Thrombosis Research 129 (2012) e1–e7

Contents lists available at SciVerse ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Risk factors for postpartum hemorrhage in a cohort of 6011 Italian women

Eugenia Biguzzi [a,*], Franca Franchi [a], Federico Ambrogi [b], Buthaina Ibrahim [a], Paolo Bucciarelli [a], Barbara Acaia [c], Tatjana Radaelli [c], Elia Biganzoli [b], Pier M. Mannucci [a,d]

[a] A. Bianchi Bonomi Hemophilia and Thrombosis Center, Department of Medicine and Medical Specialties, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico and University of Milan, Via Pace 9, 20122 Milan, Italy
[b] Institute of Medical Statistics and Biometry "G.A.Maccacaro", University of Milan and Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milan, Italy
[c] Woman, Child and Neonate Health Department, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico and University of Milan, Via della Commenda 10, 20122 Milan, Italy
[d] Scientific Direction, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico and University of Milan, Via F. Sforza 35, 20122 Milan, Italy

ARTICLE INFO

Article history:
Received 17 June 2011
Received in revised form 18 August 2011
Accepted 14 September 2011
Available online 20 October 2011

Keywords:
Post-partum hemorrhage
risk factors
ante-partum hemoglobin

ABSTRACT

Introduction: Postpartum hemorrhage is responsible for 25% of maternal pregnancy-related deaths and it is the first cause of maternal morbidity and mortality worldwide.
Objective: To define the prevalence of postpartum hemorrhage and associated risk factors after vaginal birth and to develop a risk model that improves postpartum hemorrhage prediction.
Patients and methods: All women who underwent a vaginal delivery at the Obstetric Unit of a large University hospital in Milan (Italy) between July 2007and September 2009 were enrolled. Postpartum hemorrhage was defined as ≥500 mL blood loss. A nomogram tailored to predict postpartum hemorrhage was developed, summarizing the impact of each covariate on the probability of postpartum hemorrhage.
Results: 6011 women were studied (24% had blood loss ≥500 mL and 4.8% ≥1000 mL). Nulliparity, episiotomy, retained placenta and high neonatal body weight were confirmed as risk factors for postpartum hemorrhage. The odds ratio of postpartum hemorrhage was 0.86 (95%CI 0.78-0.90) for each 1 gr/dL increase in ante-partum hemoglobin. An extensive internal validation of the developed nomogram demonstrated a good stability of the risk model.
Conclusions: Low ante-partum hemoglobin is a new potentially modifiable risk factor for postpartum hemorrhage. A nomogram to predict the probability of postpartum hemorrhage is now available for external validation.

Introduction

Postpartum hemorrhage (PPH) is responsible for 25% of maternal pregnancy-related deaths reported by the World Health Organization [1]. In spite of the fact that the prevalence of PPH varies in developed and developing countries [2], it is still the first cause of maternal morbidity and mortality worldwide [3]. Moreover, an increasing trend in PPH is observed in Australia, Canada, UK and USA [4], so that it is important that every hospital monitors the prevalence of PPH in their own department and analyzes if some changes are needed in the clinical practice to prevent PPH. Although PPH is an unpredictable event in many cases, several risk factors are described. Among them, there are such maternal characteristics as age≥35 years, Asian and Hispanic ethnicity, obesity, nulliparity, inherited coagulation disorders, uterine fibroids and a previous history of PPH [5–13]. Described intrapartum risk factors for PPH are: labour induction, prolonged first, second and third stage of labour, use of forceps or vacuum extractor, episiotomy, genital tract lacerations, retained placenta, placenta accreta, fetal macrosomia and multiple pregnancies [6,7,10,13–18]. However, the definition of PPH is not fully standardized, making comparison between studies difficult. Following the World Health Organization, most obstetricians define PPH as blood loss ≥500 mL occurring in the first 24 hours after delivery, and severe PPH as blood loss ≥1000 mL [14,19,20]. In other studies PPH is defined as the need of blood transfusion [6], or is not clearly defined [15]. Moreover, there is some variability in the methods used to estimate the amount of blood loss: visual estimation, in spite of its demonstrated inaccuracy in evaluating large volumes of blood loss [21,22], is still the most frequently used method in the USA. Alternatively, blood loss can be measured directly after its collection in a special basin or by weighing used swabs, or a combination of both. However, direct measurement may be inaccurate, because other fluids (i.e. urine) might be inadvertently collected. For this reason, some studies compare ante- and postpartum hematocrit and define PPH as a decrease in hematocrit level by 10% [7]. Finally, recent changes in the obstetricians' practice (e.g. routine use of oxytocics) or different social contexts (e.g. decreasing parity among women, home delivery for low risk pregnancies in some countries) make the comparison between studies even more difficult.

Abbreviation: PPH, postpartum hemorrhage.

* Corresponding author at: A. Bianchi Bonomi Hemophilia and Thrombosis Center, Fondazione IRCCS Ca' Granda and University of Milan, Via Pace, 9–20122 Milan Italy. Tel.: +39 02 55035464; fax: +39 02 50320723.
E-mail address: biguzzi@policlinico.mi.it (E. Biguzzi).

0049-3848/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.thromres.2011.09.010

The aim of this study was to define the prevalence of PPH and associated risk factors after vaginal birth in a large obstetric unit in Northern Italy, in order to identify women at risk for PPH and to develop a risk model that could improve the capability of PPH prediction. Such a model was integrated in a specially tailored nomogram that might be used to modify delivery guidelines and activate a specific obstetrical management if needed.

Materials and methods

Study population

The study population included all women who underwent a vaginal delivery at the Obstetric Unit of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico in Milan (Lombardia region, Northern Italy) in the period between July 2007 and September 2009. Exclusion criteria were: age <18 years, caesarean section, delivery before the 37th week of gestation, twin pregnancy, no comprehension of the Italian language, refusal to sign a written informed consent. Deliveries that occurred on Friday afternoon were not included in the study because of the impossibility to approach the puerperae on Monday morning (minimum hospitalization after delivery being two days).

Labour induction was performed by using vaginal prostaglandins or, in case of favourable Bishop score, amniotomy associated with oxytocin. In case of instrumental delivery, the Kiwi vacuum extractor was used. Third stage active management involved the use of intramuscular injection of 10 IU oxytocics after child expulsion.

Data collection

The following data were collected by obstetricians during labour and delivery or during the antenatal care visits: maternal demographics, parity, history of previous fetal loss, intra-uterine growth restriction and preeclampsia, current medical conditions, pregnancy-related diseases, fetal conditions, delivery methods, ante-partum complications, intrapartum and immediate postpartum events, blood transfusions, hematological and biochemical laboratory data. Parity was defined as follows: nulliparous in case of women who had never given birth and will deliver their first child, primiparous in case of women who had already given birth to one child and will deliver their second child, multiparous in case of women who had given birth to more than one child before the present pregnancy. A neonatal weight was defined as low when it was under the 10th percentile based on the SMILA Neonatal Standards for North East Italy (Montecatini Sept 1996). Labour was defined as induced when amniotomy, prostaglandin gel or oxytocin were used. Episiotomy was classified as midline (incision at the perineal midline) or midlateral (incision in a medio-lateral position at an angle from the posterior end of the vulva). Genital tract lacerations were recorded separately from episiotomies. The Kristeller's maneuver (also known as fundal pressure) was defined as the pressure applied with hands upon the uterine fundus synchronously with labour pains in case of weak uterine contraction during the second stage of labour. Analgesia consisted in an epidural anesthesia. Ante-partum hemoglobin and platelet levels were those obtained within one month before delivery. Maternal weight was recorded at the end of pregnancy. Beside data from medical charts, information on family and personal history of bleeding were collected by interviewing each puerpera after delivery. Results were subsequently cross-checked with the hospital administrative records. Blood loss was measured using a disposable plastic graduated basin, put under the woman's buttocks soon after delivery, and recorded in the clinical chart. PPH was defined as ≥500 mL of blood loss according to the original WHO criteria [20].

The study was approved by the Institutional Review Board of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, and a written informed consent was obtained from all participants.

Statistical analysis

Continuous variables were presented as median with minimum and maximum values, and categorical variables as counts and percentage.

To estimate the impact of each putative risk factor on the risk of PPH, a multiple logistic regression model was adopted considering PPH (blood loss of ≥500 mL) as outcome variable. As categorical risk factors (yes *vs* no unless described) we considered parity (nulliparous, primiparous, multiparous), ethnicity (non-Caucasian *vs* Caucasian), blood group (O *vs* non-O), labour induction, use of epidural analgesia, genital tract lacerations, episiotomy (no, midline, midlateral), use of vacuum extractor, Kristeller's maneuver (none, 1 or 2, >2) and retained placenta. For risk factors expressed as continuous variables (maternal age, maternal weight, neonatal birth weight, placental weight, ante-partum hemoglobin levels and ante-partum platelet number), the odds ratio and its 95% confidence intervals (95%CI) were calculated for predefined increases of the variables (5 years for maternal age, 5 Kg for maternal weight, 100 g for neonatal birth weight and placental weight, 1 g/dL for ante-partum hemoglobin, 30×10^3/μL for ante-partum platelet number). The possible presence of non-linear effects of these continuous variables on the risk of PPH was evaluated using restricted cubic spline functions with 3 knots, and the effect of each covariate on the outcome was assessed by plotting model-predicted log odds against covariate values. The Wald test was used for the presence of non-linear effects globally and for each variable. In addition, the following two-way interactions were included on the basis of their putative clinical relevance: a) parity together with episiotomy, neonatal birth weight, ante-partum hemoglobin, ethnicity, Kristeller's maneuver and use of vacuum extractor; b) episiotomy together with ethnicity, neonatal birth weight and ante-partum hemoglobin; c) ethnicity together with ante-partum hemoglobin. The predictive value capability of the logistic model was measured in terms of discrimination by means of the area under the ROC curve, correcting for optimism by using bootstrap sampling (200 replicates) [23]. Moreover, calibration of predicted probabilities was assessed by means of graphical methods, plotting them against observed outcomes. The relative contribution of each covariate on outcome variability was expressed in terms of explained variation resorting to partial R^2_{SS} coefficients [24]. In particular, the contribution of a specific covariate was obtained by observing the difference between the R^2_{SS} of the model including all covariates with respect to the model excluding that particular covariate. When a particular covariate was excluded from the model, also the corresponding interactions were excluded. The same strategy was used to assess the relative contribution of each interaction. The estimated regression coefficients of the logistic model allowed to estimate the probability of PPH for different combinations of the risk factors. This goal could be achieved by clinical staff in a direct graphical way with no calculations by means of a nomogram obtained starting from the logistic model results, summarizing the impact of each covariate on the probability of PPH. In this framework, the nomogram is particularly useful to perceive the impact of different risk factors together with individual risk assessment. The value of each risk factor is translated into a score which is directly connected to the probability of PPH, the most relevant risk factors being associated with the greatest increase in the score.

All analyses were performed with the statistical software R (release 2.9.1; R Project for Statistical Computing, Vienna, Austria).

Results

In the 2-year period of recruitment, 8530 women underwent vaginal delivery. Among them, 2495 (29%) were excluded for reasons listed in Fig. 1. For 24 additional women no information were available on blood loss during delivery due to lack of registration. Hence,