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VITAL STATISTICS: AN OVERVIEW

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INTRODUCTION

Postpartum hemorrhage constitutes a major cause of maternal mortality, particularly in the developing world, and of maternal morbidity in both the developed and the developing world. This chapter describes the incidence of primary postpartum hemorrhage, the difficulties in reporting epidemiological data on primary postpartum hemorrhage and the etiology and precipitating factors for primary postpartum hemorrhage. Because of its broad scope, this discussion will invariably include several points that are discussed in greater detail elsewhere. Regardless, these statistics should provide additional insights as many derive from secondary analyses.

DEFINING POSTPARTUM HEMORRHAGE

The traditional definition of primary postpartum hemorrhage used in most textbooks of obstetrics is a visually estimated blood loss of 500 ml or more within the first 24 h after delivery¹. Secondary postpartum hemorrhage is generally defined as 'excessive bleeding' from the genital tract after 24 h and up to 6 weeks post-delivery (see Chapter 2). As such, this latter definition only contains quantification of the time period rather than the extent of blood loss. However, according to older and commonly quoted data, measured blood loss during a vaginal delivery averages 500 ml whereas that during a Cesarean section averages 1000 ml². Thus, the 'classic' definition of primary postpartum hemorrhage is in reality a reflection of the almost universal tendency to underestimate delivery blood loss (see below and Chapters 4 and 6).

Because a loss of 500 ml at delivery for most women in the developed world does not result

in significant morbidity, one might argue that the classic definition of primary postpartum hemorrhage is clinically inappropriate and should be revised to identify a group of women who become 'ill' and at real risk of morbidity after the hemorrhage. If the classic definition were to be changed, definitions of any event leading to severe obstetric morbidity could then be based on 'pathophysiology', 'management' or a combination of both parameters³. The problem with using a management-based definition of hemorrhage, such as number of units of blood transfused, is that it can only be used retrospectively and is of no value to the clinician attempting to treat the primary postpartum hemorrhage. Further, such a definition is likely to be highly influenced by local practitioner/hospital beliefs about when to transfuse as well as the local facilities available for transfusion (see Chapter 45). Consequently, according to a recent UK position, it may be better to think of the term 'significant obstetric hemorrhage', using a definition of loss of more than 1000 ml or more than 1500 ml, rather than define primary postpartum hemorrhage as > 500 ml blood loss⁴.

In the average non-pregnant adult, circulating blood represents a total of 7% of body weight, or approximately 5 liters. Loss of 30–40% of the circulating volume (1500–2000 ml) results in tachycardia, tachypnea, a measurable fall in systolic blood pressure and alterations in mental state⁵. Therefore, the concept of defining a 'significant primary postpartum hemorrhage' as one resulting in a blood loss of 1500 ml or more is meritorious as this reflects the point when physiological compensatory mechanisms begin to fail. Whether this concept will find universal acceptance remains to be seen, however.

DIFFICULTIES OF COMPARING STUDIES

Two key factors must be considered when comparing published studies of primary postpartum hemorrhage: first, the method used to determine blood loss, and, second, the method of managing the third stage of labor. In addition, confounding represents a potential problem in case-control studies that examine risk factors for primary postpartum hemorrhage.

Determining blood loss: estimating versus measuring

Accurate measurement of blood loss at delivery is possible but must be planned for in advance (see also Chapter 4). The most obvious is collection of blood into receptacles and direct measurement. This can be combined with a gravimetric procedure which depends upon converting the increase in weight of sponges and linen into milliliters of blood on a ml/g basis. Gulmezoglu and Hofmeyr recently proposed a method for directly measuring blood loss objectively which does not interfere with routine care⁶. They suggest 'after delivery of the baby, the amniotic fluid is allowed to drain away and amniotic fluid-soaked bed linen is covered with a dry disposable 'linen saver'. A low-profile, wedge-shaped plastic 'fracture bedpan' is slipped under the woman's buttocks for blood collection, with blood and clots decanted into a measuring cylinder. Weighing of blood-soaked swabs and linen savers occurs, with the known dry weight subtracted and calculated volume added to that from the bedpan.' They particularly recommend this method for all future trials of interventions to reduce primary postpartum hemorrhage. Strand and colleagues suggested a novel method with a combination of a plastic sheet and a bucket below a cholera bed on which the woman rested during postpartum observation⁷. The BRASSS-V collection drape and instructions for use are described in Chapter 4. As with any direct measurement of blood loss, contamination with amniotic fluid and urine is not uncommon.

Laboratory-based methods for measuring blood loss include photometric techniques, whereby sanitary protection is collected and

blood pigment converted to acid or alkaline hematin and the concentration then compared in a colorimeter with the patient's own venous blood⁸. Alternatively, volumetric methods involve labelling the woman's plasma or erythrocytes with dyes or radioactive substances and then calculating the reduction in blood volume. Unfortunately, both techniques require expertise and are more time-consuming and expensive to perform than simple measurement of blood loss.

Visual estimation has long been considered to be unreliable, but only recently have data proven this to be the case. Duthie and colleagues compared visual estimation and measured blood loss using the alkaline-hematin method during normal delivery in 37 primigravid and 25 multigravid women. These investigators found that, for both groups, the mean estimated blood loss (261 ml and 220 ml, respectively) was significantly lower than the mean measured blood loss (401 ml and 319 ml, respectively)⁹. This observation is consistent with studies of simulated scenarios that suggest midwives and doctors underestimate blood loss at delivery by 30–50%¹⁰. Importantly, estimates are particularly unreliable for very small and very large amounts of blood¹¹ (see Chapter 6).

Reported rates of postpartum hemorrhage also differ widely depending on the method of measuring blood loss. Older studies that directly measured blood loss reported rates of primary postpartum hemorrhage (> 500 ml) of between 22% and 29%^{12,13} compared to rates of 5–8% with visual estimation. More recently, Prasertcharoensuk and colleagues compared visual estimation with direct measurement in 228 women who had a spontaneous vaginal delivery¹⁴. The incidences of postpartum hemorrhage > 500 ml and > 1000 ml were 5.7% and 0.44%, respectively by visual estimation, whereas direct measurements showed incidences of 27.63% and 3.51%, respectively. These differences are five and seven times higher, respectively. The authors concluded that visual estimation underestimated the incidence of postpartum hemorrhage by 89%. Razvi and colleagues conducted a similar prospective study and showed a similar degree of underestimation¹⁵.

Conduct of third stage of labor

Active management of the third stage (AMTSL) involves early clamping of the umbilical cord before pulsations have stopped, controlled cord traction using the Brandt–Andrews technique and the use of prophylactic uterotonics such as syntocinon or syntometrine, usually with the delivery of the fetal anterior shoulder (see also Chapter 11). In contrast, expectant or ‘physiological’ third stage involves late clamping of the cord after pulsations have stopped, waiting for spontaneous separation of the placenta from the uterine wall and avoidance of synthetic uterotonics. Nipple stimulation has been used to promote the release of endogenous oxytocin and reduce the length and amount of bleeding at the third stage of labor¹⁶, but is not part of active or expectant management. A meta-analysis of five randomized, controlled trials (involving over 6000 women) indicates that active management results in a reduction in maternal blood loss at delivery and a reduction in the risks of postpartum hemorrhage, defined as an estimated blood loss > 500 ml (relative risk (RR) 0.38, 95% confidence interval (CI) 0.32–0.46), severe postpartum hemorrhage, defined as an estimated blood loss ≥ 1000 ml (RR 0.33, 95% CI 0.21–0.51) and prolonged third stage¹⁷.

Clearly, the reported incidence of postpartum hemorrhage in any population is influenced by the conduct of the third stage. As active management is less widely practiced in the developing world, this must be considered when making international comparisons of postpartum hemorrhage rates.

CONFOUNDING FACTORS IN EPIDEMIOLOGICAL STUDIES

Confounding is a potential problem in epidemiologic studies exploring risk factors. A confounder is associated with the risk factor and causally related to the outcome. Thus, a researcher may attempt to relate an exposure to an outcome, but actually measures the effect of a third factor, the confounding variable¹⁸. As an example, parity, particularly grand multiparity, is generally considered a risk factor for primary postpartum hemorrhage. However, grand multiparas tend to be older and therefore have

higher rates of age-related medical diseases, such as diabetes mellitus, which could be the ‘true’ risk factors for postpartum hemorrhage.

Methods used to control confounders include:

- (1) Restriction – in the example cited in the preceding paragraph, women with diabetes mellitus could be excluded. However, restriction limits the external validity of the findings and reduces the sample size.
- (2) Matching – here, if diabetes mellitus is deemed a confounder, then for every woman recruited with diabetes mellitus who has a postpartum hemorrhage, she is matched to a control with diabetes mellitus.
- (3) Stratification – can be thought of as *post hoc* restriction performed at the analysis phase.

Multivariable analysis is a statistical tool for determining the relative contributions of different causes to a single event or outcome¹⁹. Epidemiological studies that use multivariable statistical methods are much more likely to eliminate confounders. For readers who require further information about the problems of epidemiological studies, please refer to Grimes and Schultz and Mamdani and colleagues^{20,21}.

INCIDENCE OF PRIMARY POSTPARTUM HEMORRHAGE

Denominator data

Studies that attempt to quantify the incidence and impact of postpartum hemorrhage need a denominator value over a time period to calculate rates. Common denominators used to calculate maternal mortality and morbidity rates²² are illustrated in Table 1.

Developed countries, including the United Kingdom, have the advantage of accurate denominator data, including both livebirths and stillbirths. Consequently, the UK Confidential Enquiries into Maternal Deaths have used maternities for denominator data because this enables establishment of a more detailed picture of maternal death rates. However, for many countries, particularly in the developing world, no process of stillbirth (or even livebirth) registration exists. Denominator data are, therefore,

Table 1 Denominators used in calculating maternal mortality and morbidity

<i>Denominator</i>	<i>Definition</i>	<i>Advantages and disadvantages</i>
Livebirths	Number of pregnancies that result in a live-birth at any gestation	Easier to collect than maternities
Maternities	Number of pregnancies that result in a live-birth at any gestation or stillbirths occurring at or after 24 weeks of completed gestation and required to be notified by law	Includes the majority of women at risk from death from obstetric causes but requires infrastructure for notification of stillbirths
Women aged 15–44 years	Number of women of reproductive age in a given population	Lacks rigor of confining rate to women who were pregnant Enables comparison with other causes of death

likely to be based on livebirths, rather than maternities. Indeed, in some countries even livebirth data collection may not be reliable. As a result, it is often extremely difficult to compare maternal mortality and morbidity from different geographic areas.

Maternal mortality

One method of attempting to quantify the magnitude of postpartum hemorrhage is to look at its contribution to maternal deaths around the world, and in a particular country over time. Trends over time within one country are an important audit tool in examining the care of women with postpartum hemorrhage, as can be seen from the UK Confidential Enquiries into Maternal Deaths. However, differences between countries often reflect differences in health-care provision, general economic prosperity and geographic and climactic conditions that affect access to obstetric care.

Global picture

The WHO estimates that obstetric hemorrhage complicates 10.5% of all livebirths in the world, with an estimated 13 795 000 women experiencing this complication in 2000²². Around 132 000 maternal deaths are directly attributable to hemorrhage, comprising 28% of all direct deaths. In comparison, the following numbers relate to other conditions: 79 000 deaths from sepsis, 63 000 deaths from pre-eclampsia/eclampsia, 69 000 from abortion and 42 000 from obstructed labor.

The United Kingdom

A triennial report on confidential enquiries into maternal death has been published since 1985, with reports for England and Wales commencing in 1952. Direct deaths are reported that result from obstetric complications of the pregnant state (pregnancy, labor and puerperium up to 42 days), from interventions, omissions, incorrect treatment or from a chain of events resulting from any of the above. Obstetric hemorrhage (comprising placental abruption, placenta previa and postpartum hemorrhage) is one example of direct deaths²³. In the 2000–2002 triennium, there were 106 direct maternal deaths. Seventeen (16%) were attributed to obstetric hemorrhage with ten (9.4%) attributed principally to postpartum hemorrhage. Since the UK-wide triennium report began in 1985, 83 deaths from obstetric hemorrhage have been recorded, of which half (41 women) was caused by postpartum hemorrhage, resulting in a death rate for postpartum hemorrhage of 3.1 per million maternities. Calculated death rates for postpartum hemorrhage for each triennium are shown in Table 2.

Although at first glance there appears to be a marked increase in postpartum hemorrhage in the last triennial report compared to the one that immediately preceded it, two patients had no contact at all with health services and two patients refused blood products that would probably have saved their lives. Excluding these four deaths results in a rate per million maternities comparable to the reports published between 1985 and 1996.

Table 2 Maternal mortality from postpartum hemorrhage in UK (extrapolated from CEMACH²³)

Triennium	Postpartum hemorrhage (n)	Total maternities (n)	Rate per million maternities
1985–87	6	2 268 766	2.6
1988–90	11	2 360 309	4.6
1991–93	8	2 315 204	3.4
1994–96	5	2 197 640	2.2
1997–99	1	2 123 614	0.4
2000–02	10	1 997 472	5.0

Of the eight women who sought care in the 2000–2002 cohort and ultimately died from postpartum hemorrhage, elements of sub-standard care were present in seven (88%) including:

- (1) Organizational problems – including inappropriate booking at hospitals with inadequate blood transfusion and intensive care facilities;
- (2) Poor quality of resuscitation – including inadequate transfusion of blood and blood products;
- (3) Equipment failure, e.g. malfunctioning of specimen transport system;
- (4) Inadequate staffing of recovery areas;
- (5) Failure to recognize or treat antenatal medical conditions, e.g. inherited bleeding disorders;
- (6) Failure of senior staff to attend;
- (7) Concerns about the quality of surgical treatment given.

The recognition of these diverse elements provides a blue-print to health-care authorities to institute remedial action (see Chapter 22).

United States of America

The Center for Disease Control (CDC) conducted a pregnancy-related mortality survey in the USA between 1991 and 1999²⁴. Hemorrhage in pregnancy was responsible for 17% of maternal deaths, although this figure includes hemorrhage from first-trimester pregnancy

complications. Of the 2519 maternal deaths that resulted in a livebirth and the 275 maternal deaths resulting in stillbirth, 2.7% and 21.1%, respectively, were considered to be a direct result from obstetric hemorrhage. Unfortunately, no separate data were provided about postpartum hemorrhage. Comparison with the 1987–1990 data shows a reduction in the percentage of maternal deaths from pregnancy-related hemorrhage from 28.7% to 17%²⁵.

France

A confidential enquiry into maternal deaths in five of the 22 administrative areas of France found that five deaths from 39 obstetric causes were due to postpartum hemorrhage²⁶; implicating postpartum hemorrhage in 13% of the obstetric deaths. No denominator data were collected, and therefore it is not possible to estimate rates.

Africa

Bouvier-Colle and colleagues performed a population-based survey of pregnant women from seven West African areas from 1994 to 1996²⁷. Overall, 55 women died from direct or indirect obstetric causes among 17 694 live births. Hemorrhage accounted for 17 deaths (31%), with delivery hemorrhage (third stage) and post-delivery hemorrhage (retention of placenta) accounting for six and four deaths, respectively. This equates to a maternal mortality rate of 565 per 1 000 000 livebirths, a rate approximately 100-fold higher compared to the UK.

Another study in South Africa, involving one tertiary center, reported a maternal mortality rate of 1710 per 1 000 000 livebirths during the period 1986–1992, with 25% of deaths attributed to obstetric hemorrhage²⁸. Within this setting, hemorrhage was the leading cause of death.

Maternal morbidity

Because maternal death in the developed world is a rare event, clinicians have attempted to quantify significant morbidity, which is often labelled as a maternal adverse event or a near miss (see Chapter 37). Studies have generally

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included massive obstetric hemorrhage as one indicator of severe maternal morbidity. As with mortality, comparisons between studies are often difficult because of variations in definition of 'massive obstetric hemorrhage'. Both antenatal and intrapartum bleeding are sometimes included within the definition of 'obstetric hemorrhage'.

Scotland

The Scottish Programme for Clinical Effectiveness in Reproductive Health (SPCERH) conducted a prospective investigation into 14 severe maternal morbidity categories for all maternity units in Scotland in 2003³. Within this audit, major obstetric hemorrhage was defined as estimated blood loss ≥ 2500 ml, or transfusion of ≥ 5 units of blood or the need for fresh frozen plasma or cryoprecipitate. Of the 375 events, 176 (46%) were reported to be related to obstetric hemorrhage. Because some patients experienced more than one morbid event, major obstetric hemorrhage occurred in 65% of 'near-miss patients' (176/270). Using a denominator of 50 157 livebirths, the authors calculated a rate of major obstetric hemorrhage of 3.5/1000 births (CI 3.0–4.1). Of the 176 cases notified to the investigators, full disclosure of data was obtained in 152 cases; 70% of the cases were due to primary postpartum hemorrhage, 26% to intrapartum hemorrhage and 17% to antepartum hemorrhage with some women falling into more than one category.

England

In the South East Thames region, 19 maternity units participated in a 1-year study between 1997 and 1998 to determine the incidence of severe obstetric morbidity²⁹. Severe obstetric hemorrhage was defined as estimated blood loss > 1500 ml or a peripartum fall in hemoglobin concentration of ≥ 40 g/l or the need for an acute transfusion of 4 or more units of blood. There were 588 cases of severe obstetric morbidity among 48 856 women delivered over the year, giving an incidence of 12/1000 deliveries. Hemorrhage was the leading cause of obstetric morbidity at 6.7 (CI 6.0–7.5) occurrences per 1000 deliveries, representing nearly two-thirds

of cases. However, this study did not include thromboembolic disease, which is the leading cause of direct maternal deaths in the UK.

Canada

Wu Wen and colleagues conducted a retrospective cohort study of severe maternal morbidity involving 2 548 824 women who gave birth in Canadian Hospitals over a 10-year period from 1991, using information on hospital discharges compiled by the Canadian Institute for Health Information³⁰. Their criteria for severe maternal morbidity included postpartum hemorrhage requiring hysterectomy or transfusion. Their overall rate of all severe maternal morbidity was 4.38 per 1000 deliveries. Overall rates for severe postpartum hemorrhage in the 10-year time frame are illustrated in Table 3 along with time analysis for rates at the beginning and end of the study. Within this study, rates for postpartum hemorrhage requiring transfusion halved (RR 0.5, CI 0.44–0.55), but hysterectomy rates for postpartum hemorrhage almost doubled (RR 1.76, CI 1.48–2.08). Because the definition of postpartum hemorrhage was based on management rather than pathophysiology, it is difficult to tease out whether the temporal change reflects a true reduction in the incidence of postpartum hemorrhage or simply a change in clinical management.

Africa

Filippi and colleagues conducted prospective and retrospective data extraction on near-miss obstetric events in nine referral hospitals in three countries (Benin, Cote d'Ivoire, and Morocco)³¹. Obstetric hemorrhage was defined as hemorrhage leading to clinical shock, emergency hysterectomy and blood transfusion. The incidence of near-miss cases varied widely between hospitals. Most of the women were already in a critical condition on arrival, with two-thirds being referred from another facility. The study identified a total of 507 cases of late pregnancy obstetric hemorrhage (i.e. previa, abruption and other non-classified hemorrhage and postpartum hemorrhage) from 33 478 deliveries, representing a near-miss late obstetric hemorrhage rate of 15.1/1000 deliveries. In

Table 3 Postpartum hemorrhage (PPH) rates in Canada 1991–2000. Adapted from Wu Wen³⁰

	<i>Number of cases (1991–2000)</i>	<i>Rate per 1000 deliveries (95% CI)</i>	<i>Rate per 1000 deliveries (1991–1993)</i>	<i>Rate per 1000 deliveries (1998–2000)</i>	<i>Relative risk (95% CI)*</i>
PPH requiring transfusion	2317	0.91 (0.87–0.95)	1.27	0.63	0.5 (0.44–0.55)
PPH requiring hysterectomy	892	0.35 (0.33–0.37)	0.26	0.46	1.76 (1.48–2.08)

*The 1991–1993 period was the reference period

total there were 266 cases of postpartum hemorrhage, representing a near-miss postpartum hemorrhage rate of 7.9/1000 deliveries.

Pruhal and colleagues examined severe maternal morbidity from direct obstetric causes in West Africa between 1994 and 1996³². A severe obstetric event was defined as prepartum, peripartum or postpartum hemorrhage leading to blood transfusion, or hospitalization for more than 4 days or to hysterectomy. A total of 1307 severe maternal morbidity events were identified, with obstetric hemorrhage representing the largest group involving 601 cases, 342 of which were postpartum hemorrhage. The near-miss obstetric hemorrhage rate was 30.5 (CI 28.1–33.0)/1000 live births and the near-miss postpartum hemorrhage rate was 17.4 (CI 15.6–19.3)/1000 live births.

The Pretoria region of South Africa has used the same definition of ‘near miss’ for over 5 years, allowing comparison of temporal changes³³. Rates per 1000 births for near misses plus maternal deaths over 5 years from severe postpartum hemorrhage are shown in Table 4. These rates are not dissimilar to those in Canada or the UK.

ETIOLOGY AND PRECIPITATING FACTORS

Causes of primary postpartum hemorrhage

In recent years, individual authors and academic groups have used the Four Ts mnemonic to provide a simplistic categorization of the causes of postpartum hemorrhage. This is shown in Table 5³⁴.

Table 4 Rates per 1000 births for near misses plus maternal deaths from severe postpartum hemorrhage in Pretoria. Adapted from Pattinson *et al.*³³

	<i>1997–99</i>	<i>2000</i>	<i>2001</i>	<i>2002</i>
Rate/1000 births	0.96	1.37	2.38	2.28

Table 5 The Four Ts of postpartum hemorrhage (from ALSO³⁴)

Tone – uterine atony

Trauma – of any part of the genital tract, inverted uterus

Tissue – retained placenta, invasive placenta

Thrombin – coagulopathy

Uterine atony

Uterine atony, the most common cause of postpartum hemorrhage, is reported in 70% of cases³⁴. It can occur after normal vaginal delivery, instrumental vaginal delivery and abdominal delivery. A large cohort study found an incidence of uterine atony after primary Cesarean section of 1416/23 390 (6%)³⁵. Multiple linear regression analysis demonstrates the following factors as being independently associated with risk of uterine atony: multiple gestation (odds ratio (OR) 2.40, 95% CI 1.95–2.93), Hispanic race (OR 2.21, 95% CI 1.90–2.57), induced or augmented labor for > 18 h (OR 2.23, 95% CI 1.92–2.60), infant birth weight > 4500 g (OR 2.05, 95% CI 1.53–2.69), and clinically diagnosed chorioamnionitis (OR 1.80, 95% CI 1.55–2.09).

Surprisingly, it is much more difficult to find comparable studies of risk factors for uterine

atony in women achieving vaginal delivery. A single center, case-control study from Pakistan reporting on women who had either assisted or non-assisted vaginal delivery found only two factors had a strong association with uterine atony: gestational diabetes mellitus (OR 7.6, 95% CI 6.9–9.0) and prolonged second stage of labor in multiparas (OR 4.0, 95% CI 3.1–5.0)³⁶. They found no association with high parity, age, pre-eclampsia, augmentation of labor, antenatal anemia and a history of poor maternal or perinatal outcomes.

Trauma

Trauma is reported to be the primary cause of postpartum hemorrhage in 20% of cases³⁴ (see also Chapter 9). Genital tract trauma at delivery is associated with an odds ratio of 1.7 (95% CI 1.4–2.1) for postpartum hemorrhage (measured blood loss > 1000 ml)³⁷. Similar results were found in a Dutch study with a reported OR of 1.82 (CI 1.01–3.28) for postpartum hemorrhage (\geq 1000 ml) with perineal trauma \geq first-degree tears³⁸. Trauma to the broad ligament, uterine rupture, cervical and vaginal tears and perineal tears are all associated with increased blood loss at normal vaginal delivery.

Inversion of the uterus is a rare cause of postpartum hemorrhage (see Chapter 9). The incidence of inversion varies from 1 in 1584 deliveries in Pakistan³⁹ to around 1 in 25 000 deliveries in the USA, UK and Norway⁴⁰. Blood loss at delivery with a uterine inversion is usually at least 1000 ml⁴¹, with 65% of uterine inversions being complicated by postpartum hemorrhage and 47.5% requiring blood transfusion in a large series of 40 cases⁴².

Tissue

Retained placenta accounts for approximately 10% of all cases of postpartum hemorrhage³⁴. Effective uterine contraction to aid hemostasis requires complete expulsion of the placenta. Most retained placentas can be removed manually, but rarely the conditions of placenta percreta, increta, and accreta may be responsible for placental retention (see Chapters 24 and 36). Retained placenta occurs after 0.5–3% of deliveries⁴³. Several case-control and cohort studies

show that retained placenta is associated with increased blood loss and increased need for blood transfusion. Stones and colleagues reported that retained placenta had a RR of 5.15 (99% CI 3.36–7.87) for blood loss \geq 1000 ml within the first 24 h of delivery⁴⁴. Bais and colleagues found an incidence of 1.8% for retained placenta in Holland³⁸. Using multiple regression, these authors determined that retained placenta was associated with an OR of 7.83 (95% CI 3.78–16.22) and 11.73 (95% CI 5.67–24.1) for postpartum hemorrhage of \geq 500 ml and postpartum hemorrhage \geq 1000 ml, respectively. In addition, retained placenta was found to have an OR of 21.7 (95% CI 8.9–53.2) for red cell transfusion in this Dutch cohort.

Tanberg and colleagues reported an incidence of retained placentas of 0.6% in a large Norwegian cohort of 24 750 deliveries and showed that hemoglobin fell by a mean of 3.4 g/dl in the retained placental group compared to no fall in the controls⁴⁵. In addition, blood transfusion was required in 10% of the retained placental group but only 0.5% of the control group. A similar incidence of retained placenta was found in a Saudi Arabian case-control study which demonstrated increased blood loss in women with a retained placenta (mean 437 ml) compared with controls (mean 263 ml)⁴⁶. A large study from Aberdeen of over 36 000 women reported postpartum hemorrhage in 21.3% of women with retained placenta compared to 3.5% in vaginal deliveries without retained placenta⁴⁷. Both studies confirmed that women with a history of retained placenta have an increased risk of recurrence in subsequent pregnancies^{46,47}. In the study by Adelusi and colleagues, 6.1% of the patients with retained placenta had a prior history of retained placenta, compared to none in their control group of normal vaginal deliveries⁴⁶.

Placental accreta is a rare and serious complication, occurring in about 0.001–0.05% of all deliveries^{48,49}. Makhseed and colleagues found an increasing risk for accreta with increasing numbers of Cesarean sections (OR 4.11, 95% CI 0.83–19.34) after one previous Cesarean section and an OR of 30.25 (95% CI 9.9–92.4) after two previous Cesarean sections, compared with no previous Cesarean section. Kastner and colleagues found that placenta accreta was

implicated in 49% of their 48 cases of emergency hysterectomy⁵⁰. Zaki and co-workers found an incidence of 0.05% of placenta accreta in a population of 23 000 women⁴⁹. They found that rates of postpartum hemorrhage and emergency hysterectomy were higher in the accreta group compared to the placenta previa group undergoing Cesarean section. Postpartum hemorrhage occurred in 91.7% of the accreta group compared to 18.4% of the previa group (OR 48.9, 95% CI 5.93–403.25), whereas 50% of accreta cases required emergency hysterectomy compared to 2% in the previa group (OR 48, 95% CI 7.93–290.48). Within the accreta group, 75% of patients had a previous history of Cesarean section, compared to 27.5% in the previa group (OR 7.9, 95% CI 1.98–31.34).

Thrombin

Disorders of the clotting cascade and platelet dysfunction are the cause of postpartum hemorrhage in 1% of cases³⁴. Known associations with coagulation failure include placental abruption, pre-eclampsia, septicemia and intrauterine sepsis (see Chapter 44), retained dead fetus, amniotic fluid embolus, incompatible blood transfusion, abortion with hypertonic saline and existing coagulation abnormalities^{4,51,52} (see Chapter 25).

ANTENATAL RISK FACTORS FOR PRIMARY POSTPARTUM HEMORRHAGE

Age

Increasing maternal age appears to be an independent risk factor for postpartum hemorrhage. In Japan, Ohkuchi and colleagues studied 10 053 consecutive women who delivered a singleton infant⁵³. Excessive blood loss (≥ 90 th centile) was defined separately for vaginal and Cesarean deliveries (615 ml and 1531 ml, respectively). On multivariate analysis, age ≥ 35 years was an independent risk factor for postpartum hemorrhage in vaginal deliveries (OR 1.5, 95% CI 1.2–1.9) and Cesarean deliveries (OR 1.8, 95% CI 1.2–2.7). In Nigeria, Tsu reported that advanced maternal age (≥ 35 years) was associated with an adjusted RR of 3.0

(95% CI 1.3–7.3) for postpartum hemorrhage (defined as visual estimation of ≥ 600 ml)⁵⁴. Ijaiya and co-workers in Nigeria found that the risk of postpartum hemorrhage in women > 35 years was two-fold higher compared to women < 25 years, although no consideration of confounding was made in this study⁵⁵. Rates of obstetric hysterectomy have also been reported to increase with age; Okogbenin and colleagues in Nigeria reported an increase from 0.1% at 20 years to 0.7% at ≥ 40 years⁵⁶. However, others have found no relationship between delaying childbirth and postpartum hemorrhage⁵⁷.

Ethnicity

Several studies have examined whether ethnicity is a factor for postpartum hemorrhage. Magann and co-workers, using a definition of postpartum hemorrhage of measured blood loss > 1000 ml and/or need for transfusion³⁷, found Asian race to be a risk factor (OR 1.8, 95% CI 1.4–2.2). Other studies have observed similar findings in Asians⁵⁸ (OR 1.73, 95% CI 1.20–2.49) and Hispanic races (OR 1.66, 95% CI 1.02–2.69)⁵⁸ (OR for hematocrit $< 26\%$, 3.99, 95% CI 0.59–9.26)⁵⁹.

Body mass index

Women who are obese have higher rates of intrapartum and postpartum complications. Usha and colleagues performed a population-based observational study of 60 167 deliveries in South Glamorgan, UK; women with a body mass index (BMI) > 30 had an OR of 1.5 (95% CI 1.2–1.8) for blood loss > 500 ml, compared to women with a BMI of 20–30⁶⁰. Stones and colleagues reported a RR for major obstetric hemorrhage of 1.64 (95% CI 1.24–2.17) when the BMI was 27+⁴⁴.

Parity

Although grand multiparity has traditionally been thought of as risk factor for postpartum hemorrhage, Stones and colleagues and Selo-Ojeme did not demonstrate any relation between grand multiparity and major obstetric hemorrhage^{44,61}. This observation was confirmed in a large Australian study which used

multivariate logistic regression analysis and found no association between grand multiparity (\geq five previous births) and postpartum hemorrhage (> 500 ml)⁶². Tsu reported an association with low parity (0–1 previous birth) with adjusted RR without intrapartum factors of 1.7 (95% CI 1.1–2.7) and adjusted RR with intrapartum factors of 1.5 (95% CI 0.95–2.5) but not with grand multiparity (defined as five or more births)⁵⁴. Ohkuchi also found primiparity to be associated with excessive blood loss at vaginal delivery (OR 1.6, 95% CI 1.4–1.9)⁵³. Studies from Pakistan⁶³ and Nigeria⁵⁵ have reported an association between grand multiparity and postpartum hemorrhage, but both studies failed to account for other confounding factors such as maternal age.

Other medical conditions

Several medical conditions are associated with postpartum hemorrhage. Women with type II diabetes mellitus have an increased incidence of postpartum hemorrhage of > 500 ml (34%) compared to the non-diabetic population (6%)^{64,65}. Connective tissue disorders such as Marfans and Ehlers-Danlos syndrome have also been associated with postpartum hemorrhage^{66,67}. Blood loss at delivery is also increased with inherited coagulopathies⁵². The most common inherited hemorrhagic disorder is von Willebrand's disease, with a reported prevalence of between 1 and 3%. Most (70%) have Type 1 disease characterized by low plasma levels of factor VIII, von Willebrand factor antigen, and von Willebrand factor activity. Less common inherited bleeding disorders include carriage of hemophilia A (factor VIII deficiency) or hemophilia B (factor IX deficiency) and factor XI deficiency. In their review, Economaides and colleagues suggest that the risks of primary postpartum hemorrhage in patients with von Willebrand's disease, factor XI deficiency, and carriers of hemophilia are 22%, 16%, and 18.5%, respectively, compared with 5% in the general obstetric population⁵². James also reviewed the numerous case series and the more limited case-control studies of women with bleeding disorders and came to similar conclusions⁶⁸ (see Chapter 25).

Prolonged pregnancy

A large Danish cohort study compared a post-term group (gestational age ≥ 42 weeks or more) of 77 956 singleton deliveries and a term group of 34 140 singleton spontaneous deliveries⁶⁹. Adjusted odds ratio for postpartum hemorrhage was 1.37 (95% CI 1.28–1.46), suggesting an association between prolonged pregnancy and postpartum hemorrhage.

Fetal macrosomia

Several studies confirm that fetal macrosomia is associated with postpartum hemorrhage. Jolly and colleagues examined 350 311 completed singleton pregnancies in London⁷⁰. Linear regression analysis suggested that a birth weight > 4 kg was better at predicting maternal morbidity than birth weight > 90 th centile. Postpartum hemorrhage was increased in women with fetal macrosomia (OR 2.01; 95% CI 1.93–2.10). In a large cohort of 146 526 mother-infant pairs in California, Stotland and co-workers also demonstrated an adjusted OR for postpartum hemorrhage of 1.69 (95% CI 1.58–1.82) in infants of 4000–4499 g compared to 2.15 (95% CI 1.86–2.48) and 2.03 (95% CI 1.33–3.09) with weights of 4500–4999 g and ≥ 5000 g, respectively⁷¹. In Nigeria, a case-control study of 351 infants weighing > 4 kg with 6563 term infants found an incidence of postpartum hemorrhage of 8.3% and 2.1%, respectively⁷². Bais and colleagues, in their Dutch study, also demonstrated an increase in risk for postpartum hemorrhage (≥ 500 ml) and severe postpartum hemorrhage (≥ 1000 ml) with infants with weights ≥ 4 kg (OR 2.11, 95% CI 1.62–2.76 and 2.55, 95% CI 1.5–4.18)³⁸.

Multiple pregnancies

Epidemiological studies suggest twins and higher-order pregnancies are at increased risk for postpartum hemorrhage. Walker and co-workers conducted a retrospective cohort study involving 165 188 singleton pregnancies and 44 674 multiple pregnancies in Canada⁷³. Multiple pregnancies were associated with an increased risk for postpartum hemorrhage (RR 1.88, 95% CI

1.81–1.95), hysterectomy (RR 2.29, 95% CI 1.66–3.16) and blood transfusion (RR 1.67, 95% CI 1.13–2.46). Several other studies have estimated the RR of postpartum hemorrhage associated with multiple pregnancies to be between 3.0 and 4.5^{44,58,74}. Bais and colleagues, in a Dutch population-based cohort study of 3464 women, used multiple regression analysis and found that the OR for postpartum hemorrhage ≥ 500 ml for multiple pregnancy was 2.6 (95% CI 1.06–6.39)³⁸. Albrecht and co-workers conducted a retrospective review of 57 triplet deliveries and found an incidence of 12.3% for postpartum hemorrhage requiring transfusion⁷⁵, and a case series of 71 quadruplet pregnancies conducted by Collins and colleagues estimated that the frequency of postpartum hemorrhage and transfusion to be 21% (95% CI 11–31%) and 13% (95% CI 5–21%), respectively⁷⁶. Magann and colleagues demonstrated an OR for postpartum hemorrhage of 2.2 (95% CI 1.5–3.2) in multiple pregnancies³⁷, and Stones and colleagues showed a relative risk of 4.46 (95% CI 3.01–6.61) for obstetric hemorrhage with multiple pregnancies⁴⁴.

Fibroids

Obstetric textbooks suggest that leiomyomas can be a cause of postpartum hemorrhage. This is mainly based on case reports⁷⁷, but one cohort study of 10 000 women in Japan found that women with leiomyomas had an OR of 1.9 (95% CI 1.2–3.1) and 3.6 (95% CI 2.0–6.3) for excessive blood loss at vaginal and Cesarean delivery, respectively⁵³.

Antepartum hemorrhage

Antepartum hemorrhage has been linked to postpartum hemorrhage risk with an OR of 1.8 (95% CI 1.3–2.3)³⁷. Stones and co-workers found a RR for major obstetric hemorrhage (> 1000 ml) of 12.6 (95% CI 7.61–20.9), 13.1 (95% CI 7.47–23) and 11.3 (95% CI 3.36–38.1) for proven abruption, previa with bleeding, and previa with no bleeding, respectively⁴⁴. Ohkuchi and colleagues, in their 10 000 women, demonstrated that a low-lying placenta was associated with odds ratios of 4.4 (95% CI 2.2–8.6) and 3.3 (95% CI 1.4–7.9) for

excess blood loss at the time of vaginal and Cesarean delivery, respectively⁵³. This study also reported that placenta previa was associated with an OR of 6.3 (95% CI 4.0–9.9) for excessive blood loss at Cesarean delivery.

Previous history of postpartum hemorrhage

Magann and colleagues found previous postpartum hemorrhage to be associated with an increased risk for subsequent postpartum hemorrhage (OR 2.2, 95% CI 1.7–2.9)³⁷.

Previous Cesarean delivery

The Japanese study demonstrated an odds ratio of 3.1 (95% CI 2.1–4.4) for excessive blood loss at vaginal delivery in women with a previous Cesarean section⁵³.

INTRAPARTUM RISK FACTORS FOR PRIMARY POSTPARTUM HEMORRHAGE

Induction of labor

Meta-analysis of trials of induction of labor at or beyond term indicates that induction does not increase Cesarean section or operative vaginal delivery rates⁷⁸. However, this meta-analysis did not examine blood loss at delivery. Epidemiological studies suggest a link between induction of labor and postpartum hemorrhage. Brinsden and colleagues reviewed 3674 normal deliveries and found that the incidence of postpartum hemorrhage was increased after induction of labor⁷⁹; among primipara, the incidence was nearly twice that of spontaneous labor, even when only normal deliveries were considered. The study of Magann and colleagues suggested an OR of 1.5 (95% CI 1.2–1.7) for postpartum hemorrhage after induction of labor³⁷ and Bais and co-workers found an OR of 1.74 (95% CI 1.06–2.87) for severe postpartum hemorrhage of > 1000 ml after induction of labor³⁸.

Tylleskar and colleagues performed a prospective, randomized, control trial of term induction of labor with amniotomy plus oxytocin versus waiting for spontaneous labor in 84 women and found no difference in the

amount of bleeding at the third stage⁸⁰. A Cochrane review⁸¹ of amniotomy versus vaginal prostaglandin for induction of labor reported no difference in postpartum hemorrhage rates. Another Cochrane⁸² review of amniotomy plus intravenous oxytocin included only one placebo-controlled trial, but no data on postpartum hemorrhage were reported. This review compared amniotomy plus intravenous oxytocin against vaginal prostaglandin (two trials, 160 women) and found a higher rate of postpartum hemorrhage in the amniotomy/oxytocin group (13.8% vs. 2.5% respectively, RR 5.5, 95% CI 1.26–24.07)⁸².

A review of intravenous oxytocin alone for cervical ripening⁸³ found no difference in postpartum hemorrhage rates compared to the placebo/expectant management group (three trials, 2611 women; RR 1.24, 95% CI 0.85–1.81) or vaginal PGE₂ (four trials, 2792 women; RR 1.02, 95% CI 0.75–1.4). Use of mechanical methods to induce labor⁸⁴ was not associated with any difference in postpartum hemorrhage rates when compared to placebo (one study, 240 women, RR 0.46, 95% CI 0.09–2.31), prostaglandin vaginal PGE₂ (one study, 60 women, RR 3.0, 95% CI 0.33–27.24), intracervical PGE₂ (three studies, 3339 women, RR 0.91, 95% CI 0.40–2.11), misoprostol (one study, 248 women, RR 2.34, 95% CI 0.46–11.85) or to oxytocin alone (one study, 60 patients, RR 1.0, 95% CI 0.22–4.56).

Meta-analysis⁸⁵ of trials of membrane sweeping for induction of labor found a reduction in postpartum hemorrhage compared to no intervention (three trials, 278 women, RR 0.31, 95% CI 0.11–0.89). A review of oral misoprostol for induction of labor⁸⁶ did not include any trial that compared this agent with placebo. However, one trial reported in this review, involving 692 women and using PGE₂ in the control arm, found no difference in postpartum hemorrhage rate (RR 0.98, 95% CI 0.73–1.31). Other reviews of induction of labor methods have reported no difference in postpartum hemorrhage rates between vaginal misoprostol when compared to placebo (two trials, 107 women, RR 0.91, 95% CI 0.13–6.37)⁸⁷, vaginal prostaglandins (five trials, 1002 women, RR 0.88, 95% CI 0.63–1.22), intracervical prostaglandins (two trials, 172 women, RR 1.62, 95%

CI 0.22–12.19), or with oxytocin (two trials, 245 women, RR 0.51, 95% CI 0.16–1.66). Finally, a review of vaginal PGE₂ for induction of labor suggested an increased risk of postpartum hemorrhage compared to placebo⁸⁸ (eight studies, 3437 women, RR 1.44, 95% CI 1.01–2.05).

Duration of labor

First stage

Compared with the second stage of labor, limited evidence is available regarding the influence of the duration of the first stage of labor on postpartum hemorrhage⁸⁹. Magann and colleagues defined a prolonged first stage of labor as a latent phase of > 20 h in nulliparous and > 14 h in multiparous and/or an active phase of < 1.2 cm per hour in nulliparous and < 1.4 cm in multiparous patients³⁷. These investigators found an OR of 1.6 for prolonged first stage of labor but the 95% CI ranged from 1 to 1.6.

Second stage

Several large studies have explored the relationship between the length of the second stage and adverse maternal and neonatal outcomes. Cohen analyzed obstetric data from 4403 nulliparas and found an increase in postpartum hemorrhage rate after more than 3 h in the second stage⁹⁰. He attributed this to the increased need for mid-forceps delivery. A large retrospective study involving 25 069 women in spontaneous labor at term with a cephalic presentation found that second-stage duration had a significant independent association with the risk of postpartum hemorrhage⁹¹. A more recent retrospective cohort study of 15 759 nulliparous term, cephalic singleton births in San Francisco divided the second stage of labor into 1-h intervals⁹². Postpartum hemorrhage was defined as estimated blood loss of > 500 ml after vaginal delivery or > 1000 ml after Cesarean delivery. The frequency of postpartum hemorrhage increased from 7.1% when the second stage lasted 0–1 h to 30.9% when it lasted > 4 h. The risk for postpartum hemorrhage with a second stage of > 3 h remained statistically significant when controlled for confounders (including

operative vaginal delivery, episiotomy, birth weight and fetal position) (OR 1.48, 95% CI 1.24–1.78). Myles and colleagues examined 6791 cephalic singleton births and found that the incidence of postpartum hemorrhage was 2.3% in women experiencing a second stage < 2 h compared to 6.2% in women with a longer second stage⁹³. Janni and co-workers compared 952 women with a singleton cephalic pregnancy after 34 weeks' gestation with a 'normal' second stage to 248 women with a second stage > 2 h⁹⁴. The median difference between intrapartum and postpartum hemoglobin levels was lower in the normal group (−0.79 g/dl) compared to the prolonged second-stage group (−1.84 g/dl). Multivariate binary logistic regression confirmed duration of the second stage as an independent predictor of postpartum hemorrhage (RR 2.3, 95% CI 1.6–3.3). Magann and colleagues also found an OR of 1.6 (95% CI 1.1–2.1) for prolonged second stage³⁷.

Third stage

Strong evidence indicates that, despite the use of active management, prolongation of the third stage of labor increases the risk for postpartum hemorrhage. Combs and colleagues studied 12 979 singleton, vaginal deliveries and found that the median duration of the third stage was 6 min (interquartile range 4–10 min)⁹⁵. The incidence of postpartum hemorrhage and blood transfusion remaining constant until the third stage reached 30 min (3.3% of deliveries). Thereafter, it increased progressively, reaching a plateau at 75 min⁹⁵. Dombrowski and colleagues studied the third stage in 45 852 singleton deliveries ≥ 20 weeks' gestation⁹⁶. Postpartum hemorrhage was defined as an estimated blood loss ≥ 500 ml. At all gestational ages, the frequency of postpartum hemorrhage increased with increasing duration of the third stage, reaching the peak at 40 min. Magann and colleagues performed a prospective observational study of 6588 vaginal deliveries⁹⁷. Postpartum hemorrhage was defined as a blood loss > 1000 ml or hemodynamic instability requiring blood transfusion. Postpartum hemorrhage risk was significant (and increased in a dose-related fashion with time) at 10 min (OR 2.1, 95% CI 1.6–2.6), 20 min (OR 4.3, 95% CI 3.3–5.5) and at 30 min (OR 6.2,

95% CI 4.6–8.2). Using receiver operating characteristic (ROC) curves, the best predictor for postpartum hemorrhage was a third stage of ≥ 18 min⁹⁷. Similarly, a Dutch population-based cohort study of 3464 nulliparous women suggested that a third stage of ≥ 30 min was associated with a blood loss of ≥ 500 ml (OR 2.61, 95% CI 1.83–3.72) and ≥ 1000 ml (OR 4.90, 95% CI 2.89–8.32)³⁸. Blood loss was determined by a combination of measurement and visual estimation.

Analgesia

A retrospective case–control study involving 1056 and 6261 women with and without epidural analgesia, respectively, found that use of epidural analgesia was associated with intrapartum hemorrhage > 500 ml⁹⁸. Magann and colleagues also found an OR of 1.3 for postpartum hemorrhage with epidural analgesia, but the 95% CI extended from 1 to 1.6³⁷. However, if Cesarean delivery is required, regional analgesia is superior to general anesthesia in reducing blood loss, according to evidence from one randomized, controlled trial involving 341 women⁹⁹.

Delivery method

The NICE guideline of the UK on Cesarean section examined maternal morbidity in a comparison of planned Cesarean section with planned vaginal birth from available randomized, controlled trials on an intention-to-treat basis¹⁰⁰. For maternal obstetric hemorrhage (defined as blood loss > 1000 ml), an absolute risk of 0.5% for planned Cesarean section and 0.7% for vaginal birth (RR 0.8, 95% CI 0.4–4.4) was reported, suggesting there is no difference in risk.

Magann and colleagues examined the incidence and risk factors for postpartum hemorrhage in 1844 elective Cesarean sections and 2933 non-elective Cesarean sections¹⁰¹. Two criteria were used to define postpartum hemorrhage: measured blood loss > 1000 ml and/or need for blood transfusion and measured blood loss > 1500 ml and/or need for blood transfusion. Six percent of all Cesarean deliveries were complicated by a blood loss > 1000 ml. The postpartum hemorrhage rates for elective Cesarean section (blood loss > 1000 ml –

POSTPARTUM HEMORRHAGE

4.84%, blood loss > 1500 ml – 1.9%) were lower than for non-elective Cesarean delivery (6.75% and 3.04%, respectively). During the 4-year period of this study, there were 13 868 vaginal deliveries with a postpartum hemorrhage rate of 5.15% (blood loss > 1000 ml) and 2.4% (blood loss > 1500 ml)¹⁰¹. No data on operative vaginal delivery rate were reported. Although the postpartum hemorrhage rate was higher in women undergoing non-elective Cesarean delivery than after vaginal delivery, the difference in rate for elective Cesarean delivery was not statistically significant different. Using linear regression, risk factors for postpartum hemorrhage at elective Cesarean delivery were leiomyomas, placenta previa, preterm birth and general anesthesia. For non-elective Cesarean delivery, risk factors were blood disorders, retained placenta, antepartum transfusion, antepartum/intrapartum hemorrhage, placenta previa, general anesthesia, and macrosomia.

Combs and colleagues performed a case-control study involving 3052 Cesarean deliveries¹⁰². They reported a postpartum hemorrhage incidence (based on fall in hematocrit and/or need for blood transfusion) of 6.4% for Cesarean delivery, similar to Magann and colleagues. However, Combs and colleagues did not differentiate elective from non-elective deliveries.

This group also examined 9598 vaginal deliveries and found an overall incidence of postpartum hemorrhage of 3.9%⁵⁸. Using multiple linear regression, they reported an adjusted OR of 1.66 (95% CI 1.06–2.60) for forceps or vacuum extraction use, suggesting that operative vaginal delivery is associated with postpartum hemorrhage. In addition, the use of sequential instruments (forceps after unsuccessful vacuum extraction) to achieve vaginal delivery is a further risk factor (OR 1.9, 95% CI 1.1–3.2)³⁷ or relative risk of 1.6 (95% CI, 1.3–2.0)¹⁰³ for postpartum hemorrhage.

Episiotomy

A Cochrane review argues for restrictive use of episiotomy because this policy is associated with fewer complications¹⁰⁴. Surprisingly, this meta-analysis does not address the question of postpartum hemorrhage incidence with episiotomy. Iatrogenic trauma by the indiscriminate

use of a mid-line or mediolateral episiotomy is associated with increased blood loss and postpartum hemorrhage in most studies, with blood loss increases of between 300 and 600 ml compared with no episiotomy^{105,106}. Stones and colleagues reported a relative risk of 2.06 (95% CI 1.36–3.11) for postpartum hemorrhage when episiotomy occurred⁴⁴. Bais and co-workers reported similar results with an OR of 2.18 (95% CI 1.68–2.81)³⁸, and Combs and colleagues reported that a mediolateral episiotomy is associated with an odds ratio of 4.67 (95% CI 2.59–8.43) for postpartum hemorrhage⁵⁸. However, one recent randomized, controlled trial of the use of episiotomy when perineal tears appear imminent suggested no difference in postpartum hemorrhage rates¹⁰⁷.

Chorioamnionitis

Several studies have reported an increased risk for postpartum hemorrhage in the presence of chorioamnionitis, ORs ranging from 1.3 (95% CI 1.1–1.7) at vaginal birth³⁷ to 2.69 (95% CI 1.44–5.03) at Cesarean section¹⁰² (see Chapter 44).

CONCLUSIONS

Postpartum hemorrhage remains an extremely important cause of maternal mortality and morbidity throughout the world. Sadly substandard care continues to contribute to mortality and morbidity from postpartum hemorrhage, regardless of the country in which death takes place.

Major obstetric hemorrhage complicates around 10% of live births and is responsible for 28% of direct deaths, globally. Marked differences exist between countries; in the UK there are five deaths per million maternities, whereas the figure is 100 times higher in parts of Africa. Severe obstetric hemorrhage is increasingly used as a measure of quality of health care in women. In the UK, severe obstetric hemorrhage occurs in three to seven cases per 1000 livebirths, with postpartum hemorrhage implicated in 70% of cases. In contrast, rates as high as 30.5 per 1000 livebirths are reported in parts of Africa, with postpartum hemorrhage rates of 17.4 per 1000.

References

1. Park EH, Sachs BP. Postpartum hemorrhage and other problems of the third stage. In James DK, Steer PJ, Weiner CP, Gonik B, eds. *High Risk Pregnancy: Management Options*. London: WB Saunders, 1999;1231–46
2. Pritchard JA, Baldwin RM, Dickey JC, et al. Red blood cell loss and changes in apparent blood volume during and following vaginal delivery, caesarean section and caesarean section plus total hysterectomy. *Am J Obstet Gynecol* 1962;84:1271
3. Brace V, Penney GC. Scottish Confidential Audit of Severe Maternal Morbidity: First Annual Report 2003. 22, 5–31. 2005. Aberdeen, Scottish Programme for Clinical Effectiveness in Reproductive Health
4. Griffiths D, Howell C. Massive obstetric haemorrhage. In Johanson R, Cox C, Grady K, Howell C, eds. *Managing Obstetric Emergencies and Trauma (MOET) course manual*. London: RCOG Press, 2003:151–62
5. Grady K, Cox C. Shock. In Johanson R, Cox C, Grady K, Howell C, eds. *Managing Obstetric Emergencies and Trauma*. London: RCOG Press, 2003:81–90
6. Gulmezoglu AM, Hofmeyr GJ. Prevention and treatment of postpartum haemorrhage. In MacLean AB, Neilson J, eds. *Maternal Morbidity and Mortality*. London: RCOG Press, 2002:241–51
7. Strand RT, da Silva F, Bergstrom S. Use of cholera beds in the delivery room: a simple and appropriate method for direct measurement of postpartum bleeding. *Trop Doctor* 2003;33: 215–16
8. Chua S, Ho LM, Vanaja K, Nordstrom L, Roy AC, Arulkumaran S. Validation of a laboratory method of measuring postpartum blood loss. *Gynecol Obstet Invest* 1998;46:31–3
9. Duthie SJ, Ven D, Yung GL, Guang DZ, Chan SY, Ma HK. Discrepancy between laboratory determination and visual estimation of blood loss during normal delivery. *Eur J Obstet Gynecol Reprod Biol* 1991;38:119–24
10. Glover P. Blood loss at delivery: how accurate is your estimation? *Aust J Midwifery* 2003;16:21–4
11. Higgins PG. Measuring nurses' accuracy of estimating blood loss. *J Adv Nursing* 1982;7: 157–62
12. Newton M, Mosey LM, Egli GE, Gifford WB, Hull CT. Blood loss during and immediately after delivery. *Obstet Gynecol* 1961;17:9–18
13. Hill JA, Fadel HE, Nelson MC, Nelson RM, Nelson GH. Blood loss at vaginal delivery. *South Med J* 1986;79:188–192.
14. Prasertcharoensuk W, Swadpanich U, Lumbiganon P. Accuracy of the blood loss estimation in the third stage of labor. *Int J Gynaecol Obstet* 2000;71:69–70
15. Razvi K, Chua S, Arulkumaran S, Ratnam SS. A comparison between visual estimation and laboratory determination of blood loss during the third stage of labour. *Aust N Z J Obstet Gynaecol* 1996;36:152–4
16. Irons DW, Sriskandabalan P, Bullough CH. A simple alternative to parenteral oxytocics for the third stage of labor. *Int J Gynaecol Obstet* 1994; 46:15–18
17. Prendiville WJ, Elbourne D, McDonald S. Active versus expectant management in the third stage of labour (update of Cochrane Database Syst Rev. 2000;(2):CD000007; PMID: 10796082). (Review). *Cochrane Database of Systematic Reviews* 2000;CD000007
18. Grimes DA, Schulz KF. Bias and causal associations in observational research. *Lancet* 2002;359:248–52
19. Katz MH. *Multivariable analysis: A practical guide for clinicians*. Cambridge: Cambridge University Press, 1999
20. Grimes DA, Schulz KF. Clinical research in obstetrics and gynecology: a Baedeker for busy clinicians. *Obstet Gynecol Survey* 2002;57: S35–S53
21. Mamdani M, Sykora K, Li P, et al. Reader's guide to critical appraisal of cohort studies. 2. Assessing potential for confounding. *BMJ* 2005;330:960–2
22. Anonymous. Introduction. In Lewis G, ed. *Why Mothers Die 2000–2002*. London: RCOG, 2004:1–24
23. Hall M. Haemorrhage. In Lewis G, ed. *Why Mothers Die 2000–2002*. London: RCOG Press, 2004:86–93
24. Chang J, Elam-Evans LD, Berg CJ, et al. Pregnancy-related mortality surveillance, United States, 1991–1999. CDC. <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5202a1.htm> 52(SS02), 1–8. 2003
25. Berg CJ, Atrash HK, Koonin LM, Tucker M. Pregnancy-related mortality in the United States, 1987–1990. *Obstet Gynecol* 1996;88: 161–7
26. Bouvier-Colle MH, Varnoux N, Breart G. Maternal deaths and substandard care: the results of a confidential survey in France.

- Medical Experts Committee. *Eur J Obstet Gynecol Reprod Biol* 1995;58:3-7
27. Bouvier-Colle MH, Ouedraogo C, Dumont A, et al. Maternal mortality in West Africa. Rates, causes and substandard care from a prospective survey. *Acta Obstet Gynecol Scand* 2001;80:113-19
 28. Spies CA, Bam RH, Cronje HS, Schoon MG, Wiid M, Niemand I. Maternal deaths in Bloemfontein, South Africa, 1986-1992. *South Afri Med J* 1995;85:753-5
 29. Waterstone M, Bewley S, Wolfe C. Incidence and predictors of severe obstetric morbidity: case-control study. *BMJ* 2001;322:1089-93
 30. Wen SW, Huang L, Liston R, et al. Severe maternal morbidity in Canada, 1991-2001. *Can Med Assoc J* 2005;173:759-64
 31. Filippi V, Ronsmans C, Gohou V, et al. Maternity wards or emergency obstetric rooms? Incidence of near-miss events in African hospitals. *Acta Obstet Gynecol Scand* 2005;84:11-16
 32. Prual A, Bouvier-Colle MH, de Bernis L, Breart G. Severe maternal morbidity from direct obstetric causes in West Africa: incidence and case fatality rates. *Bull WHO* 2000;78:593-602
 33. Pattinson RC, Hall M. Near misses: a useful adjunct to maternal death enquiries. *Br Med Bull* 2003;67:231-43
 34. Anderson J, Etches D, Smith D. Postpartum haemorrhage. In Damos JR, Eisinger SH, eds. *Advanced Life Support in Obstetrics (ALSO) provider course manual*. Kansas: American Academy of Family Physicians, 2000:1-15
 35. Rouse DJ, Leindecker S, Landon M, et al. The MFMU Cesarean Registry: uterine atony after primary cesarean delivery. *Am J Obstet Gynecol* 2005;193:1056-60
 36. Feerasta SH, Motiei A, Motiwala S, Zuberi NF. Uterine atony at a tertiary care hospital in Pakistan: a risk factor analysis. *J Pak Med Assoc* 2000;50:132-6
 37. Magann EF, Evans S, Hutchinson M, Collins R, Howard BC, Morrison JC. Postpartum hemorrhage after vaginal birth: an analysis of risk factors. *S Med J* 2005;98:419-22
 38. Bais JM, Eskes M, Pel M, Bonsel GJ, Bleker OP. Postpartum haemorrhage in nulliparous women: incidence and risk factors in low and high risk women. A Dutch population-based cohort study on standard (> or = 500 ml) and severe (> or = 1000 ml) postpartum haemorrhage. *Eur J Obstet Gynecol Reprod Biol* 2004;115:166-72
 39. Hussain M, Jabeen T, Liaquat N, Noorani K, Bhutta SZ. Acute puerperal uterine inversion. *J Coll Phys Surg-Pakistan* 2004;14:215-17
 40. Milenkovic M, Kahn J. Inversion of the uterus: a serious complication at childbirth. *Acta Obstet Gynecol Scand* 2005;84:95-6
 41. Beringer RM, Patteril M. Puerperal uterine inversion and shock. *Br J Anaesthes* 2004;92:439-41
 42. Baskett TF. Acute uterine inversion: a review of 40 cases. *J Obstet Gynaecol Can* 2002;24:953-6
 43. Weeks AD, Mirembe FM. The retained placenta - new insights into an old problem. *Eur J Obstet Gynecol Reprod Biol* 2002;102:109-10
 44. Stones RW, Paterson CM, Saunders NJ. Risk factors for major obstetric haemorrhage. *Eur J Obstet Gynecol Reprod Biol* 1993;48:15-18
 45. Tandberg A, Albrechtsen S, Iversen OE. Manual removal of the placenta. Incidence and clinical significance. *Acta Obstet Gynecol Scand* 1999;78:33-6
 46. Adelusì B, Soltan MH, Chowdhury N, Kangave D. Risk of retained placenta: multivariate approach. *Acta Obstet Gynecol Scand* 1997;76:414-18
 47. Hall MH, Halliwell R, Carr-Hill R. Concomitant and repeated happenings of complications of the third stage of labour. *Br J Obstet Gynaecol* 1985;92:732-8
 48. Makhseed M, el-Tomi N, Moussa M. A retrospective analysis of pathological placental implantation - site and penetration. *Int J Gynaecol Obstet* 1994;47:127-34
 49. Zaki ZM, Bahar AM, Ali ME, Albar HA, Gerais MA. Risk factors and morbidity in patients with placenta previa accreta compared to placenta previa non-accreta. *Acta Obstet Gynecol Scand* 1998;77:391-4
 50. Kastner ES, Figueroa R, Garry D, Maulik D. Emergency peripartum hysterectomy: experience at a community teaching hospital. *Obstet Gynecol* 2002;99:971-5
 51. Walker ID, Walker JJ, Colvin BT, Letsky EA, Rivers R, Stevens R. Investigation and management of haemorrhagic disorders in pregnancy. Haemostasis and Thrombosis Task Force. *J Clin Pathol* 1994;47:100-8
 52. Economides DL, Kadir RA, Lee CA. Inherited bleeding disorders in obstetrics and gynaecology. *Br J Obstet Gynaecol* 1999;106:5-13
 53. Ohkuchi A, Onagawa T, Usui R, et al. Effect of maternal age on blood loss during parturition: a retrospective multivariate analysis of 10,053 cases. *J Perinat Med* 2003;31:209-15

54. Tsu VD. Postpartum haemorrhage in Zimbabwe: a risk factor analysis. *Br J Obstet Gynaecol* 1993;100:327–33
55. Ijaiya MA, Aboyeji AP, Abubakar D. Analysis of 348 consecutive cases of primary postpartum haemorrhage at a tertiary hospital in Nigeria. *J Obstet Gynaecol* 2003;23:374–7
56. Okogbenin SA, Gharoro EP, Otoide VO, Okonta PI. Obstetric hysterectomy: fifteen years' experience in a Nigerian tertiary centre. *J Obstet Gynaecol* 2003;23:356–9
57. Roberts CL, Algert CS, March LM. Delayed childbearing – are there any risks? *Med J Aust* 1994;160:539–44
58. Combs CA, Murphy EL, Laros RK Jr. Factors associated with postpartum hemorrhage with vaginal birth. *Obstet Gynecol* 1991;77:69–76
59. Petersen LA, Lindner DS, Kleiber CM, Zimmerman MB, Hinton AT, Yankowitz J. Factors that predict low hematocrit levels in the postpartum patient after vaginal delivery. *Am J Obstet Gynecol* 2002;186:737–44
60. Usha KT, Hemmadi S, Bethel J, Evans J. Outcome of pregnancy in a woman with an increased body mass index. *Br J Obstet Gynaecol* 2005;112:768–72
61. Selo-Ojeme DO, Okonofua FE. Risk factors for primary postpartum haemorrhage. A case control study. *Arch Gynecol Obstet* 1997;259:179–87
62. Humphrey MD. Is grand multiparity an independent predictor of pregnancy risk? A retrospective observational study. *Med J Aust* 2003;179:294–6
63. Munim S, Rahbar MH, Rizvi M, Mushtaq N. The effect of grandmultiparity on pregnancy related complications: the Aga Khan University experience. *J Pak Med Assoc* 2000;50:54–8
64. Dunne F, Brydon P, Smith K, Gee H. Pregnancy in women with Type 2 diabetes: 12 years outcome data 1990–2002. *Diabet Med* 2003;20:734–8
65. Dunne F. Type 2 diabetes and pregnancy. *Semin Fetal Neonat Med* 2005;10:333–9
66. Rahman J, Rahman FZ, Rahman W, al-Suleiman SA, Rahman MS. Obstetric and gynecologic complications in women with Marfan syndrome. *J Reprod Med* 2003;48: 723–8
67. Lind J, Wallenburg HC. Pregnancy and the Ehlers-Danlos syndrome: a retrospective study in a Dutch population. *Acta Obstet Gynecol Scand* 2002;81:293–300
68. James AH. More than menorrhagia: a review of the obstetric and gynaecological manifestations of bleeding disorders. *Haemophilia* 2005;11: 295–307
69. Olesen AW, Westergaard JG, Olsen J. Perinatal and maternal complications related to post-term delivery: a national register-based study, 1978–1993. *Am J Obstet Gynecol* 2003;189: 222–7
70. Jolly MC, Sebire NJ, Harris JP, Regan L, Robinson S. Risk factors for macrosomia and its clinical consequences: a study of 350,311 pregnancies. *Eur J Obstet Gynecol Reprod Biol* 2003;111:9–14
71. Stotland NE, Caughey AB, Breed EM, Escobar GJ. Risk factors and obstetric complications associated with macrosomia. *Int J Gynaecol Obstet* 2004;87:220–6
72. Fakeye O. The incidence, sociobiological factors and obstetric complications associated with large infants at Ilorin, Nigeria. *Int J Gynaecol Obstet* 1988;27:343–7
73. Walker MC, Murphy KE, Pan S, Yang Q, Wen SW. Adverse maternal outcomes in multifetal pregnancies. *Br J Obstet Gynaecol* 2004;111: 1294–6
74. Klapholz H. Blood transfusion in contemporary obstetric practice. *Obstet Gynecol* 1990;75: 940–3
75. Albrecht JL, Tomich PG. The maternal and neonatal outcome of triplet gestations. *Am J Obstet Gynecol* 1996;174:1551–6
76. Collins MS, Bleyl JA. Seventy-one quadruplet pregnancies: management and outcome. *Am J Obstet Gynecol* 1990;162:1384–91
77. Akrivis C, Varras M, Bellou A, Kitsiou E, Stefanaki S, Antoniou N. Primary postpartum haemorrhage due to a large submucosal non-pedunculated uterine leiomyoma: a case report and review of the literature. *Clin Exp Obstet Gynecol* 2003;30:156–8
78. Crowley P. Interventions for preventing or improving the outcome of delivery at or beyond term (Review). *Cochrane Database of Systematic Reviews* 2000;CD000170
79. Brinsden PR, Clark AD. Postpartum haemorrhage after induced and spontaneous labour. *Br Med J* 1978;2:855–6
80. Tylleskar J, Finnstrom O, Leijon I, Hedenskog S, Ryden G. Spontaneous labor and elective induction – a prospective randomized study. I. Effects on mother and fetus. *Acta Obstet Gynecol Scand* 1979;58:513–18
81. Bricker L, Luckas M. Amniotomy alone for induction of labour. (Review). *Cochrane Database of Systematic Reviews* 2000;CD002862

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82. Howarth GR, Botha DJ. Amniotomy plus intravenous oxytocin for induction of labour. (Review). *Cochrane Database of Systematic Reviews* 2001;CD003250
83. Kelly AJ, Tan B. Intravenous oxytocin alone for cervical ripening and induction of labour. (Review). *Cochrane Database of Systematic Reviews* 2001;CD003246
84. Boulvain M, Kelly A, Lohse C, Stan C, Irion O. Mechanical methods for induction of labour. (Review). *Cochrane Database of Systematic Reviews* 2001;CD001233
85. Boulvain M, Stan C, Irion O. Membrane sweeping for induction of labour.[update of Cochrane Database Syst Rev. 2001;(2):CD000451; PMID: 11405964]. (Review). *Cochrane Database of Systematic Reviews* 2001;CD000451
86. Alfirevic Z. Oral misoprostol for induction of labour.[update of Cochrane Database Syst Rev. 2000;(4):CD001338; PMID: 11034716]. (Review). *Cochrane Database of Systematic Reviews* 2001;CD001338
87. Hofmeyr GJ, Gulmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour.[update of Cochrane Database Syst Rev. 2001;(3):CD000941; PMID: 11686970]. (Review). *Cochrane Database of Systematic Reviews* 1905;CD000941
88. Kelly AJ, Kavanagh J, Thomas J. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term.[update of Cochrane Database Syst Rev. 2001;(2):CD003101; PMID: 11406078]. (Review). *Cochrane Database of Systematic Reviews* 2001;CD003101
89. Mahon TR, Chazotte C, Cohen WR. Short labor: characteristics and outcome. *Obstet Gynecol* 1994;84:47–51
90. Cohen WR. Influence of the duration of second stage labor on perinatal outcome and puerperal morbidity. *Obstet Gynecol* 1977;49:266–9
91. Saunders NS, Paterson CM, Wadsworth J. Neonatal and maternal morbidity in relation to the length of the second stage of labour. *Br J Obstet Gynaecol* 1992;99:381–5
92. Cheng YW, Hopkins LM, Caughey AB. How long is too long: Does a prolonged second stage of labor in nulliparous women affect maternal and neonatal outcomes? *Am J Obstet Gynecol* 2004;191:933–8
93. Myles TD, Santolaya J. Maternal and neonatal outcomes in patients with a prolonged second stage of labor. *Obstet Gynecol* 2003;102:52–8
94. Janni W, Schiessl B, Peschers U, *et al.* The prognostic impact of a prolonged second stage of labor on maternal and fetal outcome. *Acta Obstet Gynecol Scand* 2002;81:214–21
95. Combs CA, Laros RK Jr. Prolonged third stage of labor: morbidity and risk factors. *Obstet Gynecol* 1991;77:863–7
96. Dombrowski MP, Bottoms SF, Saleh AA, Hurd WW, Romero R. Third stage of labor: analysis of duration and clinical practice. *Am J Obstet Gynecol* 1995;172:1279–84
97. Magann EF, Evans S, Chauhan SP, Lanneau G, Fisk AD, Morrison JC. The length of the third stage of labor and the risk of postpartum hemorrhage. *Obstet Gynecol* 2005;105:290–3
98. Ploekinger B, Ulm MR, Chalubinski K, Gruber W. Epidural anaesthesia in labour: influence on surgical delivery rates, intrapartum fever and blood loss. *Gynecol Obstet Invest* 1995;39:24–7
99. Lertakyamanee J, Chinachoti T, Tritrakarn T, Muangkasem J, Somboonnanonda A, Kolatat T. Comparison of general and regional anesthesia for cesarean section: success rate, blood loss and satisfaction from a randomized trial. *J Med Assoc Thailand* 1999;82:672–80
100. Anonymous. Women – centred care. In National Collaborating Centre for Women’s and Children’s Health, ed. *Caesarean Section*. London: RCOG Press, 2004:20–5
101. Magann EF, Evans S, Hutchinson M, Collins R, Lanneau G, Morrison JC. Postpartum hemorrhage after cesarean delivery: an analysis of risk factors. *S Med J* 2005;98:681–5
102. Combs CA, Murphy EL, Laros RK Jr. Factors associated with hemorrhage in cesarean deliveries. *Obstet Gynecol* 1991;77:77–82
103. Gardella C, Taylor M, Benedetti T, Hitti J, Critchlow C. The effect of sequential use of vacuum and forceps for assisted vaginal delivery on neonatal and maternal outcomes. *Am J Obstet Gynecol* 2001;185:896–902
104. Carroli G, Belizan J. Episiotomy for vaginal birth. (Review). *Cochrane Database of Systematic Reviews* 2000;CD000081
105. Myers–Helfgott MG, Helfgott AW. Routine use of episiotomy in modern obstetrics. Should it be performed?. *Obstet Gynecol Clin N Am* 1999;26:305–25
106. House MJ, Cario G, Jones MH. Episiotomy and the perineum: A random controlled trial. *J Obstet Gynaecol* 1986;7:107–10
107. Dannecker C, Hillemanns P, Strauss A, Hasbargen U, Hepp H, Anthuber C. Episiotomy and perineal tears presumed to be imminent: randomized controlled trial. *Acta Obstet Gynecol Scand* 2004;83:364–8