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Postpartum Hemorrhage: A Life-Threatening Condition, Challenges, and Solutions

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Abstract: Postpartum hemorrhage (PPH) is an obstetric emergency that can happen following a vaginal or cesarean delivery. Postpartum hemorrhage is the leading cause of morbidity and mortality among mothers globally, and it is still prevalent in many undeveloped countries. According to estimates by the World Health Organization (WHO), PPH is responsible for 25% of maternal fatalities worldwide. PPH can result in significant morbidity in addition to death because of side effects such hypopituitarism of postpartum, respiratory distress syndrome of adults, congelation, shock state. The primary cause of this disease is uterine atony, which also raises the risk of this disease for iatrogenic trauma. In order to significantly lower morbidity caused by maternal reasons and extinction, it is necessary to be aware of these facts like, anticipate and prevent uterine atony, avoid unnecessary cesarean sections, episiotomies, and other genital tract trauma, and closely monitor the vital signs of mother. Lab tests, particularly testing for clotting of blood, and prompt detection of the source of Postpartum bleeding are also significant. We analyzed machine learning methods for predicting postpartum hemorrhage. A machine learning algorithm can predict postpartum bleeding following vaginal birth. Further Conduct research to examine relevant factors and prepare large amounts of data, including hundreds of thousands of instances.

Keywords: Postpartum hemorrhage, Coagulopathy, Uterine atony, Tranexamic acid, Maternal, Atony, Gestation

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Introduction

Maternal mortality is mostly caused by postpartum hemorrhage, which accounts for 25% of all maternal fatalities from obstetric causes. Postpartum bleeding is now technically described as abnormal loss of blood exceeding more than 1000 ml. However, both Revitalize and ACOG

emphasize that loss of blood (500-999 ml) is abnormal and should prompt heightened observation and, if clinically required, treatments. Postpartum complications, such as hemorrhage and sepsis, increase the risk of morbidity and death for women in 24 h after giving birth. In other words, upto1000 ml or more loss of blood, or loss of blood with concomitant indications of hypovolemia, that happens within a day following delivery, regardless of mode of delivery, is now described as postpartum hemorrhage (Alfirevic *et al*., 2007). These amount of blood loss creates hemodynamic instability in the mother. The majority of PPH instances, or "primary PPH," happen within a day following delivery and following birth, secondary PPH occurred between the next day and six weeks. Postpartum bleeding remains the leading cause of maternal mortality in developing countries. It now ranks second or third in wealthy nations for direct motherly fatalities, after thromboembolic and hypertensive problems. Two problems make estimating the prevalence of Postpartum bleeding more difficult: an absence of a standard definition for the condition and imprecise clinical assessments of loss of blood at the time of birth (Westcott *et al*., 2022). Even when all precautions are taken, roughly 3% of vaginal births result in serious post-partum bleeding.

Risk factors:

Any pregnancy that lasts longer than 20 weeks gestation may result in postpartum hemorrhage. PPH is related with a number of risk factors, but it's crucial to remember that it often strikes suddenly (Anderson *et al*., 2007; Van Steijn *et al*., 2021)

The study's limitation is that risk factors can only be assessed in retrospect. According to one study (Pavord et al., 2015), just thirty-nine out of hundreds of Postpartum bleeding-affected women had any independent risk factor for the condition identified. It is justified to use preventive techniques to all parturients due to the incapacity to precisely identify women with a chance of developing this disease.

Antenatal risk factors: The only recognized prenatal risk factors for PPH in the clinical case were higher BMI and fetal macrosomia. Despite being iron deficient, the patient was not anemic. The immediate estimated postpartum blood loss was significant, indicating a PPH, and the bleeding did not cease after uterine massage and therapeutic uterotonics (Bannow *et al*., 2018; Watkins *et al*., 2020).

Failure to perform an early coagulation test: A coagulation test can assist diagnose unanticipated coagulopathy. A VE-POC test can offer a result in 15 min if it is available. Even if a traditional laboratory-based fibrinogen assay is delayed by 60 min, it may still be useful if the PPH is not controlled by the first maneuvers (Perlman *et al*., 2019; Polic *et al*., 2022).

Causes:

There are several possible causes of PPH, but uterine atony is by far the most frequent (Sentilhes *et al*., 2015). Another easy and successful technique to recall and recognize the precise reasons is the "Four Ts"-(1-Tone, 2-Tissue, 3-Trauma, and 4-Thrombin).

Tone (*Uterine atony*): Uterine atony, as well as inability to contract and retract myometrial muscle fibers, can result in severe bleeding and hypovolemic shock. Absolute or relative uterine overdistension is a key risk factor for atony. An estimated 70% of PPH cases are thought to be caused by this (Blomberg , 2011). After birth, a deficiency in contraction of uterine restricts the uterus from contracting normally, obstructing the gaping arteries and stopping the bleeding, thereby ensuring mechanical halting of bleeding. Several other possible factors for uterine inertia are as follows:

- Uterine overdistention
- consumption of large amounts of oxytocin
- Rapid or prolonged labor
- Myometrial laxity that is associated with multiparity

- Chorioamnionitis

Trauma: Damage to the vaginal tract can develop naturally or as a result of delivery interventions (Borovac-Pinheiro *et al*., 2018). The biggest risk comes from internal version and extraction of a second twin; nevertheless, uterine rupture can also occur as a result of exterior version.

The main reason for develop ingtrauma to the genital tract of upper portion is uterine rupture, which can happen when a scar from a previous cesarean section or myomectomy separates. Additionally, bleeding might result from direct uterine injury during the cesarean delivery or from damage to nearby vascular structures like the uterine artery or wide ligament varicosities. Perineal, cervical, or vaginal lacerations are examples of lower genital tract trauma (Oyelese *et al*., 2010; Sentilhes *et al*., 2016). These injuries can happen on their own or as a result of episiotomies, obstetric procedures, or surgical instrumented births.Some elements of dangerare as follows:

- Caesarean birth
- Fetal malposition
- Fetal macrosomia
- Perineotomy

Tissue: The placenta detaches and is expelled as a result of uterine contraction and retraction. Complete placental separation and evacuation allows for continuous retraction and adequate blood vascular occlusion. Retained placental pieces hinder proper uterine contraction, resulting in uterine atony and PPH. This system of classification is based on the invasion depth; also this is readily recalled by alliteration (Wetta *et al*., 2013).

Thrombosis: Coagulation problems are an uncommon cause of PPH that is generally detected before birth. Idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), von Willebrand disease, and hemophilia are examples of these illnesses (Callaghan *et al*., 2010). Patients who have a history of menorrhagia or who have a family history of similar abnormalities should be suspected of having coagulation issues. Those women who have factor XI deficiency or hemophilia, they are at an elevated danger of both early and late PPH (16%-22% for early and 11%-24% for late). Massive antepartum hemorrhage (PPH), sepsis, severe preeclampsia, amniotic fluid embolism, tissue necrosis, placental abruption, and acute fatty liver of pregnancy are examples of these.

Obesity: Obesity is becoming more prevalent on a worldwide scale. An examination of births showed that over 25% of women who gave birth were fat.

Advanced maternal age: A pregnancy in a woman older than 35 is referred to as advanced maternal age (AMA) (Shakur *et al*., 2010; Butwick *et al*., 2021). Due to the use of assisted reproductive technologies and postponed childbirth, AMA pregnancies are on the rise. It increases 8 times in last 30 years.

Precautions that should be taken during postpartum hemorrhage:

It is important to take precautions to reduce the effects of postpartum hemorrhage, including as recognizing and treating anemia prior to delivery, understanding the mother's views regarding blood transfusions, and stopping routine episiotomy. Actively managing the third stage of labor (number needed to treat [NNT] to prevent one occurrence of postpartum hemorrhage) is the best preventive measure.

Diagnostic Managements for PPH:

Many women will lose more than 500 ml in the presence of no medical consequences, while others will loss a less amount of blood but remain at risk of poor outcomes.

Ultrasonography: Each woman in the study had ultrasonography and physical examination. Commercially accessible real-time equipment was used for all ultrasound testing, which included a 5-MHz vaginal test and a 3,5-MHz transabdominal convex test (Sharma *et al*., 2003; Smith *et al*.,

2013).

Magnetic resonance imaging (*MRI*): Information gathered included patient demographics, obstetric history, gestational age at imaging, surgical grading of PAD, operation details, anticipated blood loss, blood transfusion requirements, and specimen histopathology reports (if specimens were submitted for testing).

Treatment of Postpartum Hemorrhage (*Table 1*):

Many trials and interventions in postpartum hemorrhage control have focused on the introduction of drills and therapies. However, the diagnosis of bleeding is of major significance, and the accuracy of blood loss estimation is critical to enable proper response by warning of imminent hemorrhagic shock (Turgut *et al*., 2013; D'Alton *et al*., 2021).

Since blood loss may not be apparent in the postpartum period, especially following a caesarean operation, it is crucial to accurately estimate the hemodynamic condition (Usha, 2019). Early clinical diagnosis of PPH-related conditions is necessary to start appropriate therapy (pharmacological and/or surgical).

Pharmacological treatment or Drugs use in Postpartum Hemorrhage:

Oxytocin: In addition to being used as a first-line treatment, during the third stage oxytocin (also known as pitocin) is frequently prophylactically given as part of active labor management. Oxytocin injections as a single intravenous dosage may result in severe hypotension (de Groot et al., 1998). It does not seem that oxytocin injections into the umbilical vein are helpful for preventing PPH.

Carbetocin: Carbetocin possesses comparable pharmacologic qualities to oxytocin, but it additionally benefits from thermal stability and a half-life that is four to ten times longer, could be less harmful than oxytocin while yet being more effective. A single, gradual intravenous injection of 100 mg is advised (Blum *et al*., 2007; Stewart *et al*., 2021).

Ergot alkaloids (*ergometrine, ergonovine, methylergonovine*): These drugs cause prolonged uterine contractions by partially agonizing alpha-adrenergic receptors, weakly antagonizing dopaminergic receptors, and agonizing serotonergic receptors. These drugs should never be injected intravenously; instead, they should be taken orally or intramuscularly. When treating PPH, 0.2 mg should be injected intramuscularly (including directly into the myometrium) and repeated every two to four hours as needed.They typically take 1 to 3 min to start acting, and their half-lives are prolonged to 30 to 120 min.

Prostaglandin analogue: The PG analogues of PGF2α, PGE2, and PGE1, carboprost, sulprostone, and misoprostol are frequently used in clinical practice for the prevention and treatment of PPH.

Injectable prostaglandins (*PGs*): When treating PPH, injectable PG analogs such as carboprost and sulprostone are typically thought of as second-line uterotonics. Their effectiveness has been reported to be between 87 and 92%, and they cause powerful, prolonged myometrial contractions. PGs which are injectable, should be considered only when oxytocin else any other first-line uterotonics fail to induce enough uterine tone.

Carboprost: Natural PGs' quick metabolism restricts their therapeutic utility and encourages the creation of analogs with extended durations of action.The combination of 15-methyl PGF2 and tromethamine is known as carboprost tromethamine.

Misoprostol: To prevent PPH, misoprostol (Cytotec), an analog of prostaglandin E1, can be administered orally, sublingually, rectally, or buccally. The American College of Obstetricians and Gynecologists (ACOG) advises taking 800–1000 mg rectally; dosages range from 200–1000 mg.

Sulprostone: In situations of chronic bleeding despite oxytocin therapy, of sulprostone, a PGE2 analog, is used. Sulprostonecan be considered a safe treatment for people having PPH in various

Table 1: Possible pharmacological agents for prevention and treatment of PPH

DRUGS	DOSES	PREVENT / TREAT	CAUTIONS
Oxytocin	I.U., I.M. or 5 to10 I.U., I.V. to 40 I.U. in 1L Normal saline, 500 -250 ml at a chance	'Preventio n and reatment	In large doses, long-term use can cause water intoxication. Possible fall in blood pressure.
Cyclohexanecarboxylic acid, 4-(aminomethyl)	1 g I.V, over 10 min, might be again give after 30 min (Driessen *et al*., 2011)	Treatment only	Use three hours after the bleeding starts. When administering to individuals who have renal impairment or who also have another coagulation factor, such as prothrombin complex, use care.
Methylergonovine	).2 mg Intra Muscular, recurrent every 2-4 h	reatment	C/I in patients with high blood pressure or cardiac disease Use with care in individuals taking protease inhibitors for human immunodeficiency virus infection.
Carboprost	every 15 to 90 min, administer 2 250 mcg intramuscularly or intramyometrially, for a total dosage of 2 mg.	Treatment only	Patients with severe renal, hepatic, or cardiac illness should avoid to use this medication.
Misoprostol	Prevent: Take 600 mcg by mouth Treatment options include 600–800 mcg taken orally, sublingually, or via injection.		only use at time oxytocin is not present. Use with C/I in patients with cardiac disease

population-based trials with strict medication monitoring.

Surgical approach for treatment of PPH:

Arterial ligation techniques: One of the simplest and most successful surgical procedures for managing PPH that is resistant to early attempts to stop the bleeding is uterine artery ligation. Unilateral artery ligation controls bleeding in 10% to 15% of instances, whereas bilateral ligation controls an additional 75% of cases.

Hysterectomy: In around 1 in 1000 births, a hysterectomy is necessary to treat PPH. The treatment should be reserved for situations when other efforts have failed, and the American College of Obstetricians and Gynecologists advises that if hysterectomy is performed for uterine atony, there should be confirmation that alternative therapy were first tried (Devanayagi, 2020).

Massive Transfusion therapy:

Professional associations generally concur that multidisciplinary bleeding protocols are necessary for managing trauma and PPH. Obstetric hemorrhage protocols are recommended by the American College of Obstetrics and Gynecology,

the European Society of Anaesthesiology, the French National College of Gynaecologists and Obstetricians, the UK Confidential Enquiry into Maternal and Child Health, and The Joint Commission. These regimens use a stepwise escalation of obstetric, surgical, and medicinal measures to avoid PPH development.

The CMQCC Obstetric Hemorrhage Toolkit and other societies recommend a 1:1-1:2 transfusion ratio, which differs from prior recommendations of 6:4:1 or 4:4:1.2

Methods: Time of PPH period and the rate of transfusion are expected to range between 0.4% and 1.6%. Cryo-preservation, a rich supply of Coagulation factor F8, and factor VIII-related antigen (von Willebrand factor), is effective for treatment of low fibrinogen activity (usually<100 mg per dL in patients) and circulated intravenous agglomeration. Depending on the time required for lab tests, clinical accuracy usually dictates the triggerers and models of blood transfusion in the acute phase of Postpartum hemorrhage.

Recombinant factor VIIa (*rFVIIa*): It has been discovered that obstetric hemorrhage regimens that do not respond to transfusion use recombinant factor VIIa (rFVIIa). Although the recommended intravenous bolus dose of rFVIIa during pregnancy is unclear, research in the obstetrical literature suggests a range of 40 to 90 micrograms/kg over 3-5 min. Despite the lack of RCTs, the literature that is currently available shows notable reductions in blood loss, indicating that rFVIIa may be useful in the treatment of severe PPH.

Result and analysis of (*MTP*): Evensen *et al.* (2017) outlined the MTP for institution's labor and delivery unit. To sum up, the decision to activate the MTP is made by the on-site attending obstetrician and/or anesthesiologist.

Side effects of post-partum hemorrhage:

There are many side effects suggested for post-partum hemorrhage:

1. Over-distended uterus (Multiple gestations, polyhydraminos, macrosomia)
2. Primigravitidy
3. Chorioamnionitis
4. Prolonged rupture of membranes
5. Fibroids
6. Previous cesarean delivery,
7. Coagulation disorders
8. Anticoagulant therapy
9. Labor induction and augumentation
10. Prolonged labors
11. Preeclampsia
12. Obesity

Machine Learning (*AI*) *in Postpartum Hemorrhage*:

Current approaches for predicting postpartum hemorrhage rely on risk stratification. Using conventional statistics and machine learning techniques could enhance the ability to forecast (Manjula, 2005). Recent advances in machine learning, which uses advanced computer-driven algorithms to detect patterns in data, have gained popularity due to their superior predictive ability, particularly in determining intensive care unit admission and hospital readmission compared to statistical models. However, these novel techniques have yet to be thoroughly evaluated in obstetrics (Leduc *et al*., 2009).

Methods:

(i) This retrospective cohort study by Westcott *et al*. (2022) was conducted at a single tertiary care facility. The study covered deliveries made by women between the ages of 18 and 55 at New York University Langone Health Tisch Hospital between July 1, 2013, and October 31, 2018 (Kadir *et al*., 1998). Individuals who failed to meet the age requirements and those for whom a blood loss value was either unreported or unavailable were excluded. 497 variables in all were gathered from various sources during the electronic medical record collection process.

Table 2: All models operate at their best when employing gradient enhanced decision trees

MODEL	Precision	AUROC*	Response
Starting	0.982	0.978	0.764
2nd stage	0.981	0.956	0.738
C-section	0.819	0.738	0.321
Normal delivery (1 h)**	0.983	0.838	0.255
Normal delivery (2nd stage)	0.984	0.845	0.255

*AUROC: area under the receiver operating curve; **within one hour of the anticipated admission for a vaginal birth (PPH_040_PMSB)

Table 3: All studies summary

Study No.	Author	Country	Study Population &Sample Size	Definition of PPH	Types of ML Used	Best ML Performance	Performance Parameters	Predicting Factors
1	Venkatesh *et al.* (2020)	USA	152,279 women delivering vaginally or by cesarean section	Blood loss ≥ 1000 mL within 24 hrs	RF, EGBM	EGBM	AUC: 0.931	Antepartum maternal weight; Fetal macrosomia diagnosis during pregnancy
2	Akazawa *et al.* (2021)	Japan	9,894 women delivering vaginally	Blood loss ≥ 1000 mL within 24 hrs	DL, LR, RF, BT, DT	DL	AUC: 0.7065; FPR: 32.64%; FNR: 37.91%	Gestational age; Weight of mother at birth; Weight of mother before pregnancy
3	Liu *et al.* (2022)	China	25,098 women delivering vaginally or by cesarean section	Blood loss ≥ 1000 mL within 24 hrs	RF, KNN, LR, LGB	LGB + LR	AUC: 0.729; Sensitivity: 69.4%	Hematocrit; Shock index; Frequency of contractions; WBC count; Pregnancy-related hypertension; Newborn mass; Amniotic fluid index; Second stage of labor duration; BMI
4	Westcott *et al.* (2022)	USA	30,867 women delivering vaginally or by cesarean section	Blood loss ≥ 1000 mL within 24 hrs	LR, RF, GB, DT, SP	GB	AUC: 0.979; Accuracy: 98.1%; Sensitivity: 76.3%	Body mass index; Admission hematocrit; Cesarean delivery prior to delivery or rupture; Status of the cesarean delivery schedule; Platelet count upon admission

AUC: Area under curve; FPR: False positive rate; FNR: False negative rate; ML: machine learning; RF: Random forest; EGBM: Extreme gradient boosting models; DL: Deep learning; LR: Logistic regression; BT: Boosted tree; DT: Decision tree; KNN: K nearest neighbor; LGB: Light gradient boost; SP: support vector.

Table 4: Regional estimated data of PPH in 2012

	Occurrence of PPH >500 ml		Occurrence of PPH >1000 ml	
Areas	females giving birth: No.	blood loss of >500 ml in women	Areas	females giving birth: No.
Overall	1,003,694	89378	503,046	6,505
Region				
Africa	2738	645	1889	99
Latin America and the Caribbean	23129	2076	15551	386
Northern America	28580	5934	21744	939
Asia	215611	9494	11416	293
Europe	378617	51204	452116	4779
Oceania	355019	20025	330	9

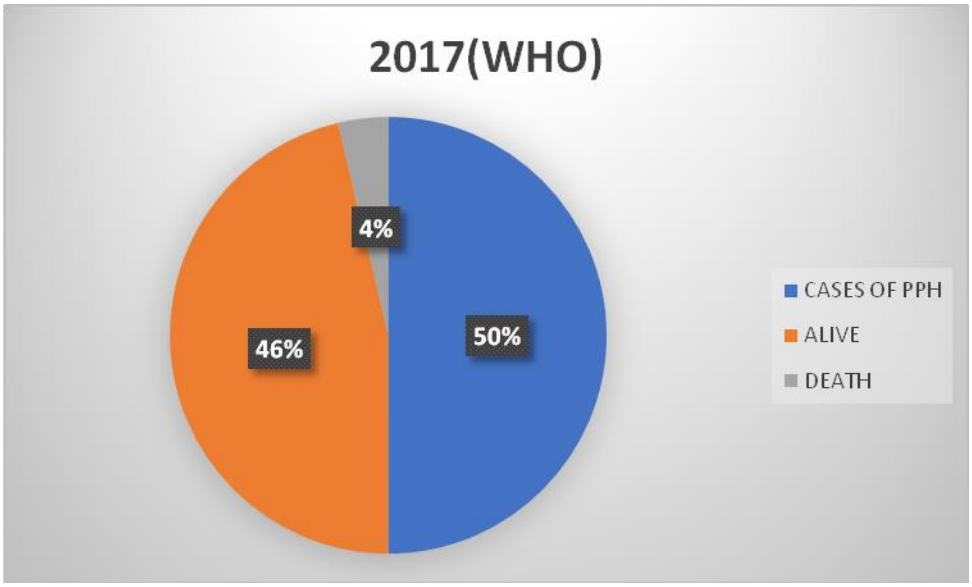

Fig. 1: Worldwide stats of PPH (20170by WHO).

Developed model: The final performance was evaluated by measuring the accuracy, sensitivity, and area under the receiver operating curve (AUROC) for correctly detecting postpartum hemorrhage in an independent test cohort (4631/30,867, 15%; Table 2) (Knight *et al*., 2009).

For the purpose of initial model creation, the delivery cohort was split into training, validation, and test cohorts, consisting of 21,606 (70%), 4630 (15%), and 4631 (15%) patients, respectively. (Table 3) (Stewart *et al*., 2021).

Only one obstetrician who is knowledgeable in electronic medical records made the decision to include the pertinent factors.

(ii) The U.S. Consortium for Safe Labor (2002-2008) dataset was used in a retrospective analysis published in the AJOG (American Journal of Obstetrics and Gynecology) (Nyfløt et al., 2017). A maternal bleeding event was considered severe if at least one blood transfusion unit was required (Grillo-Ardila *et al*., 2012). Patient data from 2002 to 2006 was used for model training, and it was assessed throughout the course of the following two years, excluding patients whose transfusion records were missing (Manjula, 2005; Lamba *et al*., 2016; Bank *et al*., 2023). The area under the precision-recall curve (AUPRC) and the area under the receiver operating characteristic (AUROC)

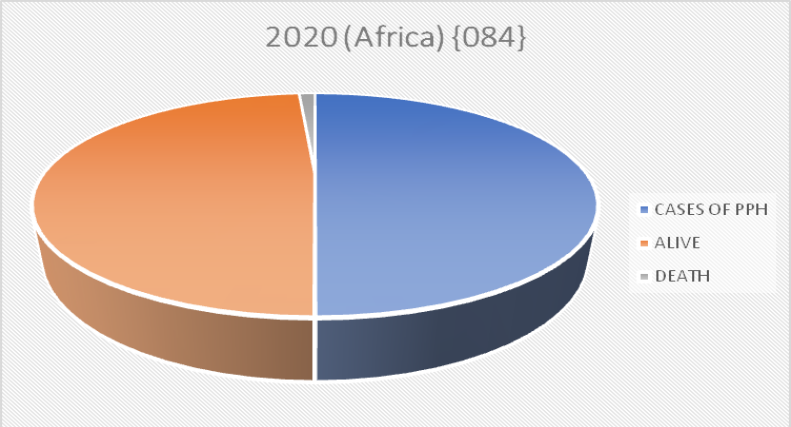

Fig. 2: Worldwide stats of PPH (2020 –Africa, 084).

were used to assess the model (Liabsuetrakul *et al*., 2018).

Of the 142,137 newborns, 3.7% required a blood transfusion. The model performed well in terms of AUROC(0.80) and AUPRC (0.11), demonstrating a roughly threefold development over the previous model (Hancock *et al*., 2015). However, the model underperformed in minority populations when compared to the white patients as the reference when comparing the model's performance and fairness measures with regard to race (AUROC: W:.75, B:0.83, H:0.75, A:0.85 and AUPRC: W:0.11 B:0.11, H:0.08, A:0.06; H= Hispanic, W= White, B= Black, A=Asian)(Table 3).

Global Statistics:

The main cause of maternal death worldwide is severe bleeding after childbirth, known as postpartum hemorrhage (PPH) (Lao *et al*., 2014). PPH affects around 14 million women each year, accounting for over 70,000 maternal deaths worldwide (Jin *et al*., 2016). Even if women survive, they frequently require emergency surgical procedures to stop the bleeding and may be left with a permanent reproductive impairment (Table 4).

Worldwide stats of PPH:

Figures 1 and 2 depict worldwide stats of PPH.

Conclusion

A major contributing factor to maternal morbidity and mortality in both developed and developing nations is postpartum hemorrhage. It is advised to identify patients who are at risk of postpartum hemorrhage, but all expectant mothers should be regarded as at risk as many will experience postpartum hemorrhage even in the absence of known risk factors. While there is no way to prevent postpartum hemorrhage, there are several aspects that can help with optimal care. These include the rate of blood loss, clinical indicators, patient symptoms, shock index, and the physiological reaction to hemorrhage (McLintock, 2020). All of these elements are crucial for identifying a high-risk condition early on. While it is impossible to prevent postpartum hemorrhage (PPH), uterine atony is the main cause of PPH, with most occurrences being preventable. Trauma increases PPH, especially iatrogenic trauma from episiotomies and cesarean deliveries. PPH risk is increased by trauma, particularly iatrogenic trauma following cesarean birth and episiotomies (Jones *et al*., 2023).

Ethical Statement

This is a review article hence no Ethical Approval needed.

Author Contributions

Each author has contributed equally to the study's planning, analysis, writing, and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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