

## A SYSTEMATIC REVIEW ON EPIDEMIOLOGY, PREVENTION AND MANAGEMENT OF EARLY POSTPARTUM HEMORRHAGE

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### **ABSTRACT**

Early Postpartum Hemorrhage (EPH) is one of the leading causes of postpartum mortality. It is defined as blood loss of at least 500 mL after vaginal or 1000 mL following cesarean delivery within 24 hours postpartum. The following paper includes literature review aimed to estimate the incidence and predictors of early postpartum hemorrhage (EPH). Available prevention and treatment methods were also assessed. The inclusion criteria for the study were met by 52 studies. The exact frequency of EPH in different populations varies from 1.2% to 12.5%. Maternal, pregnancy-associated, labor- correlated and sociodemographic risk factors seem to be important predictors of EPH. In these cases appropriate prophylaxis should be considered. However, EPH may occur without previous risk factors. The main reason for

EPH is uterine atony which contributes to up to 80% of cases of postpartum hemorrhage (PPH). Other common reasons for PPH include genital tract injuries, placenta accreta or coagulopathies. Interestingly, the majority of uterotonics seem to have a similar effect. However, carbetocin seems to be the most effective in certain situations. Appropriate diagnosis of EPH is the most important issue. The treatment should be causative. The first-line treatment should include uterotonics. Surgical interventions, if required, should be performed without delay, although preoperative uterine tamponade should be considered due to its high effectiveness. Medical staff training in medical simulation centers is an important

factor that improves the outcomes of EPH treatment. It provides adaptation to hospital protocols, team work improvement, self-confidence building, more accurate blood loss evaluation and reduced perception of stress. The implementation of systematic trainings provides better outcomes in the future.

**KEYWORDS:** Postpartum hemorrhage; delivery; perinatology; medical simulation.

## INTRODUCTION

Early postpartum hemorrhage (EPH) is usually defined as blood loss of at least 500 mL following vaginal delivery (VD) or 1000 mL following a cesarean section (CS) within 24 hours postpartum.<sup>[1-3]</sup> Late postpartum hemorrhage (LPH) occurs after 24 hours following labor and complicates 0.23% of deliveries. According to the American College of Obstetricians and Gynecologists, EPH may be recognized with the presence of signs of hypovolemia within 24 hours after delivery.<sup>[4]</sup> EPH may be divided into minor (500–1000 mL), moderate (1001–2000 mL) and severe (> 2000 mL).<sup>[3]</sup> This complication significantly impacts global women's health as the most frequent reason for perinatal deaths all over the world.<sup>[2]</sup>

The volume of blood loss is usually estimated visually. However, this method is connected with a high possibility of error. The underestimation occurs in 30 to 50% if it is only visual.<sup>[1]</sup> To make the assessment more objective it is highly advisable to count utilized medical materials, such as surgical towels and drapes. Estimating weight difference of dry unused materials and those soaked with blood seems to be another effective method. Using a calibrated collector bag is also recommended for a more accurate blood loss estimation. Gravimetric blood loss measurement includes weighing bags after delivery.<sup>[5]</sup> Modified Brecher's formula consists in hemoglobin measurement after delivery which makes the evaluation more accurate.

Undiagnosed abnormal postpartum blood loss (UP- PBL) is defined as decrease in hemoglobin level of at least 2 g/dL without any symptoms or signs of EPH.<sup>[6]</sup> Apart from an increased risk of maternal mortality (12 to 17.2%) EPH may lead to further serious complications related to severe anemia, such as acute kidney injury (29.3%), hepatic failure, Sheehan Syndrome, adult respiratory distress syndrome (24.6%) and disseminated intravascular coagulopathy (DIC) (11.7%).<sup>[2]</sup>

The following paper includes a literature review of recent studies regarding PPH. The main aim of the study was to estimate the incidence and predictors of EPH. Available prevention and treatment methods of EPH were also assessed.

## MATERIAL AND METHODS

The authors searched PubMed database for articles concerning postpartum hemorrhage published from June 2014 to April 2019. Searching with 'postpartum hemorrhage' query revealed 186 original studies. The inclusion criteria for the study were: a uniform definition of EPH (blood loss of at least 500 mL after VD or 1000 mL following CS within 24 hours postpartum), a study group  $\geq 250$  patients and the English language of the manuscripts. 52 studies met the inclusion criteria (Fig. 1).

## RESULTS

According to the WHO postpartum hemorrhage is one of the leading reasons for postpartum mortality, especially in developing countries of Asia (30.8%) and Africa (33.9%). Conversely, in developed countries the average mortality rate was estimated to 13.4% of all PPHs (1.2–49.6%). The exact frequency of EPH in different populations is shown in Table 1<sup>[6–10]</sup> and varies from 0.4% to 33%.

### Etiology

The leading cause of EPH is uterine atony which contributes 60 to 80% of those complications and 20–30% of mothers' deaths.<sup>[10]</sup> Childbirth via CS may also lead to PPH. There are only few papers concerning PPH occurrence after CS in which PPH ratio amounted to 0.3–6%.<sup>[11]</sup> The prevalence of PPH has increased over the past few years, which may be caused by an increased incidence of uterine atony and CS. The number of emergency hysterectomies (5.8–6.3/10,000 births), blood transfusions, performing B-Lynch sutures (10.7/10,000 births) and uterine artery embolizations are the most correlated with uterine atony. Other common causes of EPH are genital tract injuries or episiotomy (16.7%), placental abnormalities (4 to 36% of retained placenta, abnormal placental implantation or placental abruption) or coagulopathies (e.g. anticoagulant treatment or DIC) (7.4%).<sup>[10]</sup>

### Risk factors

Unmodifiable risk factors of EPH include a history of EPH (OR = 2.3–10.5) and a delivery of a large for gestational age.

**Table 1: Frequency of PPH [3, 10, 13, 15, 17–35] identified using a multivariable analysis, were: retained placenta (OR 3.5, 95% CI 2.1–5.8.**

Country	Years	Population	PPH frequency
Israel	1988–2002	154 311	0.4%
Africa Asia Europe	2008	505 379	Severe EPH: 0.3–3.8% 2.7% 5.5%
Asia, Africa, Middle East, Latin America (data from 28 countries)	2010–2011	274 985	VD: 1.2%
WHO	2012		2%
USA	1995–2004	870 000	2.93%
USA	1999–2008	8 500 000	3%
USA	2006–2012	1 339 397	CS: 2%
Canada	2003–2010	2 200 000	6.2%
Norway	1999–2004	307 415	Severe EPH: 1.1%
Norway	2008–2011	43 105	Severe EPH: 2.5%
United Kingdom	2003–2013	24 230	CS: 12.4%
France	2004–2006	146 781	6.4%
France	2016	3 917	VD UPPBL: 11% VD EPH: 11.2%
Nederland	2000–2008	1 599 867	4.5%
Denmark	2008	147 132	CS: 2.24% VD: 1.75%
Ireland	1999–2009	649 019	2.6%
Spain	2017	1 352 691	3%
Brazil	2010	9 555	12.5%
RPA	2012	15 725	2.5%
Nigeria	2014	4 889	3.4%
India	2010–2012	96	CS: 1.8% VD: 1.3% Instrumental: 5.3%
Tunisia	2010–2013	39	Severe PPH included to the study
Japan	2011	1 294	VD: 33%
German	2010–2013	1 550	8.4%

Fetus (> 4000 g) (OR = 1.7–1.9). Uterine abnormalities such as uterine fibroids (OR = 2.0–2.7) also played an important role in the incidence of EPH.<sup>[6]</sup> Pregnancy complications, such as maternal anemia (hemoglobin level below 9 [g/dL]) (OR = 4.1), hypertensive disorders (OR = 1.6–3.6), gestational diabetes mellitus (OR = 1.6), a multiple gestation (OR = 1.5–3.7), polyhydramnios (OR = 2.6) and preterm delivery (OR = 2.6) were significantly correlated with EPH.<sup>[12]</sup> Maternal fever (OR=1.7–2.5), labor induction (OR=1.5–1.7) and instrumental (OR = 1.2–2.9) or operative delivery (OR = 1.4–5.7) increase the risk of EPH.

Retained placenta increase the risk of hemorrhage immediately after delivery (OR = 3.5–4.1) as well as after subsequent pregnancy.<sup>[12]</sup> Sociodemographic factors, such as obesity [BMI > 35 (kg/m<sup>2</sup>)] (OR = 2.3), mother's age over 35 years (OR = 1.5–1.7) and Middle Eastern ethnicity (OR = 1.8) increase the risk of EPH.<sup>[13]</sup> Conversely, smoking (OR = 0.8) during pregnancy seems to reduce the risk of EPH.<sup>[6,13]</sup> All the mentioned risk factors of PPH are shown in Table 2.<sup>[6,10,14]</sup> Risk factors of UPPBL are similar to those in EPH and include Asian ethnicity (aOR = 2.3), previous cesarean section (aOR = 3.4), episiotomy (aOR = 2.6), primiparity, prolonged labor, instrumental delivery and retained placenta.<sup>[6]</sup>

### Prevention

WHO guidelines for the prevention of EPH include a thorough assessment of possible risk factors as the primary prophylaxis of this complication. Moreover, pharmacological prophylaxis includes 10 IU of oxytocin in bolus (intravenously or intramuscularly), 100 µg of carbetocin (intravenously or intramuscularly), misoprostol (400 µg or 600 µg, per os), ergometrine/methylergometrine (200 µg, intramuscularly or intravenously) or oxytocin and ergometrine together (5 IU and 500 µg, intramuscularly).<sup>[15]</sup> According to German guidelines 3–5 IU of intravenous oxytocin or 100 µg of intravenous carbetocin should be recommended (Tab. 3.).<sup>[1]</sup> Conversely, RCOG suggested 0.5–1 g of intravenous injection of tranexamic acid, carboprost or misoprostol to be superior to oxytocin prophylaxis. However oxytocin and/or ergometrine or 100 µg of intravenous carbetocin is highly advised, similarly to the guidelines of the Society of Obstetricians and Gynaecologists of Canada.<sup>[3]</sup> RCOG guidelines suggest that the prevention of minor EPH with 5 IU and 10 IU of oxytocin has comparable results.<sup>[3]</sup> ACOG recommends to prevent EPH by using 10 IU of oxytocin intramuscularly or intravenously as the most effective.<sup>[4]</sup> An intravenous bolus of tranexamic acid at a dose of 0.5–2 g (15–30 mg/kg BW) should also be considered.<sup>[2,3]</sup> Moreover, it could be used as prophylaxis of EPH after VD.