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Risk factors analysis and a scoring system proposal for the prediction of retained placenta after vaginal delivery



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ABSTRACT

Introduction: Retained placenta (RP) is an obstetric complication of third stage of labour. We aimed to evaluate risk factors for RP and to propose a scoring system in order to predict this potentially fatal disorder.

Methods: This was a retrospective case-control study, comparing women with RP after vaginal delivery (≥ 24 weeks of gestation) and women with regular placental separation. Data were collected from January 2007 to October 2017, in two 2nd level University Hospitals. Eligibility was limited to singleton pregnancies in vertex presentation with no major foetal anomaly. A nomogram was developed to predict RP risk.

Results: Among 22,749 women who delivered vaginally, 138 (0.6%) had RP. RP was directly related with previous uterine curettage (OR = 1.92, 95% CI 1.04–3.54, $p = 0.04$) and labour induction with prostaglandins (OR = 4.29, 95% CI 1.83–10.02, $p = 0.001$), while vaginal spontaneous delivery (OR = 0.03, 95% CI 0.01–0.15, $p = 0.0001$) and higher Apgar score at 1 min (OR = 0.5, 95% CI 0.33–0.76, $p = 0.001$) were inversely related to RP. Our predictive model showed an overall diagnostic accuracy of 0.803.

Discussion: RP is associated with several maternal, pregnancy, foetal and placental risk factors. The development of a new scoring system, with a high predictive power, able to identify the risk of RP, could be a useful tool for physicians in order to promptly face this life-threatening condition.

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Introduction

Retained placenta (RP) is an obstetric complication associated with a high risk of post-partum haemorrhage [1,2], which complicates 0.5–3% of all vaginal deliveries [2,3–6]. Although no consensus has been declared for the time required to consider a prolonged third stage of labour, the National Institute of Health and Care Excellence (NICE) defines RP as the condition in which the placenta is retained after 30 min of active management or 60 min of physiological management [7,8]. Indeed, in case of RP, the management may involve manual or operative removal, with a high risk of haemorrhage, post-partum infections and prolonged hospitalization [9–13].

In previous studies, several risk factors have been associated with RP after vaginal delivery, such as advanced maternal age,

previous uterine dilation and curettage, previous caesarean section, preterm delivery, labour induction, premature rupture of membranes (PROM), abnormal adherent placenta as well as hypertensive disorders [14,15]. Nevertheless, RP is still today an obstetric pathology difficult to predict.

The aim of this study was to evaluate the risk factors correlated with RP after vaginal delivery. Moreover, a new scoring system to predict pregnant women at high risk of RP was proposed.

Materials and methods

A retrospective case control study was conducted between January 2007 and October 2017 in two 2nd level University Hospitals, the Department of Obstetrics and Gynecology, Perugia, Italy, and the Department of Obstetrics and Gynecology, Terni, Italy, both belonging to the University of Perugia, Italy.

Study design, analysis, interpretation of data, drafting and revisions were done following the strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies, available through the EQUATOR (Enhancing the QUALity and Transparency Of health Research) network [16]. The study design was in accordance with

Abbreviations: RP, retained placenta; E/P, estro-progestins; D&C, dilatation and curettage; PG, prostaglandins; OXT, oxytocin; PPH, post-partum haemorrhage; PROM, premature rupture of membranes.

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the Helsinki Declaration, conforms the committee on publication ethics (COPE) guidelines. Institutional Review Board approval was obtained for data collection.

Singleton pregnancies in vertex presentation, with no major foetal anomaly, which vaginally delivered and diagnosed with RP were considered eligible for the analysis. RP cases were identified going back to the codes established by the ICD-9-CM (International Classification of Diseases- 9th revision- Clinical Modification). Histological diagnosis of placenta accreta was considered as exclusion criteria.

According to the International guidelines, an active management of the third stage of labour was offered to all women after delivery: 10 IU of oxytocin were administered intramuscularly immediately after birth; the cord was clamped after 1–2 min, unless immediate clamping was required for maternal and/or newborn indication and a controlled cord traction after signs of separation of the placenta was performed [7]. If the placenta was not delivered within 30 min, active management with manual removal was performed (earlier in case of heavy bleeding).

The control group was selected referring to the pregnant woman who vaginally delivered, treated by an active management of the third stage of labour, with a physiological placental separation, following the inclusion of a patient with RP in the study group.

For each woman, the following data were recorded: maternal age, ethnicity, history of estro-progestins therapy, previous uterine dilation and curettage, labour induction with prostaglandins, duration of oxytocin administration, instrumental vaginal delivery, post-partum blood loss, birth weight, Apgar score at 1 and at 5 min, placental weight, placental implantation site, umbilical cord insertion.

Statistical analysis

The Shapiro-Wilk test was used to assess the normal distribution of variables. The Chi-square test with Yate's continuity correction and Fisher's exact test were used for comparisons of categorical variables and the Mann-Whitney's *U*-test was used for

comparisons of non-normally distributed continuous variables. Bivariate and multivariate logistic regression models were fitted for the prediction of the presence of RP incorporating all the variables that showed a p -value ≤ 0.25 in bivariate analysis (Hosmer DW, Lemeshow S. Applied Logistic Regression. John Wiley & Sons, New York, 2000) as explanatory variables. To decrease the overfit bias and internally validate our results, all bivariate and multivariate regressions were subjected to 200 bootstrap resamples and the goodness-of-fit of logistic models was checked using Hosmer and Lemeshow test. Odds ratios (ORs) with 95% confidence intervals were also calculated.

Furthermore, multivariate logistic regression coefficients were used to develop a RP based nomogram (Orange software, version 3.4.2, 2017; <https://orange.biolab.si/>) (Demsar J, Curk T, Erjavec A, Gorup C, Hocevar T, Milutinovic M, Mozina M, Polajnar M, Toplak M, Staric A, Stajdohar M, Umek L, Zagar L, Zbontar J, Zitnik M, Zupan B (2013) Orange: Data Mining Toolbox in Python. Journal of Machine Learning Research 14(Aug):2349 – 2353) and its predictive accuracy was quantified as the area under the receiver operating characteristics curve (AUC).

All statistical analysis was performed using IBM-SPSS® version 23.0 (IBM Corp., Armonk, NY, USA, 2015). In all analyses, a two-sided p -value < 0.05 was considered significant.

Results

During the study period, 22,749 women met inclusion criteria. Among these, 147 cases of RP were diagnosed, but 9 cases were excluded from the study due to the histological diagnosis of accretism. Thus, 138 cases were eligible for the analysis and the rate of RP in our study was 0.6%.

Maternal characteristics analyzed are shown in Table 1. Comparing the two groups, a higher maternal age ($p = 0.011$) and a lower rate of previous estro-progestins therapy ($p = 0.026$) were found in women with RP. The rate of prior gynaecological procedures was significantly higher in the RP group, in term of previous uterine curettage ($p = 0.016$). No differences were observed regarding previous caesarean sections and fertility

Table 1
Maternal, pregnancy and delivery characteristics.

	Retained placenta (n = 138)	Control group (n = 150)	<i>p</i> value
Maternal age (years)	34 (20-44)	32 (20-45)	0.011
Ethnicity			0.029
caucasian	127 (92.0)	142 (94.7)	
african	7 (5.1)	1 (0.7)	
hispanic	4 (2.9)	3 (2.0)	
asiatic	0 (0.0)	4 (2.7)	
E/P therapy	60 (43.5)	86 (57.3)	0.026
Previous uterine D&C			0.016
0	96 (69.6)	129 (86.0)	
1	27 (19.6)	17 (11.3)	
2	9 (6.5)	3 (2.0)	
≥ 3	6 (4.3)	1 (0.7)	
Labor induction PG	28 (20.3)	14 (9.3)	0.014
Time of OXT (min)	0.0 (0-720)	0.0 (0-605)	0.048
Instrumental delivery	33 (23.9)	2 (1.3)	0.0001
PPH			0.0001
< 500 cc	79 (57.2)	131 (87.3)	
500-1000 cc	21 (15.2)	16 (10.7)	
1000-2000 cc	31 (22.5)	3 (2.0)	
> 2000 cc	7 (5.1)	0 (0.0)	
Hypertension disorders	10 (7.2)	3 (2.0)	0.06
Previous cesarean section	5 (3.6)	4 (2.7)	0.9
PROM-delivery interval (h)	0.0 (0-390)	0.0 (0-150)	0.14
Gestational diabetes	5 (3.6)	1 (0.7)	0.18
Fertility treatments	4 (2.9)	1 (0.7)	0.32

Data are reported as number (%) or median (minimum-maximum).

E/P, estro-progestins; D&C, dilatation and curettage; PG, prostaglandins; OXT, oxytocin; PPH, post-partum hemorrhage; PROM, premature rupture of membranes.

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