Chapter 14

POSTPARTUM HEMORRHAGE

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Postpartum hemorrhage (PPH) is one of the leading causes of maternal mortality and morbidity worldwide. This condition occurs in approximately 1%-2% of deliveries and is responsible for around 150,000 deaths annually, representing 25% of global maternal deaths (Corvino *et al.*, 2021). PPH is characterized by blood loss exceeding 500 mL after vaginal delivery or 1000 mL after cesarean section, primarily occurring within the first 24 hours postpartum (Watkins; Stem, 2020). Alternatively, any blood loss from the genital tract that compromises hemodynamic stability within this period also defines PPH. The causes of postpartum hemorrhage can be classified using the mnemonic of the 4 Ts: tone, trauma, tissue, and thrombin, with uterine atony being the most common cause, responsible for up to 80% of cases (Watkins; Stem, 2020). PPH can be classified as early postpartum hemorrhage, occurring within the first 24 hours after delivery, and late postpartum hemorrhage, occurring between 24 hours and 12 weeks postpartum. In terms of volume, massive PPH is defined by blood loss exceeding 2,000 mL in 24 hours, the need for a minimum transfusion of 1,200 mL, a hemoglobin drop of ≥ 4 g/dL, or the occurrence of coagulation disorders (Watkins; Stem, 2020). Given the potential risk, understanding the classification and manifestations of PPH is essential to ensure an effective management approach.

Postpartum hemorrhage stands out in the field of obstetric emergencies due to its high incidence and potential for severe complications. It demands rapid and effective interventions to prevent multi-organ failure and ensure maternal survival. Uterine atony, for example, is caused by the dysfunctional hypocontractility of the myometrium during the immediate postpartum period and is initially treated with measures such as uterine massage, uterotonics (oxytocin, carbetocin, methylergonovine maleate, prostaglandins), and administration of tranexamic acid (Li; Chang; Wang, 2022). However, it has been found that prolonged administration of oxytocin, especially for more than 4 hours in spontaneous deliveries and more than 7 hours in induced deliveries, is associated with a significant increase in the risk of PPH, regardless of the duration of hospitalization or the second stage of labor (Erickson; Carlson, 2020). The management of PPH involves a set of strategies, ranging from conventional medical treatments to advanced interventional procedures such as pelvic arterial embolization (Corvino *et al.*, 2021). Even in the absence of robust evidence, international protocols agree on the main initial steps in the treatment of PPH, which include manual uterine exploration, visual evaluation of the genital tract, insertion of a bladder catheter, administration of supplemental oxygen, and infusion of crystalloids for maternal stabilization (Corvino *et al.*, 2021). A multidisciplinary approach is fundamental for hemodynamic control and effective treatment of the underlying causes of hemorrhage (Erickson; Carlson, 2020). In this context, it is crucial to integrate different medical specialties to provide the best possible care for patients.

Postpartum hemorrhage (PPH) significantly affects maternal health globally, with incidences varying according to the definition and accuracy of blood loss measurement. Population studies indicate that the incidence of PPH can reach up to 10% when blood loss is precisely quantified. Risk factors include advanced maternal age, multiple pregnancies, and an increasing number of cesarean sections (Giurazza *et al.*, 2021). PPH occurs in approximately 6% of all deliveries, with severe cases in 1%-2% (Corvino *et al.*, 2021). Survivors of severe PPH often face physical and emotional sequelae, including sterility, hormonal and organ dysfunctions, post-traumatic stress disorder, and depression (Brenner et al., 2023). Recent studies also suggest that women who do not receive oxytocin during labor (physiological delivery) may not benefit as much from prophylactic postpartum oxytocin in preventing PPH as those who received oxytocin during labor, indicating that previous exposure to oxytocin can influence the effectiveness of postpartum prophylaxis (Erickson; Carlson, 2020). These factors underscore the need for preventive interventions and long-term emotional support.

Early and accurate diagnosis of PPH is crucial for the implementation of immediate interventions. Traditional methods, such as clinical evaluation and measurement of blood loss, are complemented by emerging technologies, including the use of artificial intelligence for continuous monitoring and early diagnosis (Li; Chang and Wang, 2022). Imaging tools like ultrasound and computed tomography play a vital role in assessing the causes and determining appropriate treatment (Corvino *et al.*, 2021). Additionally, when hemorrhage persists after 15 to 30 minutes of initial treatment, the use of tranexamic acid, volume resuscitation, and intrauterine balloon tamponade are recommended before resorting to more invasive interventions such as surgery or radiological management. These strategies have been shown to reduce the need for procedures like pelvic arterial embolization (Corvino *et al.*, 2021). Technological advancements, therefore, play an increasingly important role in the early detection and personalized treatment of PPH.

Treatment options for PPH include aggressive fluid resuscitation, administration of uterotonic medications, and in severe cases, pelvic arterial embolization. The evolution of endovascular techniques offers an effective minimally invasive approach, preserving future fertility and reducing the need for hysterectomy (Brenner *et al.*, 2023). However, when conservative measures fail, surgical interventions such as arterial ligation and procedures like the B-Lynch suture may be necessary, although these techniques have variable success rates due to the complex pelvic vasculature (Corvino *et al.*, 2021). The use of nanotextile-based biosensors represents a new frontier in the sensitive diagnosis and targeted treatment of PPH (Watkins; Stem, 2020). With the adoption of these emerging technologies, the treatment of PPH is becoming increasingly effective and less invasive.

Current trends in managing PPH include the growing integration of advanced technologies such as artificial intelligence and nanotechnology to enhance early diagnosis and personalized treatment. The use of machine learning algorithms for continuous surveillance and identification of risk patterns promises to revolutionize the approach to PPH, improving maternal outcomes (Li; Chang and Wang, 2022). Additionally, the development of new therapeutic agents and strategies based on pharmacogenomics aims to combat drug resistance and optimize treatment efficacy (Erickson; Carlson, 2020). These innovations promise to transform the landscape of obstetric medicine in the coming years.

Prophylactic administration of uterotonics immediately after delivery significantly reduces the incidence of PPH. Oxytocin is frequently used, although its excessive use can lead to complications (Li; Chang and Wang, 2022). However, the effectiveness of prophylactic oxytocin may be reduced in women who were not exposed to oxytocin during labor, highlighting the complexity of prophylactic management of PPH and the importance of individualizing therapeutic approaches. Early diagnosis of PPH is crucial and involves continuous monitoring of vital signs and precise estimation of blood loss (Erickson; Carlson, 2020). This preventive approach could be key to reducing the mortality and morbidity associated with PPH.

The initial management of postpartum hemorrhage (PPH) involves investigating the causes and implementing supportive measures, such as the insertion of a urinary catheter and the administration of supplemental oxygen. The use of crystalloids for volume resuscitation is preferred, and tranexamic acid has shown significant benefits when administered within the first three hours after the onset of hemorrhage (Giurazza *et al.*, 2021). The WOMAN study, which recruited more than 20,000 women with PPH, corroborated these findings by demonstrating that intravenous tranexamic acid reduces deaths from bleeding by about one-third when administered promptly (Brenner *et al.*, 2023). Additional measures include the use of sulprostone, intrauterine balloon tamponade, and, if necessary, surgical procedures such as B-Lynch suture and pelvic artery embolization (Brenner *et al.*, 2023). When conservative approaches fail to control the hemorrhage, surgical and radiological interventions, such as pelvic artery embolization (PAE) and vessel ligation, are recommended, despite limited evidence supporting their efficacy. PAE, for example, aims to reduce uterine blood flow to allow uterine involution to occur, but the rich vascularization of the female pelvis may limit the effectiveness of this technique (Corvino *et al.*, 2021).

In extreme situations where all conservative interventions fail, peripartum hysterectomy may be necessary as a last resort. This procedure is performed to ensure hemostasis and save the patient›s life, but it results in infertility and can be associated with substantial morbidity and psychosocial sequelae. The decision to perform a hysterectomy is complex and must consider all risks and benefits, as well as the long-term impact on the patient›s quality of life (Corvino *et al.*, 2021).

Thus, postpartum hemorrhage remains a significant challenge in obstetrics, requiring a multidisciplinary approach and the integration of new technologies to improve maternal outcomes. The prevention and early management of PPH, combined with individualized therapeutic interventions, are crucial to reducing the mortality and morbidity associated with this condition. As medical and technological innovations continue to evolve, it is expected that the management of PPH will become even more effective, providing better outcomes for women worldwide.

EPIDEMIOLOGY

Postpartum hemorrhage (PPH) occurs in approximately 6% of all deliveries, with severe cases accounting for 1%-2%. It is the leading cause of maternal mortality worldwide, responsible for about 25% of pregnancy-related deaths, totaling approximately 70,000 annual deaths (Neary *et al.*, 2021). The prevalence is higher in developing countries but is also increasing in developed countries. PPH predominantly affects women of reproductive age, with higher incidence among those with risk factors such as multiparity, previous cesarean sections, and multiple pregnancies (Feduniw *et al.*, 2020). In the United States, Black women have a threefold higher risk of dying from pregnancy complications compared to White women.

Historically, PPH has been a persistent concern in obstetrics. Recently, there has been an increase in the incidence of PPH in developed countries, possibly due to factors such as rising cesarean rates and advanced maternal age. Changes in obstetric practice and improvements in early diagnosis and treatment have also influenced these trends (Ashwal *et al.*, 2022).

Risk factors for PPH include uterine atony, which accounts for 70% of cases, followed by placental problems, trauma, and coagulopathies (Feduniw et al., 2020). Other risk factors include obesity, advanced maternal age, multiparity, prolonged or very rapid labor, and medical conditions such as maternal hypertension and prepartum anemia (Chainarong; Deevongkij and Petpichetchian, 2022).

The maternal mortality rate due to PPH is significant. It is estimated that PPH is responsible for about 25% of maternal deaths globally, with higher incidence in low- and middle-income countries. In the United States, the mortality rate is higher among Black women, reflecting racial and socioeconomic disparities in access to and quality of obstetric care (Borovac-Pinheiro *et al.*, 2021). Prevention and early diagnosis are crucial in reducing the morbidity associated with PPH. Prophylactic administration of uterotonics immediately after delivery reduces the incidence of PPH by 50% and severe PPH by 40% (Omotayo *et al.*, 2021). Diagnosis is based on clinical evaluation, with visual estimation of blood loss and weighing blood-soaked products being common methods, though often imprecise.

Protocols for managing PPH include medical interventions, intravenous fluid and blood product resuscitation, the use of uterotonic medications, and surgical options. Uterine artery embolization stands out as a minimally invasive treatment that preserves the uterus. In more severe cases, hysterectomy may be necessary, though it is associated with high morbidity and psychosocial sequelae (Franke *et al.*, 2021). PPH represents a significant challenge in modern obstetrics. Effective prevention, early diagnosis, and appropriate management are essential for improving maternal outcomes and reducing the mortality associated with this critical condition (Liu *et al.*, 2021).

DIAGNOSIS

The diagnosis of postpartum hemorrhage (PPH) is a daily challenge faced by obstetric care worldwide. This condition is often undetected or detected late, compromising prognosis and maternal health. Severe maternal hemodynamic changes can be avoided with early diagnosis and rapid treatment, accelerating the return to health, preventing further consequences, and reducing maternal morbidity and mortality rates (Ruiz *et al*., 2023; Gallos *et al*., 2023). Effective measurement of blood loss, performed in various ways, is crucial to avoid a late diagnosis but also poses one of the biggest challenges in correctly diagnosing PPH, as blood loss is often underestimated. It is most commonly performed through visual estimation, weighing of surgical sponges and drapes, the use of graduated collectors along with clinical criteria and shock index, and recent diagnostic advances such as the use of artificial intelligence systems with colorimetry (Ruiz *et al*., 2023; Gallos *et al*., 2023).

PPH is characterized by significant blood loss following delivery, specifically defined as blood loss exceeding 1,000 mL accompanied by signs of hypovolemia within the first 24 hours postpartum. During a cesarean section, it is crucial to accurately quantify blood loss and continuously monitor the woman's hemodynamic status to prevent PPH. Distinguishing between blood and amniotic fluid is essential, usually performed using separate suction containers or measuring amniotic fluid prior to collection.

Strict monitoring of vital signs (heart rate, blood pressure) and the shock index is essential for diagnosing PPH. The physiological response to hemorrhage plays a crucial role in the early identification of high-risk cases. Measurement of hemoglobin (Hb) and/or hematocrit (Ht) before and after delivery is highly accurate for assessing blood loss. Healthcare teams trained in postpartum blood loss quantification methods show more robust results. Current methods use prenatal data, such as medical history and risk factors, to predict severe PPH. Ultrasound and magnetic resonance imaging (MRI) can be used to evaluate conditions such as placenta previa and uterine anomalies, effectively excluding certain factors (Pingray *et al*., 2024; Alvez *et al*., 2020; Lu *et al*., 2024).

To effectively evaluate and manage postpartum hemorrhage, frequent monitoring of women's hemodynamic status is crucial, ideally every 15 minutes during the first 2 hours postpartum, and observation of clinical signs of internal bleeding, such as assessment of uterine fundal height. It is vital to evaluate postpartum vaginal blood loss using quantitative methods or estimates such as counting and weighing surgical sponges. In cases of suspected internal hemorrhage, urgent ultrasound is recommended for early diagnosis. The Obstetric Shock Index (OSI), calculated by dividing heart rate by systolic blood pressure, can be used as a clinical decision support tool. Prenatal platelet count has proven useful in predicting severe PPH, with low levels associated with a higher risk of complication. Various methods are used to estimate blood loss, including visual assessment, weighing surgical sponges, using calibrated collection devices, and comparing hemoglobin (Hb) and/

or hematocrit (Ht) levels. The application of technologies such as colorimetry using digital devices can enhance the accuracy of blood loss quantification.

Pregnant women with a history of previous cesarean sections should undergo ultrasound to locate the placenta, especially in cases of placenta previa or suspected placenta accreta, indicating the need for delivery in a tertiary care setting due to the high risk of PPH. These strategies aim to improve early diagnosis and appropriate management of PPH, reducing complications and improving outcomes for patients (de Moreuil *et al*., 2023; Ruiz *et al*., 2023).

Various gestational conditions can lead to postpartum hemorrhage (PPH) and consequently make it difficult to distinguish symptoms in their early stages. Uterine atony, placenta accreta, lacerations of the birth canal, placental disorders, and coagulopathy are examples of conditions that, like PPH, present with heavy vaginal bleeding, low heart rate, sweating, dizziness, and altered consciousness. In these cases, a comprehensive ultrasound evaluation, physical examination, and vital signs assessment are necessary to accurately detect the etiology of the bleeding, ensure the correct diagnosis, and provide specific treatment for each situation (Pingray *et al*., 2024; Alvez *et al*., 2020; Lu *et al*., 2024).

With the established consensus on a single definition, independent of the specific characteristics of each delivery, new protocols are being implemented, from early detection to treatment. Regarding the initial response phase, an individualized approach is expected, evaluating blood loss through quantitative measurements (counting and weighing), complemented by monitoring the woman's hemodynamic status (ideally every 15 minutes during the first 2 hours) and clinical signs (assessing the height of the uterine fundus). In addition, quantitative measurement and monitoring should be incorporated into routine practice, along with strategies to prevent PPH. It is also crucial to consider coagulopathy as a possible cause of hemorrhage, requiring specific guidelines on the appropriate blood products for the woman's context (Pingray *et al*., 2024).

Regarding biomarkers linked to severe postpartum hemorrhage, platelet count was the only one significantly associated. It was observed to be low in women in the prepartum phase, and consequently, those who had severe PPH in the postpartum phase. This mechanism is explained by the formation of clots and hemorrhage control conducted by platelets (de Moreuil *et al*., 2023).

Analysis of the teams present at delivery shows that the better trained the care team is in postpartum blood loss quantification methods, the fewer discrepancies and more reliable the quantifications will be. This leads to early diagnosis, determination of the cause of the hemorrhage, and the best course of action for each case, reducing maternal mortality rates due to postpartum hemorrhage (Ruiz *et al*., 2023).

TREATMENT

In the occurrence of abnormal postpartum uterine bleeding, conservative treatment is initially performed. To reduce bleeding, the Hamilton maneuver is performed on anesthetized patients or those with higher tolerance to bimanual uterine compression, or the Chantrapitak maneuver is used. Continuous monitoring of the patient is essential for calculating the shock index, and two large-bore intravenous accesses are established for the infusion of crystalloids, medications, and blood tests (blood typing, crossmatching, complete blood count, coagulation profile, fibrinogen, electrolytes, clot test, and in severe cases, lactate analysis and blood gas analysis). Oxygenation with a face mask (100% O2 at a flow rate of 8 to 10 liters per minute) and permanent urinary catheterization should also be instituted. Additionally, measures such as elevating the lower limbs, warming the patient, evaluating antibiotic prophylaxis, estimating blood loss, and quickly assessing the etiology with localization of the hemorrhage focus are employed according to the cause of the hemorrhage (Alvez *et al*., 2020; Hofer *et al*., 2023).

Uterine massage is a technique used to stimulate uterine contraction and reduce blood loss. To perform bimanual uterine compression, either the Hamilton or Chantrapitak maneuver can be used (Lu *et al*., 2024). Another mechanical therapy is the use of an intrauterine balloon for tamponade. Its primary indication is when medications do not adequately control the hemorrhage or cannot be administered due to contraindications. These devices apply pressure to the vasculature by expanding against the internal walls of the uterus for 12 to 24 hours. Contraindications include pregnancy, internal genital infections, abnormalities that distort the uterine cavity, uterine rupture, allergy to balloon components, and arterial bleeding requiring surgical treatment or embolization (D'Alton *et al*., 2021; Alvez*et al*., 2020).

Additionally, the NASG (Non-Pneumatic Anti-Shock Garment) is a segmented neoprene garment that covers the lower limbs and abdomen from the ankle to the last rib, applying external compression. It is a low-cost, easy-to-use device that aids in volume resuscitation and the treatment of severe forms of PPH (Alvez *et al*., 2020).

Tranexamic acid (TXA) is an antifibrinolytic medication that reduces bleeding by inhibiting the interaction of plasminogen with fibrin, thereby reducing plasmin activation and consequently clot breakdown. The WOMAN study demonstrated that early administration within 3 hours after birth reduces PPH-related deaths and the need for surgical intervention to control hemorrhage without increasing the risk of vascular occlusive events (McLintock, 2020). This placebo-controlled clinical trial conducted in 21 countries analyzed the impact of TXA on 20,021 women with PPH > 500 mL after vaginal delivery or > 1,000 mL after cesarean section. The World Health Organization (WHO) recommends the intravenous administration of 1g of TXA diluted in 100mL of 0.9% saline solution. If bleeding continues after 30 minutes or restarts within 24 hours, a second intravenous dose of 1g is recommended (Roberts; Brenner and Shakur-Still, 2023; D'Alton *et al*., 2020).

Uterotonics and tranexamic acid should be the first medications administered. As a first choice, oxytocin should be infused slowly (5 units over three minutes), followed by 20 to 40 units in 500 mL of saline solution infused at 250 mL/hour. A maintenance dose of 125 mL/hour for 4 hours should be administered. In more severe cases of uterine atony, this maintenance can be considered for up to 24 hours (67.5 mL/hour or 3 units/hour) with monitoring for water intoxication (Alvez *et al*., 2020).

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If there is no response to oxytocin and if there is no hypertension or use of protease inhibitors, the second-choice medication is methylergonovine at a dose of 0.2 mg intramuscularly, which can be repeated after 20 minutes. The third and final option for uterotonic medication is prostaglandin, with rectal administration of 800 to 1,000 mcg of misoprostol or sublingual administration of 600 mcg (Alvez *et al*., 2020).

Blood component transfusion is essential for patients with significant blood loss. Early consideration of coagulopathy treatment is crucial, especially in etiologies with a higher risk of coagulopathy, such as abruptio placentae. The use of red blood cells, fresh frozen plasma, and platelets in women with PPH > 1,500 mL has been shown to be effective in reducing progression to severe PPH (McLintock, 2020).

Common hemostatic methods include tamponade of the uterine cavity, uterine compression sutures, uterine artery ligation, and blood volume supplementation. Uterine compression sutures are widely used in obstetrics to achieve hemostasis by compressing the uterus with sutures. However, there is still room for improvement due to the complexity of the procedure, long recovery time, and increased risk of infection following maternal exposure (Liu *et al*., 2024).

A vacuum intrauterine device, known as the Jada System, uses low-level vacuum to induce uterine myometrial contraction and control postpartum uterine bleeding. This device is designed to offer rapid and effective treatment of hemorrhage, being applied for at least 1 hour. A multicenter prospective study conducted in 12 centers in the United States evaluated the effectiveness of this device, observing a success rate in treatment in 96% of participants (D'Alton *et al*., 2020).

Another device studied to control PPH is the Bakri Balloon, which can mechanically compress the uterine wound and promote local coagulation. Among various conservative procedures, the Bakri Balloon has notable advantages, such as minimal local requirements, little training needed, and high efficacy in maintaining fertility. A retrospective study conducted in China demonstrates that precise and timely intervention in the placement of the Bakri Balloon was crucial to control PPH in cesarean deliveries, especially in women with placenta accreta (Chen *et al*., 2023).

Treating pathological conditions related to uterine hemorrhage, especially PPH, presents several significant challenges. One of the main obstacles is the early and accurate diagnosis of the underlying cause of the hemorrhage. It is essential to quickly identify whether the cause is due to uterine atony, cervical trauma, retained products of conception, or another etiology to initiate appropriate treatment as soon as possible. Administering medications such as uterotonics and using established protocols are crucial steps in the first line of treatment. However, when these measures fail, prompt referral to a specialized tertiary center is necessary. In these centers, trained teams are prepared to intervene with more advanced techniques, such as using an intrauterine balloon for tamponade or aspiration systems. The additional challenge lies in the need for rapid and effective intervention, especially due to the potential hypovolemic shock that can occur quickly in severe cases of PPH. Coordination among healthcare professionals, the availability of adequate resources, and the knowledge to apply these techniques effectively are fundamental to ensuring the best possible health outcomes (Gallos *et al*., 2023; Alvez*et al*., 2020; Brenner *et al*., 2023).

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