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The incidence, aetiology, and coagulation management of massive postpartum haemorrhage: A 2-year national prospective cohort study

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Abstract

Introduction

This 2-year prospective cohort study describes the maternal outcomes of all women experiencing massive postpartum haemorrhage (PPH) in Wales between 2017 and 2018. During this period, a national quality improvement initiative was introduced which incorporated the use of point of care viscoelastic haemostatic assays (VHA) to guide blood product transfusion. Laboratory coagulation profiles, reported use and results of VHA and administration of blood products were investigated to assess how the introduction of VHA informed resuscitation management of these complex cases.

Methods

A database was designed to capture information for all women experiencing PPH >1000mL in Wales. In the current study, cases of massive PPH (≥ 2500 mL blood loss and/or ≥ 5 units red blood cell (RBC) transfusion) were identified.

Results

Between 2017 and 2018 there were 349 cases of massive PPH among 60914 maternities. The incidence of massive PPH was 5.7 per 1000 maternities. There were no deaths from PPH. Intensive care unit admission and or hysterectomy occurred in 34/311 (10.9%) and 16/347 (4.6%) of cases, respectively. The leading cause of massive PPH was genital tract trauma (107/349, 30.6%). The majority of women with massive PPH required RBC transfusion (279/346, 80.6%) and 79/345 (22.9%) received at least one blood coagulation product. Results of VHA were recorded in 245/349 (70.2%), with 44/98 (44.9%) women tested in the first 6 months vs 63/77 (81.8%) in the final 6 months of the 2-year period reported. Hypofibrinogenemia (Claus fibrinogen <2g/L or Fibtem A5 <12mm) was observed in 56/328 (17.1%) of women, thrombocytopenia (platelet count <75x10⁹) in 17/334 (5.1%) and either PT or aPTT >1.5x the reference range in 10/293 (3.4%).

Conclusion

This study provides a comprehensive summary of the management of all massive PPH cases in Wales. Previous studies of massive PPH report coagulation product transfusion in 39-99% of women. In this study the use of VHA increased over time, enabling clinicians to adopt a targeted, patient specific approach to blood product administration with only 22.9% of women receiving blood coagulation products and 17.1% with documented clotting abnormality.

Keywords: Coagulopathy, fibrinogen, hysterectomy, intensive care, postpartum haemorrhage

Highlights

- Massive PPH incidence in Wales (2017-2018) was 5.7 per 1000 maternities
- Red blood cell transfusion was received by 80.6%
- Blood coagulation products were received by 22.9%
- Point of care coagulation testing was recorded in 70.2% and increased over time
- Hypofibrinogenemia was the most frequent coagulation deficit, occurring in 17.1%

Introduction

Postpartum haemorrhage (PPH) is the leading cause of maternal death worldwide.^{1,2} In many regions of the world the incidence of PPH is increasing.²⁻⁵

Massive PPH can be defined as blood loss of $\geq 2500\text{mL}$ and or the transfusion of ≥ 5 units of packed red blood cells (RBC).³ In 2012, the Scottish Confidential Audit of Severe Maternal Morbidity observed high rates of both hysterectomy (6%) and intensive care admission (11.8%) in patients experiencing massive PPH, highlighting the contribution of massive PPH to major maternal morbidity. Improvements in PPH management are therefore vital to improve outcomes in these women.

Routine United Kingdom (UK) data do not provide an incidence for massive PPH, with only severe ($>1500\text{mL}$) rates reported.⁶ A limited number of international publications describe massive PPH using entry criteria based on blood transfusion ($\geq 4, 5$ or 8 units red blood cell (RBC) transfusion), however none of these reports include routine use of bedside viscoelastic haemostatic assays (VHA) such as rotational thromboelastometry (ROTEM) or thromboelastography (TEG) to guide management of coagulopathy.⁷⁻¹¹ One study has described the introduction of VHA in women with severe PPH and observed a reduction in blood product transfusion, but data were only reported for women treated for coagulopathy.¹² In order to optimise PPH resuscitation strategies, further research is required to understand the use of empirical blood product administration compared to targeted transfusion utilising bedside tests of coagulation.^{4,13,14}

The current study describes the maternal outcomes of all women experiencing massive PPH ($\geq 2500\text{mL}$ blood loss and or ≥ 5 units RBC transfusion) between 2017 and 2018 in multiple obstetric units in Wales. Outcome data were collected as part of the Obstetric Bleeding Strategy for Wales (OBS Cymru) quality improvement project and included maternal death, critical care admission, surgical procedures, and transfusion administration.¹⁵ Viscoelastic testing (ROTEM, Werfen, Barcelona) was introduced as standard care for all women with PPH. Details of laboratory coagulation studies, VHA results and PPH aetiology were also recorded. The purpose of this study is to describe the impact of VHA guided blood product transfusion (rather than empirical administration) during all cases of massive PPH, with the aim of improving understanding for coagulation product transfusion and maternal outcomes.

Methods

The OBS Cymru quality improvement project combined learning from a 10 year research programme with themes from international PPH quality improvement initiatives to create a care bundle that was adopted by all 12 obstetric units in Wales between 2017 and 2018.¹⁵⁻²⁰ The OBS Cymru project promoted risk assessment of all mothers admitted to the obstetric unit, quantitative measurement of blood loss for all births (incorporating validated gravimetric and volumetric techniques),²¹ escalation of clinical care at specific blood loss volumes and point of care VHA at 1000mL loss or clinical concern, to enable patient specific blood product management.¹⁵ In addition, tranexamic acid was infused at 1000mL blood loss.²² Cell salvage was available in all obstetric units, although no specific criteria for use were advocated by the OBS Cymru project. The lead research and development office at the University Hospital of Wales designated OBS Cymru a quality improvement project and service evaluation according to NHS guidance, therefore ethical approval, and individual consent to collect and report data was not required. The design, uptake and consequent improvements in maternal outcomes have been previously reported and include reductions in the $\geq 2500\text{mL}$ PPH rate and blood transfusion.^{16,23}

The Welsh Maternity Indicators Dataset (National Health Service (NHS) Wales Informatics Service) provided data regarding number of births, mode of delivery and PPH $\geq 2500\text{mL}$.²⁴ An All-Wales database was established by Improvement Cymru and collected data from January 1st, 2017 until December 31st, 2018 as part of OBS Cymru.¹⁵ The two databases were compared to ensure reliable data collection. Women experiencing blood loss $1000-1500\text{mL}$ or in whom there was concern about abnormal bleeding had a limited dataset recorded to describe uptake of the OBS Cymru project and are not reported in this study. Women with blood loss $\geq 2500\text{mL}$ or those who received any blood product transfusion had additional data collected

including mode, date, time and site of delivery, cause(s) of bleeding and critical care admission, surgical interventions, blood component transfusion and coagulation results.

Massive PPH was defined as women with total measured blood loss $\geq 2500\text{mL}$ and or those receiving ≥ 5 units RBC transfusion. High Dependency Unit (HDU, Level 2) and Intensive Care Unit (ICU, Level 3) admission was defined according to the Intensive Care Society Guidelines (2002).²⁵ Haemostatic impairment was defined as Clauss fibrinogen $< 2\text{g/L}$ or Fitem A5 $< 12\text{mm}$ (the lowest or most abnormal of either result was used), platelet count $< 75 \times 10^9$, or PT or aPTT $> 1.5 \times$ reference range (equating to prolonged PT $> 16.5\text{s}$ or aPTT $> 48\text{s}$) according national and international guidelines.^{4,14}

During the first 6 months of 2017, the OBS Cymru project was introduced into all 12 obstetric units in Wales. The introduction of VHA point of care coagulation devices (ROTEM) was staggered over this time, supported by a validated interpretation algorithm and All Wales PPH guideline.²⁶ A revised interpretation algorithm was introduced in 2018 to emphasise the importance of correction of hypofibrinogenemia before Fresh Frozen Plasma (FFP) administration.²⁷

Data are summarised descriptively with continuous variables reported as median, inter-quartile range (IQR) and range and categorical variables as number and percent or per 1000 maternities. Incomplete data is presented with denominators adjusted for available data and not imputed. Data were analysed using Microsoft Excel 365 (Redmond, Washington, USA).

Results

Between 1st January 2017 and 31st December 2018, 61094 women delivered in Wales, with 337 women recorded as having PPH $\geq 2500\text{mL}$ in the Maternity Indicators Dataset. There were 339 episodes of PPH $\geq 2500\text{mL}$ recorded in the OBS Cymru database and a further 10 women who received ≥ 5 units RBC transfusion. Thus, the total number of women with massive PPH was 349, giving an incidence of 5.7 per 1000 maternities. In this cohort, 18 (5.2%) were twin pregnancies and 331 (94.8%) were singletons. There were 331 women (94.8%) who delivered in an obstetric unit, 15 (4.3%) in a midwifery led unit and 3 (0.9%) at home. Blood loss was quantified in 333 (95.4%) of cases. The median ([IQR], range) total blood loss was 2814mL ([2602-3202], 841-7806). The mode of delivery was unassisted vaginal (121, 34.7%), emergency caesarean section (107, 30.7%), instrumental vaginal (83, 23.8%), elective caesarean (37, 10.6%) and not recorded (1, 0.3%). A greater proportion of deliveries occurred during the daytime hours of 8am to 8pm (212, 60.7%), and this was seen for all modes of birth.

Aetiology of postpartum haemorrhage

The cause of bleeding related to RBC transfusion, median total blood loss and blood coagulation product transfusion are shown in Table 1. Amniotic fluid embolism (AFE) and abnormal placentation (praevia and or increta or accreta) had the highest proportions of women requiring RBC transfusion and number of units of RBC administered per transfusion, with placenta increta or accreta leading to the highest median total blood loss. Placenta increta or accreta, AFE and placental abruption were associated with the greatest proportion of women transfused coagulation products.

Blood transfusion

Transfusion data are summarised in Table 2. A total of 110/346 (31.8%) women who experienced massive PPH received transfusion of ≥ 4 units RBC, 55/346 (15.9%) received ≥ 5 units RBC, 39/346 (11.3%) received ≥ 6 units RBC and 16/346 (4.6%) received ≥ 8 units RBC. No RBC transfusion was administered to 67/346 (19.4%) women with massive PPH. Cell salvage blood was recorded as being received by 11/98 (11.2%) women. The median [IQR] total blood loss for women receiving cell salvage blood was 3500mL [2900-5500], with a median [IQR] volume of blood returned to the woman of 300mL [200-489.5]. Of these 11 women, 9 (81.2%) also received allogenic blood transfusion and 5/11 (45.4%) women received blood coagulation products.

Coagulation profiles and coagulation product transfusion

The blood results recorded in the OBS Cymru database found 328/349 (94.0%) women having either fibrinogen or Fibtem. Two hundred and forty-five (70.2%) had a VHA (Fibtem), 293 (84.0%) had a laboratory coagulation studies (PT, aPTT and fibrinogen) and 334 (95.7%) had a platelet count. The most frequently observed coagulation deficit was hypofibrinogenemia (defined as laboratory fibrinogen <2g/L and or Fibtem <12mm), which was seen in 56/328 (17.1%) of cases. The median ([IQR], range) first laboratory fibrinogen level after delivery was 3.9g/L ([3.1-4.6], 0.4-7.1). Recorded PPH aetiology and documented hypofibrinogenemia is shown in Table 1. Only 10/293 (3.4%) women had a highest recorded PT >16.5s and 9/293 (3.1%) had an aPTT >48s. All the women who had PT >16.5s or aPTT >48s also had hypofibrinogenemia and they all received coagulation products. Of the 17/334 (5.1%) women with a lowest platelet count of <75 x10⁹/L, 11 had concurrent hypofibrinogenemia and 7 received platelet transfusion. One woman declined allogenic blood products and received recombinant factor 7a, she was not included in the number of women receiving coagulation products.

Review of the coagulation results in the 16 women receiving ≥8 units RBC transfusion identified 12/15 (80.8%) that had hypofibrinogenemia, whilst 5/14 (35.7%) had either PT or aPTT 1.5x the reference range and 5/14 (35.7%) had a platelet count <75 x10⁹.

There were 49 women who received a single type of coagulation product, 5 of these received no RBC transfusion and 30 women received multiple coagulation products. Of the 79/345 (22.9%) women who received coagulation products, 77 had laboratory coagulation indices or VHA recorded. In the 47/77 (61%) women who had documented hypofibrinogenemia, blood coagulation products administered were fibrinogen concentrate or cryoprecipitate alone in 16/47 (34%) and fibrinogen concentrate or cryoprecipitate with either FFP or platelets in 44/47 (93.6%). VHA results were recorded in 40/47 (85.1%). Thirty women did not have documented hypofibrinogenemia but received blood coagulation products. The majority were given FFP alone, 20/30 (66.7%). VHA results were recorded in 17/30 (56.7%) of these cases.

Over the course of the study, the number of women with a VHA result recorded increased to >80%: 44/98 (44.9%) in the first 6 months of 2017, then 70/92 (72.1%), 70/82 (85.4%) and 63/77 (81.8%) in the final 6 months of 2018. The proportion of women receiving FFP alone fell (11/27 (40.7%) in the first 6 months of 2017, then 5/18 (27.8%), 1/13 (7.7%) and 6/21 (28.5%) in the final 6 months of 2018. The proportion of women receiving fibrinogen concentrate or cryoprecipitate alone increased (6/27 (22.2%) in the first 6 months of 2017 then 2/18 (15.4%), 7/13 (53.8%) and 10/21 (47.6%) in the final 6 months of 2018.

Obstetric intervention and maternal critical care utilisation

Obstetric intervention and maternal critical care admissions are summarised in Table 3. A total of 19 hysterectomies were performed in Wales during 2017 - 2018, of whom 16/19 (84.2%) experienced massive PPH. The most common PPH aetiology for women who had a hysterectomy for massive PPH was placenta praevia and or increta or accreta (9, 56.3%). Comparison between 2017 and 2018 shows 7/190 (3.5%) vs 9/159 (5.7%) hysterectomies performed for massive PPH. There were 37 women who required ICU Level 3 admissions for PPH and 34/37 (91.9%) of these had massive PPH. During the first year of the study, 21/190 (11.0%) women were admitted to ICU compared to 13/159 (8.2%) in the second year. The median [IQR], range of ICU Level 3 care was 24 hours [18-25], 0-168. No woman died from PPH.

Impact of changes in PPH management during OBS Cymru quality improvement intervention

Comparison of the first 6 months of 2017 with the last 6 months of 2018 shows a reduction in massive PPH rate from 98/15,204 (6.5 per 1000 maternities) to 77/15,150 (5.1 per 1000 maternities) and a decrease in the number of women receiving ≥ 5 units RBC transfusion from 16/15,204 (1.1 per 1000 maternities) to 11/15,150 (0.7 per 1000 maternities).

Discussion

This report describes maternal outcomes of all women experiencing massive PPH in Wales between 2017 and 2018. The overall incidence was 5.7 per 1000 maternities with almost 5% of women requiring hysterectomy and 11% admitted to ICU (Level 3). Most women received RBC transfusion whilst rates of blood coagulation product administration and coagulation abnormalities were approximately 20%. Bedside VHA testing was incorporated into massive PPH management in the majority of cases, and results indicate that this approach enabled a targeted, patient specific approach to blood product transfusion, rather than empirical administration.

The major strength of this report is the inclusion of all women in Wales experiencing massive PPH during a 2-year period, with a denominator maternity population of 61,094. There was close agreement between the national reporting system (Maternity Indicators Dataset) and the OBS Cymru database, indicating robust data capture of women experiencing PPH ≥ 2500 mL. The OBS Cymru database was created to analyse implementation and uptake of the OBS Cymru quality improvement initiative, with a reduction in rates of ≥ 2500 mL PPH and blood transfusion reported.²⁸ The OBS Cymru database captured detailed information regarding women experiencing massive PPH, which has not been previously reported. This analysis is important because there are only a limited number of large, published datasets available that describe cases of massive PPH, with a single study incorporating use of VHA to inform coagulation product administration.^{3,7-12}

The limitation of this study is the lack of a control arm to allow comparison of PPH management before OBS Cymru intervention, with VHA gradually adopted by obstetric units during the first 6 months of the 2-year period. Other PPH management strategies such as uterotonic and surgical management of PPH (except hysterectomy), detailed patient demographic data, resuscitation fluids (other than blood products), uterotonics and neonatal outcomes were not recorded.

The hysterectomy rate was low in this study (0.3 per 1000 maternities) when compared to published international rates (0.36 to 1.04 per 1000 maternities), whilst the high numbers of abnormal placentation contributing to hysterectomy followed international trends.²⁹⁻³¹ The high percentage of women requiring HDU care on the obstetric unit highlights the importance of appropriate staff training and skills to avoid the psychological implications of physical separation of mother and baby at birth.³²

The mean number of RBC transfused per patient in this cohort was 3.4 units per woman. Causes of bleeding associated with the highest proportion of units of RBC transfused per patient were amniotic fluid embolism, placenta increta and abruption. As seen in the Scottish Maternal Morbidity Audit, almost 20% of women with massive PPH did not require any RBC transfusion, highlighting the importance of monitoring the haemoglobin level and targeted blood transfusion.³

The two leading causes of massive PPH were genital tract trauma and surgical trauma, a finding supported by the high rates of massive PPH observed in instrumental and emergency caesarean section. Instrumental and caesarean delivery have both been previously identified as risk factors for PPH.^{33,34} The substantial

contribution of instrumental delivery to massive PPH rates was also observed by Flood et al, although the low rates of coagulopathy and blood coagulation product transfusion seen in this cohort have not been previously reported.³⁵ Further studies are required to understand whether the risk, and indeed rate of massive PPH associated with genital tract trauma and instrumental delivery is related to second stage duration, the intervention performed or a combination.

Not all women in this cohort were treated using the VHA algorithm, since some cases were managed prior or during introduction of the device and use of the device increased over the duration of the project. Thirty (8.7%) women received blood coagulation product therapy with no recorded coagulopathy, the majority of whom were administered FFP. In these cases, women were given FFP empirically, with clinicians following trauma-based protocols. Most of the women (93.6%) with hypofibrinogenemia received coagulation products that included targeted fibrinogen replacement (either fibrinogen concentrate or cryoprecipitate), indicating the adoption of patient specific, VHA guided blood fibrinogen replacement in cases of coagulopathy. Review of the changes in management in the first and last 6 months of the project showed increased use of VHA, a reduction in FFP transfusion and increase in targeted fibrinogen administration supporting a phased uptake of the intervention.

Postpartum haemorrhage may be exacerbated by coagulation failure. Clauss fibrinogen of less than 2 g/L is associated with progression of PPH,¹⁸ whilst deficiencies of other clotting factors and platelets are less common.^{36,37} Hypofibrinogenemia was the most frequently observed coagulation deficit in this cohort, whilst less than 3.5% of women had either PT or aPTT of >1.5x the reference range and in all cases fibrinogen levels were also abnormal. These findings are similar to McNamara et al who report the introduction of VHA into management of major obstetric haemorrhage.¹² They identified hypofibrinogenemia in 23% of women with estimated blood loss ≥ 1500 ml and deficiencies in other clotting factors in only 5% (prolonged Extem CT). In this study, only 5% of women had a platelet count $< 75 \times 10^9$, with 4% receiving platelet transfusion. This finding is consistent with an analysis performed by Jones et al.³⁷ Lascia et al analysed women receiving ≥ 8 units RBC transfusion for PPH and found higher rates of coagulation deficit, with hypofibrinogenemia present in up to 52% of cases, platelet counts $< 50 \times 10^9$ in 16%, INR > 1.5 x normal in 18% and aPTT > 57 seconds 13%.¹¹ Women receiving ≥ 8 units RBC transfusion in this study had even higher rates of coagulopathy.

Causes of coagulopathy in this cohort were varied, reflecting both consumptive and dilutional processes. Hypofibrinogenemia was most frequently seen in abruption, AFE and uterine inversion, whilst coagulation products were most likely to be administered to cases of abruption, AFE and placenta increta or accreta. These observations are consistent with two recent UK based reports, in which coagulation changes differed substantially according to cause.^{8,12} Due to the diversity of coagulopathies (both consumptive and dilutional) observed in massive PPH the authors suggest VHA for all PPH cases to inform targeted blood product administration.

Delays in obtaining timely laboratory coagulation results have resulted in the integration of formulaic plasma transfusion with fixed ratios of FFP to RBC into PPH care; extrapolated from trauma-based protocols.^{4,38} The use of an empirical approach is reflected in massive PPH reports, in which 39-99% of women receive FFP.^{3,7-11} Several publications have now challenged this approach. A recent cohort study found no improvement in maternal outcomes associated with early FFP transfusion and theoretical modelling of PPH suggests that administration of FFP may dilute fibrinogen levels in some instances.^{39,40} Collins et al performed a multicentre PPH randomised controlled study, in which only 55 of the 663 women recruited with > 1000 ml PPH and bleeding ongoing were found to have Fibtem ≤ 15 mm (approximately fibrinogen < 3 g/L).¹⁸ Withholding FFP in those without evidence of coagulopathy on VHA did not result in clinically significant

haemostatic impairment and avoided unnecessary blood coagulation products exposure.¹⁹ McNamara et al published four years of observational data following introduction of VHA to inform treatment of coagulopathy in major obstetric haemorrhage and identified improvements in outcomes and reduced FFP administration with adoption of this strategy.¹² This report supports the findings of McNamara et al but also suggests that an individualised management approach using a VHA based algorithm to inform coagulation product administration can be adopted by multiple obstetric units.

In conclusion, we describe a cohort of 349 women experiencing massive PPH in Wales. Management of PPH included routine quantification of blood loss from delivery and use of bedside testing of coagulation to guide blood product replacement. This report suggests that this approach has enabled proactive identification and treatment of coagulopathy, whilst minimising empirical coagulation product administration in the majority. To understand the impact of VHA in PPH, standardised reporting of PPH rates incorporating quantification of blood loss volumes and or blood product transfusion is needed. Furthermore, randomised controlled trials to evaluate the impact of VHA on maternal outcomes are urgently required.

References

1. Say L, Chou D, Gemmill A, et al. Global causes of maternal death: A WHO systematic analysis. *Lancet Global Health* 2014;**2(6)**:e323-e33.
2. Kramer MS, Berg C, Abenheim H, et al. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. *Am J Obstet Gynecol* 2013;**209(5)**:449.e1-7.
3. Marr L, Lennox C, McFadyen AK. Quantifying severe maternal morbidity in Scotland: a continuous audit since 2003. *Curr Opin Anaesthesiol* 2014;**27(3)**:275-81.
4. Mavrides E, Allard S, Chandraran E, et al. Prevention and management of postpartum haemorrhage. *BJOG* 2016;**124**:e106-e49.
5. WHO. WHO recommendations for the prevention and treatment of postpartum haemorrhage 2012. Available at https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548502/en/. Accessed November 6th, 2020.
6. NMPA Project Team. National Maternity and Perinatal Audit: Clinical Report 2019. Based on births in NHS maternity services between 1 April 2016 and 31 March 2017. London: RCOG; 2019.
7. Green L, Knight M, Seeney FM, et al. The epidemiology and outcomes of women with postpartum haemorrhage requiring massive transfusion with eight or more units of red cells: a national cross-sectional study. *BJOG* 2016;**123(13)**:2164-2170.
8. Green L, Knight M, Seeney F, et al. The haematological features and transfusion management of women who required massive transfusion for major obstetric haemorrhage in the UK: a population based study. *Br J Haematol* 2015;**172(4)**:616-24.
9. Ramler PI, van den Akker T, Henriquez DDCA, et al (TeMpOH-1 study group). Women receiving massive transfusion due to postpartum hemorrhage: A comparison over time between two nationwide cohort studies. *Acta Obstet Gynecol Scand* 2019 ;**98(6)**:795-804.
10. Deleu F, Deneux-Tharaux C, Dhiesia-Dubruille C, Seco A, Bonnett M. P. A population-based analysis of French transfusion practices for women experiencing severe postpartum haemorrhage. *Int J Obstet Anesth* 2020;**42**:11-19.
11. Lascia M Sparrow R L, Tacey M, Pollock WE, Wood EM, McQuilten ZK. Haematological features, transfusion management and outcomes of massive obstetric haemorrhage: findings from the Australian and New Zealand Massive Transfusion Registry. *BJHaem* 2020;**190(4)**:618-628.
12. McNamara H, Kenyon C, Smith R, et al. Four years' experience of a ROTEM®-guided algorithm for treatment of coagulopathy in obstetric haemorrhage. *Anaesthesia* 2019;**74(8)**:984-91.
13. Muñoz M, Stensballe J, Ducloy-Bouthors AS, et al. Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement. *Blood Transfus* 2019;**17(2)**:112-136.

14. Collins P, Kadir R, Thachil J. Management of coagulopathy associated with postpartum haemorrhage: guidance from the SSC of ISTH. *Journal of Thrombosis and Haemostasis* 2016;**14**:205-10.
15. Bell SF, Kitchen T, M. J, et al. Designing and Implementing an All Wales Postpartum Haemorrhage Quality Improvement Project: OBS Cymru (The Obstetric Bleeding Strategy for Wales) *BMJ Quality* 2020;9:e000854.
16. Collins PW, Bell SF, Lloyd d, et al. Management of postpartum haemorrhage: from research into practice, a narrative review of the literature and the Cardiff experience. *Int J Obstet Anesth* 2018;**37**:106-17.
17. Collins PW, Cannings-John R, Bruynseels D, et al. Viscoelastometric-guided early fibrinogen concentrate replacement during postpartum haemorrhage: OBS2, a double-blind randomized controlled trial. *Br J Anaesth* 2017;**119(3)**:411-21.
18. Collins PW, Lilley G, Bruynseels D, et al. Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study. *Blood* 2014;**124(11)**:1727-36.
19. Collins PW, Cannings-John R, Bruynseels D, et al. Viscoelastometry guided fresh frozen plasma infusion for postpartum haemorrhage: OBS2, an observational study. *Br J Anaesth* 2017;**119(3)**:422-34.
20. Main EK, Cape V, Abreo A, et al. Reduction of severe maternal morbidity from hemorrhage using a state perinatal quality collaborative. *Am J Obstet Gynecol* 2017;**216(3)**:298.
21. Bell SF, Watkins A, John M et al. Incidence of postpartum haemorrhage defined by quantitative blood loss measurement: a national cohort. *BMC Pregnancy Childbirth* 2020; **20**:271.
22. Shakur H, Roberts I, Fawole B, et al. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2017;**389(10084)**:2105-16.
23. Bell SF, Collis RE, Pallmann P et al. Reduction in massive postpartum haemorrhage and red blood cell transfusion during a national quality improvement project, Obstetric Bleeding Strategy for Wales, OBS Cymru: an observational study. *Under peer review*.
24. Maternity Indicators Data Set for Wales 2018. Available at <https://stats.wales.gov.wales/Catalogue/Health-and-Social-Care/NHS-Primary-and-Community-Activity/Maternity/numberofdeliveries-by-ageofmother-deliverymethod>. Accessed November 6th, 2020.
25. The Intensive Care Society. Guidelines for the provision of intensive care services. Edition 2, 2019. Available at <https://www.ficm.ac.uk/sites/default/files/gpics-v2.pdf>. Accessed November 6th, 2020.
26. Maternity Network Wales 2017. Prevention and management of postpartum haemorrhage. Available at http://www.wisdom.wales.nhs.uk/sitesplus/documents/1183/All%20Wales%20Prevention%20of%20Postpartum%20Haemorrhage%20%281.4%29_2018.pdf. Accessed November 6th, 2020.
27. Obstetric Anaesthetist Association. OBS Cymru checklist and Rotem protocol 2019. Available at <https://www.oaa-anaes.ac.uk/ui/content/content.aspx?ID=76>. Accessed November 6th, 2020.
28. Bell SF, Collis RC, Pallmann P et al. Reduction in massive postpartum haemorrhage and red blood cell transfusion during a national quality improvement project, Obstetric Bleeding Strategy for Wales, OBS Cymru: an observational study. *In press*.
29. Briley A, Seed PT, Tydeman G, Ballard, H, Waterstone, M, Sandall I, Poston L, Tribe RM, Bewley S. Reporting errors, incidence and risk factors for postpartum haemorrhage and progression to severe PPH: a prospective observational study. *BJOG* 2009;**121(7)**:876-888.
30. Smith J, Mousa HA. Peripartum hysterectomy for primary postpartum haemorrhage: incidence and maternal morbidity. *J Obstet Gynaecol* 2007;**27(1)**:44-7.
31. Reale SC, Easter SR, Xu X, Bateman BT, Farber MK. Trends in Postpartum Hemorrhage in the United States From 2010 to 2014. *Anesth Analg* 2020;**130(5)**:e119-e122.
32. Hinton L, Locock L, Knight M. Maternal critical care: what can we learn from patient experience? A qualitative study. *BMJ Open* 2015;**5(4)**:e006676.
33. Kramer MS, Berg C, Abenheim H, Dahhou M, Rouleau J, Mehrabadi A, Joseph KS. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. *Am J Obstet Gynecol* 2013;**209(5)**:449.e1-7.
34. Miller CM, Cohn S, Akdagli S, Carvalho B, Blumenfeld YJ, Butwick AJ. Postpartum hemorrhage following vaginal delivery: risk factors and maternal outcomes. *J Perinatol* 2017;**37(3)**:243-248.

35. Flood M, McDonald SJ, Pollock W, Cullinane F, Davey MA. Incidence, trends and severity of primary postpartum haemorrhage in Australia: A population-based study using Victorian Perinatal Data Collection data for 764 244 births. *Aust N Z J Obstet Gynaecol* 2019 ;**59(2)**:228-234.
36. De Lloyd L, Bovington R, Kaye A, et al. Standard haemostatic tests following major obstetric haemorrhage. *Int J Obstet Anesth* 2011;**20(2)**:135-41.
37. Jones R, Hamlyn V, Collis R, et al. Platelets count and transfusion requirements during moderate or severe postpartum haemorrhage. *Anaesth* 2016;**71**:648-56.
38. Pacheco LD, Saade GR, Costantine MM, Clark SL, Hankins GD. An update on the use of massive transfusion protocols in obstetrics. *Am J Obstet Gynecol* 2016;**214(3)**:340-344.
39. Henriquez DDCA, Caram-Deelder C, le Cessie S, et al. Association of Timing of Plasma Transfusion With Adverse Maternal Outcomes in Women With Persistent Postpartum Hemorrhage. *JAMA Netw Open* 2019;**2(11)**:e1915628.
40. Collins PW, Solomon C, Sutor K, et al. Theoretical modelling of fibrinogen supplementation with therapeutic plasma, cryoprecipitate, or fibrinogen concentrate. *Br J Anaesth* 2014;**113(4)**:585-95

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Tables and Figures

PPH aetiology	n (%)	Total blood loss, mL	Women transfused RBC (%)	Total RBC transfused, units (mean, per woman)	Women transfused any coagulation products (%)	Women with hypo-fibrinogenaemia (%)
ALL	349	2814 [2602-3202]	279/346 (80.6)	944 (3.4)	79/345 (22.8)	56/328 (17.0)
Atony alone	80 (22.9)	2792 [2603-3087]	64/79 (81.0)	208 (3.3)	17/79 (20.8)	10/71 (14.1)
Surgical trauma	85 (24.9)	2778 [2549-3005]	68/85 (80.0)	229 (3.4)	20/85 (23.5)	15/71 (21.1)
Genital tract trauma	107 (30.6)	2877 [2644-3294]	86/107 (80.3)	275 (3.2)	16/106 (15.0)	10/100 (10.0)
Retained products of conception	49 (14.0)	2945 [2681-3243]	39/49 (79.5)	130 (3.3)	12/49 (24.4)	7/48 (14.9)
Placental abruption	19 (5.4)	2800 [2628-3173]	14/19 (73.6)	50 (3.6)	9/19 (47.3)	7/19 (36.8)
Placenta praevia	12 (3.5)	3000 [2580-3588]	10/12 (83.3)	38 (3.8)	2/12 (16.7)	1/12 (8.3)
Placenta increta or accreta	13 (3.7)	4000 [3000-5543]	13/13 (100)	60 (4.6)	5/13 (38.4)	5/13 (38.5)
Uterine rupture	4 (1.2)	3081 [2725-3552]	3/4 (75)	12 (4)	1/4 (25)	1/4 (25)
Uterine inversion	2 (0.6)	3195 [3158-3121]	1/2 (50)	4 (4)	0/2 (0)	1/2 (50)
Amniotic fluid embolism	1 (0.3)	3865	1/1 (100)	8 (8)	1/1 (100)	1/1 (100)
Extragenital bleeding alone	1 (0.3)	3161	1/1 (100)	2 (2)	0/1 (0)	0/1 (0)

Table 1 PPH aetiology, total blood loss, RBC transfusion, blood coagulation product transfusion and hypofibrinogenemia in women with massive PPH (women could have multiple PPH aetiologies recorded)

Values are n (%), median [IQR], n (mean). PPH: Postpartum haemorrhage, RBC: Red blood cell, hypofibrinogenemia: Fibtem <12mm or Clauses fibrinogen <2g/L

Blood product	Women transfused, n (%)	Total transfused, units/g	Transfusion per woman, units/g
RBC	279/346 (80.6)	944	2 [2-4, (0-15)]
Fibrinogen concentrate	43/346 (12.4)	220	0 [0-0, (0-14)]
FFP	43/345 (12.4)	194	0 [0-0, (0-12)]
Cryoprecipitate	11/345 (3.1)	27	0 [0-0, (0-5)]
Platelets	15/345 (4.3)	23	0 [0-0, (0-3)]

Table 2 Blood product transfusion in women with massive PPH

Values are n (%), median [IQR, (range)]. RBC: Red blood cell, FFP: Fresh frozen plasma

	n (%)
Obstetric intervention	
Haemostatic uterine suture	24/310 (7.7)
Bakri balloon insertion	74/259 (28.5)
Internal artery ligation	3/332 (0.9)
Interventional radiology	8/ 338 (2.3)
Hysterectomy for PPH	16/347 (4.6)
Critical care admission	
HDU (Level 2) care delivered on obstetric unit	301/341 (88.2)
HDU (Level 2) care delivered on adult critical care unit	17/315 (5.3)
ICU (Level 3) care	34/311 (10.9)

Table 3 Obstetric interventions and critical care utilisation for women with massive PPH

Values are n (%). PPH: Postpartum haemorrhage, HDU: High dependency unit, ICU: Intensive care unit