsia, or cardiovascular disease due to its vasopressor effects [8,9].

The highest bleeding risk occurs in the first 48–72 hours postpartum, due to a rapid decline in VWF and FVIII levels. This drop can trigger secondary hemorrhage, even in patients who were stable during delivery. Close clinical and laboratory follow-up and, if needed, extended replacement therapy are crucial during this window [10].

A multidisciplinary team, obstetrician, hematologist, and anesthesiologist, is vital for effective care. A delivery plan should be developed early, including substitution protocols, transfusion access, and rapid response strategies.

Recent advances in clinical research and updated international guidelines have led to significant improvements in the management of pregnancy for women with VWD. These include clearer therapeutic thresholds, standardized monitoring schedules, subtype-specific interventions, and a stronger focus on postpartum surveillance. Table 1 summarizes the main differences between earlier practices and the most current, evidence-based recommendations

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Prognosis in Pregnancy with von Willebrand Disease:

With proper management, pregnancy outcomes in women with VWD are generally favorable. In type 1, spontaneous rises in VWF and FVIII levels during late pregnancy often reduce bleeding risk without the need for therapy [3,4]. In contrast, patients with type 2 or type 3 require planned replacement therapy to avoid complications during and after delivery [5].jfgjjjgf

The postpartum phase is the most critical period. If factor levels fall rapidly, timely treatment can prevent hemorrhagic complications [10]. Neonatal outcomes are typically good, but infants born to mothers with type 3 VWD or affected fathers should be tested to assess their own bleeding risk [7].

In the postpartum period, non-hormonal contraception, such as a copper intrauterine device or barrier methods, is often preferred for women with von Willebrand disease. This approach helps avoid the potential impact of hormones on coagulation, reduces thrombotic risk, and allows sufficient time for hemostatic parameters to return to normal before a subsequent pregnancy [11].

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Conclusion:

Von Willebrand disease is not a contraindication to pregnancy, but it requires careful planning and close management. Successful outcomes depend on anticipating risks, tailoring follow-up to each patient, and involving a multidisciplinary team. With recent advances in treatment and monitoring, pregnancy can now be managed safely and effectively

Table 1 – Comparison between “Old” and “Updated” management of pregnancy in women with von Willebrand disease (VWD)

Theme	"Old" approach (≈ before 2015)	Updated approach (2018–2025)
Frequency of laboratory monitoring (VWF/FVIII)	Infrequent measurements, often only 1–2 times during the third trimester.	Quarterly from early pregnancy, with increased frequency in the third trimester and peripartum; defined factor level targets for procedures and delivery [11].
Target levels for delivery / neuraxial anesthesia	Variable and poorly harmonized thresholds.	Explicit targets (e.g., VWF/FVIII ≥ 0.50 IU/mL depending on context) for delivery, minor/major surgery, and neuraxial anesthesia [11].
Type 1 vs Types 2/3 management	General recognition that types 2/3 have higher bleeding risk, without structured algorithms.	Clear algorithms: type 1 often without replacement therapy if targets are achieved; types 2/3 require planned VWF (±FVIII) replacement around delivery [3,4,11].
Desmopressin (DDAVP) use	Broad use, heterogeneous guidance; contraindications less clearly defined.	Prior test dose to confirm responsiveness; restricted to type 1 and selected type 2 cases; contraindicated in preeclampsia, eclampsia, or cardiovascular disease; monitor for hyponatremia [4,6,7].
Postpartum period (48–72 h)	Clinical monitoring with variable duration; factor decline not systematically addressed.	Recognized as a critical window due to rapid VWF/FVIII drop; requires close clinical/laboratory follow-up and extended replacement therapy if needed [10,11].
Care organization	Ad hoc local coordination without standardized protocols.	Multidisciplinary team (obstetrics, hematology, anesthesiology) with a written delivery plan, including replacement protocols, transfusion access, and escalation strategy [8,9,11].
Postpartum anticoagulation (if VTE indication)	Cautious approach with limited VWD-specific recommendations.	Individualized decision-making balancing hemostatic benefit and VTE risk, based on 2021 guidelines and obstetric risk factors [11].

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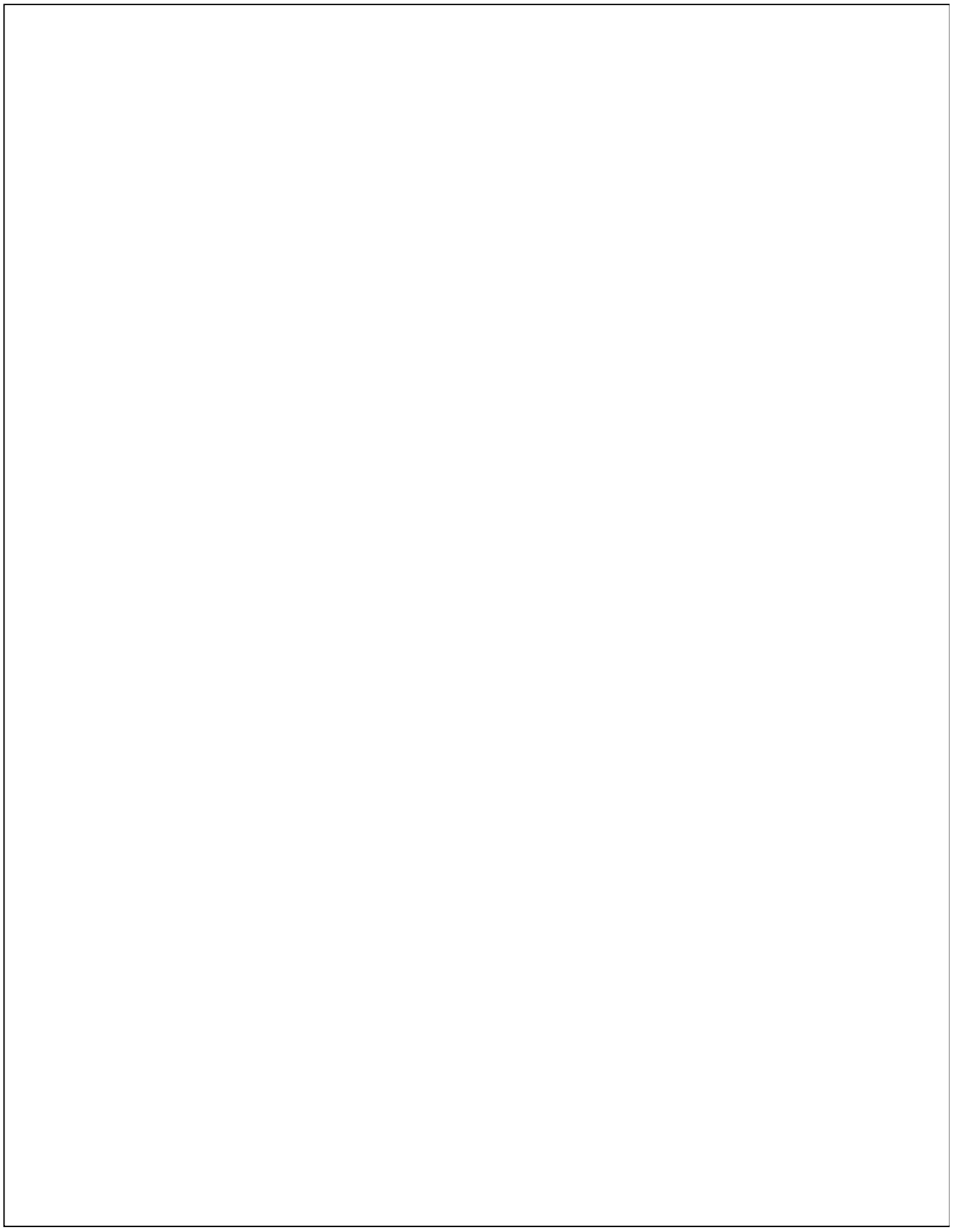

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