

## RISK FACTORS FOR ATONIC POSTPARTUM HEMORRHAGE: A SYSTEMATIC REVIEW

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### Abstract

**Introduction:** Postpartum bleeding occurs in 3-10% of all deliveries. Although numerous causes exist, uterine atony is the most frequent, accounting for about 70% of all instances.

**Objective:** This study aimed to identify and quantify risk variables for atonic postpartum hemorrhage.

**Methods:** The databases PubMed, CINAHL, EMBASE, Web of Science, and ClinicalTrials.gov were searched for English language studies with no date or geographical constraints. Randomized trials, prospective or retrospective cohort studies, and case-control studies of pregnant individuals who suffered atonic postpartum hemorrhage and reported at least one risk factor were included in the studies. This review contained 16 studies out of the 1,977 records evaluated. A qualitative synthesis of research with low and moderate risk of bias rates each risk factor as definite, likely, unclear, or not a risk factor.

**Results:** This research found 47 potential risk factors for atonic postpartum hemorrhage, 15 of which were deemed definite or likely risk factors. The remaining 32 risk factors were unrelated to atonic postpartum hemorrhage or had inconsistent or inconclusive data.

**Conclusion:** A significant proportion of postpartum bleeding occurs without known risk factors. Many risk variables for atonic hemorrhage contained in existing risk assessment tools were confirmed, with past postpartum hemorrhage of any cause, placenta previa, placental abruption, uterine rupture, and multiple pregnancies conferring the largest risk. Hypertension, diabetes, and ethnicity were new risk factors not previously included in risk-assessment systems. In this study, obesity and magnesium were not associated with to atonic postpartum hemorrhage.

**Keywords:** postpartum hemorrhage, uterine hemorrhage, uterine atony, incidence, factors

## INTRODUCTION

Postpartum hemorrhage affects 3–10% of deliveries and accounts for nearly 20% of maternal deaths worldwide.<sup>1,2</sup> Although there are many etiologies, uterine atony is the most common and accounts for nearly 70% of cases.<sup>3</sup> Patients who experience postpartum hemorrhage can have increased morbidity and mortality, which can be attenuated by identifying patients at risk, early preparation, and increased vigilance.<sup>1-4</sup> Risk stratification for postpartum hemorrhage is commonly performed using an assessment tool from one of several organizations, such as the California Maternal Quality Care Collaborative, Association of Women's Health, Obstetric and Neonatal Nurses, or the American College of Obstetricians and Gynecologists.<sup>5</sup> Although these risk-assessment tools have the support of major medical societies, recent evidence suggests that the tools have only moderate predictive value for severe hemorrhage in the highest risk groups and that a significant portion of hemorrhages (up to 43%) occur in those deemed low risk.<sup>6,7</sup> This limitation may be partly due to the tools' development via expert consensus opinion and a lack of systematically reviewed evidence to support or refute the included risk factors.

A recently published meta-analysis that evaluated the association between maternal demographics and comorbidities, and postpartum hemorrhage evaluated only four potential risk factors and found body mass index, nulliparity, and hypertensive disorders to confer risk of postpartum hemorrhage.<sup>8</sup> Additionally, existing tools assess the risk of all postpartum hemorrhage etiologies simultaneously, which may confound attempts at risk prediction because each etiology of postpartum hemorrhage is likely associated with different risk factors. Furthermore, current tools fail to account for the relative contribution of each risk factor or to provide mechanisms to quantify risk for a given patient when more than one risk factor is present. Because each etiology of postpartum hemorrhage likely has a unique set of risk factors, evaluating each etiology separately may improve the ability to delineate individual patient risk.

The systematic identification and quantification of risk factors for atonic postpartum hemorrhage may allow the development of more reliable, weighted risk stratification tools. Thus, this systematic review aimed to identify risk factors that increase the odds of a patient developing postpartum hemorrhage due only to uterine atony after vaginal or cesarean delivery.

## Methods

### Protocol and Registration

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.<sup>9</sup>

### Search Strategy

The PubMed (National Library of Medicine), CI-NAHL (EBSCO), EMBASE (Ovid), Web of Science (Clarivate), and ClinicalTrials.gov (National Institutes of Health) databases were searched in July 2023 for English language studies with no restrictions on date or geographic location. PubMed MeSH headings included, but were not limited to, postpartum hemorrhage; uterine hemorrhage; uterine inertia; causality; epidemiology; incidence; methylergonovine; misoprostol; oxytocin; prevalence; probability; risk assessment; risk factors; and risk, in addition to corresponding keywords. The PubMed search was translated for CINAHL, EMBASE, Web of Science, and clinicaltrials.gov.

### Eligibility Criteria

Eligibility for inclusion was limited to randomized clinical trials, prospective or retrospective cohort studies, and case-control studies written in the English language with pregnant patients who developed postpartum uterine atony or atonic postpartum hemorrhage. Definitions of atonic postpartum hemorrhage varied by study and included some combination of clinical diagnoses, second-line uterotonic administration, estimated blood loss, need for transfusion, or International Classification of Diseases codes.

Studies were excluded if they reported postpartum hemorrhage data without specifying etiology or if they did not report the incidence of at least one risk factor for postpartum hemorrhage in a uterine atony subgroup. Case reports, case series, and unpublished meeting abstracts were excluded.

The research selection was carried out in three successive phases. The titles and abstracts of all search results were initially screened and evaluated for relevance. Second, complete access was gained to all potentially eligible studies. Finally, the systematic review included only those studies that met our inclusion criteria.

### Data Extraction and Parameter Measured

All data were collected independently by co-investigators into a study spreadsheet and verified by a separate author. In addition to baseline study characteristics including country of origin, study design, the number of patients, and inclusion and exclusion criteria, data were collected on all risk factors for atonic postpartum hemorrhage reported in the study. For each risk factor, adjusted or unadjusted odds ratios (aOR, uOR), relative risks (aRR, uRR), or rate ratios (arr, urr) were recorded when available. If not explicitly reported, uOR and 95% CI were calculated with a 2×2 table using the number of patients with and without a given risk factor who developed atonic postpartum hemorrhage.<sup>10</sup> The primary outcome assessed in all studies was the OR, RR, or rr of risk factors associated with atonic postpartum hemorrhage. For each identified risk factor, low and moderate risk of bias studies were synthesized qualitatively to label each risk factor as

definite, likely, unclear, or not a risk factor based on the number of total studies evaluating the factor and percentage of studies showing a positive association.

**Results**

Initially, 1,977 publications were chosen with the possibility of being included in this study, with 1,239 surviving the following exclusion by repetition. The titles and abstracts were examined, and 871 publications were eliminated for failing to meet the inclusion criteria suggested by these writers, leaving 368 articles. As a result, 352 articles was rejected because not available of full text articles, left 16 publications to be read in full, all of which were included in the research (Figure 1). Table 1 presents an overview of the main findings of the selected studies.

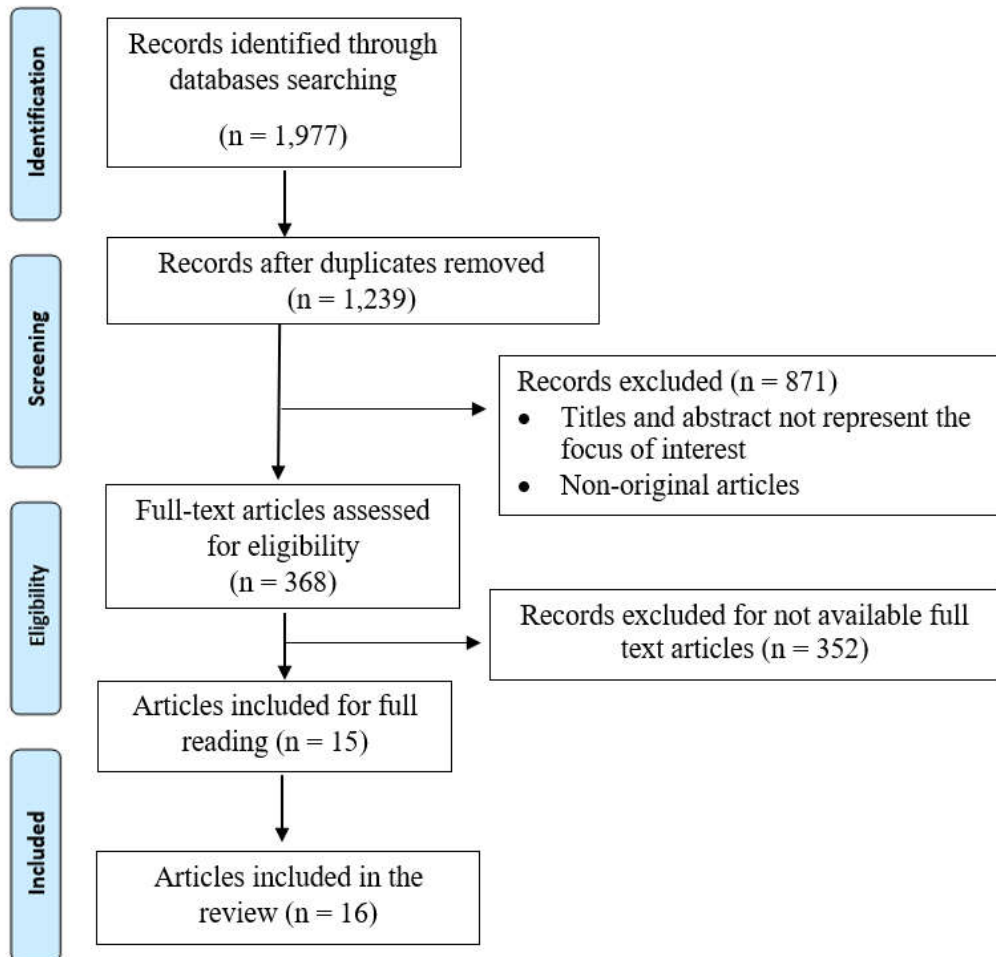


Figure 1. PRISMA flow diagram

Table 1. Summary of Article Characteristic

Author and Year	Study Design	Study Country and Years	Risk Factor Assessed	Covariates Adjusted For
Bateman et al, <sup>2</sup> 2010	Retrospective cohort	United States; 1995–2004 (2004 data for risk factor analysis)	Age, mode of delivery, HDP, diabetes, uterine leiomyoma, prior Cesarean Delivery (CD), polyhydramnios, chorioamnionitis, precipitous delivery, long labor, medical induction of labor, multiple gestation, stillbirth, antepartum hemorrhage, retained placenta	Logistic regression included all risk factors assessed
Bateman et al, <sup>11</sup> 2013	Retrospective cohort	United States; 2000–2007	Calcium channel blocker administration	Age, race, ethnicity, HDP, diabetes, obesity, renal disease, leiomyomas, prior CD, placenta previa, multiple gestation, mode of delivery, induction of labor
Bryant et al, <sup>12</sup> 2012	Retrospective cohort	United States; 2005–2008	Race and ethnicity (African American, Hispanic, Asian or Pacific Islander)	Induction of labor, multiple gestation, polyhydramnios, diabetes, chorioamnionitis, stillbirth, grand multiparity, preeclampsia, obesity,

				leiomyomas, placental abruption, placenta previa, previous CD, chronic anemia, retained placenta, prolonged labor
Foley et al, <sup>13</sup> 2018	Retrospective cohort	United States; 2015	Predelivery oxytocin exposure	Nulliparity, hypertension, diabetes, multiple gestation, polyhydramnios, premature rupture of membranes, preterm rupture of membranes, prolonged rupture of membranes, placenta previa, placental abruption, chorioamnionitis, macrosomia
Joseph et al, <sup>14</sup> 2015	Retrospective case- control	Canada; 1998–2009	Maternal medication use (antidepressants, aspirin, nonsteroidal antiinflammatory drugs, beta-agonists, and antihistamines), multiple pregnancies, placenta previa or abruption, polyhydramnios, prolonged labor, preeclampsia or eclampsia, epidural, labor induction, perineal trauma, uterine rupture, mode of delivery, chorioamnionitis, alcohol use disorder, liver disease, thrombocytopenia, asthma	Age, welfare status, rural vs urban residence, prior CD, alcoholism, liver disease, thrombocytopenia, multiple gestation, preeclampsia, polyhydramnios, placenta previa, placental abruption, epidural analgesia, labor induction, prolonged first stage, prolonged second stage, mode of delivery, uterine rupture, cervical laceration, severe perineal tear, chorioamnionitis
Kahr et al, <sup>15</sup> 2018	Prospective cohort	Switzerland; 2015–2016	Blood group O	None
Kovacheva et al, <sup>16</sup> 2013	Retrospective cohort	United States; 2009	Serum uric acid level	Uric acid level, use of magnesium, duration of oxytocin, polyhydramnios, oligohydramnios, chorioamnionitis, abnormal placentation, gestational age, birth weight
Looft et al, <sup>17</sup> 2017	Retrospective cohort	Sweden; 2008–2014	Length of the second stage Length of pushing	Age, height, BMI, smoking, induction of labor, oxytocin use during first stage of labor, gestational age, birth weight
Wetta et al, <sup>18</sup> 2013	Secondary analysis of randomized controlled trial	United States; 2008–2010	Age, oxytocin dose, BMI, ethnicity, race, augmentation, induction, birthweight, parity, preeclampsia, magnesium use, twin gestation, chorioamnionitis, hydramnios, amnioinfusion, epidural anesthesia, breastfeeding, artificial rupture of membranes	Logistic regression included all risk factors assessed
Tran et al, <sup>19</sup> 2017	Retrospective cohort	Canada; 2013–2015	Length of the oxytocin recovery period, BMI	Preeclampsia, chorioamnionitis, morbid obesity, macrosomia, multiple gestation, polyhydramnios, oxytocin induction, dose and duration of oxytocin augmentation
Regalia et al, <sup>20</sup> 2001	Retrospective cohort	Italy; 1995–1999	Maternal age, BMI, gestational age, parity, fetal weight, prior atony, prior CD or uterine scar, uterine leiomyomas, preeclampsia, fever in labor, hydramnios, labor induction, labor velocity of progress, use of Kristeller maneuvers, nonvertex cephalic presentation	Logistic regression included all risk factors assessed
Oberg et al, <sup>21</sup> 2014	Retrospective cohort	Sweden; 1997–2009	History of PPH according to type	Year of birth, age, civil status, country of origin, chronic hypertension, diabetes, coagulopathy, leiomyomas
Guillaume et al, <sup>22</sup> 2015	Retrospective cohort	France; 2011–2013	Cord blood collection	Age, grand multiparity, diabetes, induction of labor, long labor, oxytocin

				augmentation, prophylactic postpartum oxytocin, instrumented delivery, birth weight, vaginal tearing, placental retention
Vendittelli et al, <sup>23</sup> 2016	Prospective cohort	France; 2011	Mode of delivery	None
Chalouhi et al, <sup>24</sup> 2015	Retrospective cohort	United States; 2009–2012	Ethnicity (Native American)	None
Mehrabadi et al, <sup>25</sup> 2013	Retrospective cohort	Canada; 2001–2010	Maternal age, parity, birthweight, BMI, gestational age, smoking status, multiple gestation, mode of delivery, prior CD, epidural analgesia, induction, oxytocin augmentation, uterine rupture, third or fourth degree perineal tear, high vaginal laceration, cervical laceration, placenta previa, placental abruption, breech, transverse lie, polyhydramnios, prolonged first stage, prolonged second stage, preeclampsia, chorioamnionitis, forceps, vacuum, forceps and vacuum	Logistic regression included all risk factors assessed

**Table 2. Complete List of Studies Reporting on Each Risk Factor**

<b>Patient History and Demographic Risk Factors</b>	
<b>Young Age</b>	Bateman et al, <sup>2</sup> 2010, Wetta et al, <sup>18</sup> 2013, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Old Age</b>	Bateman et al, <sup>2</sup> 2010, Wetta et al, <sup>18</sup> 2013, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Hispanic</b>	Bryant et al, <sup>12</sup> 2012, Wetta et al, <sup>18</sup> 2013
<b>Asian</b>	Bryant et al, <sup>12</sup> 2012
<b>Native American</b>	Chalouhi et al, <sup>24</sup> 2015
<b>African American</b>	Bryant et al, <sup>12</sup> 2012, Wetta et al, <sup>18</sup> 2013
<b>Nulliparity</b>	Wetta et al, <sup>18</sup> 2013, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Prior PPH</b>	Oberg et al, <sup>21</sup> 2014, Regalia et al, <sup>20</sup> 2001
<b>Prior Cesarean Delivery</b>	Bateman et al, <sup>2</sup> 2010, Wetta et al, <sup>18</sup> 2013, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Blood Group O</b>	Kahr et al, <sup>15</sup> 2018
<b>Calcium Channel Blocker exposure</b>	Bateman et al, <sup>11</sup> 2013
<b>Antidepressant Exposure</b>	Joseph et al, <sup>14</sup> 2015
<b>Aspirin Exposure</b>	Joseph et al, <sup>14</sup> 2015
<b>NSAID Exposure</b>	Joseph et al, <sup>14</sup> 2015
<b>Doxylamine Exposure</b>	Joseph et al, <sup>14</sup> 2015
<b>Patient Comorbidity Risk Factors</b>	
<b>Hypertension</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Diabetes</b>	Bateman et al, <sup>2</sup> 2010
<b>Anemia</b>	Wetta et al, <sup>18</sup> 2013
<b>Obesity</b>	Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Fibroids</b>	Bateman et al, <sup>2</sup> 2010, Regalia et al, <sup>20</sup> 2001
<b>Liver Disease</b>	Joseph et al, <sup>14</sup> 2015
<b>Thrombocytopenia</b>	Joseph et al, <sup>14</sup> 2015
<b>Asthma</b>	Joseph et al, <sup>14</sup> 2015
<b>Elevated Uric Acid</b>	Kovacheva et al, <sup>16</sup> 2013
<b>Alcohol Use Disorder</b>	Joseph et al, <sup>14</sup> 2015
<b>Smoking</b>	Mehrabadi et al, <sup>25</sup> 2013
<b>Pregnancy-Related Risk Factors</b>	
<b>Polyhydramnion</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Multiple Gestation</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Mehrabadi et al, <sup>25</sup> 2013
<b>Malpresentation</b>	Mehrabadi et al, <sup>25</sup> 2013
<b>Macrosomia</b>	Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Placental Disorders</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Mehrabadi et al, <sup>25</sup> 2013
<b>Antepartum Hemorrhage</b>	Bateman et al, <sup>2</sup> 2010
<b>Stillbirth</b>	Bateman et al, <sup>2</sup> 2010
<b>Labor-Related Risk Factors</b>	
<b>Chorioamnionitis</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Mehrabadi et al, <sup>25</sup> 2013

<b>Uterine Rupture</b>	Joseph et al, <sup>14</sup> 2015, Mehrabadi et al, <sup>25</sup> 2013
<b>Pre-Delivery Oxytocin Exposure</b>	Foley et al, <sup>13</sup> 2018, Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Induction of Labor</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Wetta et al, <sup>18</sup> 2013, Tran et al, <sup>19</sup> 2017, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Prolonged Labor</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Looft et al, <sup>17</sup> 2017, Wetta et al, <sup>18</sup> 2013, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Epidural</b>	Joseph et al, <sup>14</sup> 2015, Wetta et al, <sup>18</sup> 2013, Mehrabadi et al, <sup>25</sup> 2013
<b>Magnesium Exposure</b>	Wetta et al, <sup>18</sup> 2013
<b>Tocolytic Exposure</b>	Joseph et al, <sup>14</sup> 2015
<b>Delivery-Related Risk Factors</b>	
<b>Gestational age</b>	Wetta et al, <sup>18</sup> 2013, Regalia et al, <sup>20</sup> 2001, Mehrabadi et al, <sup>25</sup> 2013
<b>Genital Tract Trauma</b>	Joseph et al, <sup>14</sup> 2015, Mehrabadi et al, <sup>25</sup> 2013
<b>Instrumented Vaginal Delivery</b>	Wetta et al, <sup>18</sup> 2013, Mehrabadi et al, <sup>25</sup> 2013
<b>Cesarean Delivery</b>	Bateman et al, <sup>2</sup> 2010, Joseph et al, <sup>14</sup> 2015, Vendittelli et al, <sup>23</sup> 2016, Mehrabadi et al, <sup>25</sup> 2013
<b>Cord Blood Collection</b>	Guillaume et al, <sup>22</sup> 2015
<b>Breastfeeding</b>	Wetta et al, <sup>18</sup> 2013

**Discussion**

A total of 47 unique risk factors were identified in the search: 15 relating to maternal history or demographics, 11 to maternal comorbidities, six pregnancy-related factors, eight labor-related factors, and six delivery-related factors. For qualitative comparison, the authors characterized each risk factor as definite, likely, unclear, or not a risk factor based on the number of low and moderate risk of bias studies that showed statistically significant evidence that the risk factor was associated with atony.

Definite risk factors included being of Asian race, a history of prior postpartum hemorrhage of any etiology in a previous pregnancy, preexisting or gestational diabetes mellitus, placental disorders (including retained placenta, placenta previa, vasa previa, and placental abruption, but excluding abnormal placentation), prolonged labor, and genital tract trauma sustained during delivery. An additional nine variables were deemed likely associated with atonic postpartum hemorrhage, and these included being of Hispanic ethnicity, nulliparity, hypertensive diseases of pregnancy, multiple gestation, chorioamnionitis, uterine rupture, predelivery oxytocin exposure, induction of labor, and instrumented vaginal delivery. Some variables that are traditionally considered risk factors for postpartum hemorrhage were not found to be associated specifically with atonic postpartum hemorrhage in this review but may confer risk for hemorrhage due to other etiologies. These included maternal obesity, leiomyomas, polyhydramnios, prolonged second stage of labor, magnesium exposure, and cesarean delivery.

This systematic analysis identifies numerous newly unknown risk variables for atonic postpartum hemorrhage that are not included in current risk-assessment tools, and it raises the question of whether additional risk factors included in current systems are supported by published research. This review also provides further evidence to support the validity of numerous risk factors already included in risk-stratification methods and quantitative estimates of their contribution to the risk of atonic postpartum hemorrhage. Although several risk factors listed, such as genital tract trauma or aberrant placentation, may induce postpartum bleeding independently, they contribute to uterine atony and are thus included in this review.

Perhaps most crucially, current risk-assessment systems do not account for several definite or plausible risk factors that appear to be well-established in the literature. In this study, Hispanic ethnicity and Asian race were related to atonic postpartum hemorrhage but were not included in existing risk-assessment methods. Given the evidence of discrepancies in minority women's treatment, we may underestimate the higher risk of postpartum hemorrhage in these communities.<sup>26</sup> When adding race or ethnicity to risk-prediction systems, special caution must be taken because new evidence suggests these algorithms may perpetuate healthcare disparities.<sup>27</sup>

Hypertensive disease and diabetes mellitus, both of which are known to be associated with vascular and perfusion abnormalities, also emerged as previously underappreciated risk factors for atonic postpartum hemorrhage.<sup>28-30</sup> Interestingly, high vaginal lacerations and cervical trauma are not included in current risk-assessment tools. However, high vaginal and cervical lacerations demonstrated higher OR than either instrumented delivery or perineal trauma, both of which are included in the Association of Women's Health, Obstetric and Neonatal Nurses' risk-stratification tool.<sup>5</sup> Although nulliparity and prolonged first stage of labor were found to be associated with atonic postpartum hemorrhage and are not included in the current risk-assessment tools, they may be associated with other risk factors that are included, such as induction of labor, oxytocin use, and chorioamnionitis. Finally, uterine rupture was found to be associated with atonic postpartum hemorrhage. Although not specifically described in the studies that reported this association, hemorrhage attributable to uterine atony presumably occurred after repair of the uterine defect.

Most risk-assessment systems include obesity and magnesium intake as additional risk factors; however, none revealed relationships with atonic postpartum hemorrhage in this research. The underlying diseases (such as diabetes and

hypertension) are probably the true risk factors, giving the clinical perception that obesity and magnesium increase the risk of postpartum hemorrhage and leading some studies to discover a favorable effect.

Intrapartum cesarean delivery is associated with factors (eg, prolonged labor and oxytocin exposure) shown to increase the risk of atonic postpartum hemorrhage, this may contribute to a positive association in studies or a clinical impression that cesarean delivery is significantly associated with atonic postpartum hemorrhage. The occurrence of leiomyomas varies significantly in size, location, vascularity, and previous surgical interventions, which may influence the ability to determine the significance of leiomyomas as a risk factor in published studies.

Many risk factors already included in widely adopted risk-assessment tools are further confirmed in this systematic review as associated with atonic postpartum hemorrhage—prior postpartum hemorrhage, multiple gestation, placental disorders (previa or abruption), chorioamnionitis, predelivery oxytocin exposure, induction of labor, prolonged labor, perineal trauma, and instrumented vaginal delivery. Although some of these factors (eg, abnormal placentation, birth canal trauma) are etiologies for postpartum hemorrhage themselves, the evidence presented here suggests that they are additionally associated with the development of uterine atony.

The data for oxytocin exposure, which also are already included in current risk-assessment tools, presented the most significant challenge in the interpretation of results for this systematic review. It is essential also to consider the mechanism by which oxytocin likely contributes to atonic postpartum hemorrhage, namely that tachyphylaxis to oxytocin occurs during labor, thereby decreasing efficacy of the primary drug used for the active management the third stage of labor.<sup>31–33</sup> Further investigation is needed to determine the cut-offs for the amount or duration of oxytocin that leads to an increased risk of atony.

The strengths of this systematic review include the systematic approach to identifying all publications that included risk factors for atonic postpartum hemorrhage and the division of risk factors into maternal, pregnancy-related, labor-related, and delivery-related conditions to provide a logical progression of possible etiologies of atonic postpartum hemorrhage. The results of this systematic review must be considered in the context of several limitations: we had to accept the authors' definitions of atonic postpartum hemorrhage, which varied from study to study and we restricted our search to English-language studies, which contributed to publication bias.

## Conclusion

In conclusion, this systematic analysis of risk variables for postpartum hemorrhage owing to uterine atony provides important insights that can help guide future obstetric care. We hoped to provide more clear evidence supporting or disputing supposed risk factors by narrowing our emphasis to solely atonic postpartum hemorrhage, given that each etiology of postpartum hemorrhage likely has a distinct combination of contributing factors. These findings should encourage academics and physicians to improve current risk-assessment systems. Future tools should include weighted risk factor values or risk levels based on the etiology of postpartum hemorrhage. Finally, the genetic basis for postpartum hemorrhage deserves more exploration and possible incorporation into risk-adjustment methods.

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