

ORIGINAL RESEARCH ARTICLE

Spontaneous hemoperitoneum in pregnancy: Italian prospective population-based cohort study

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Funding information

Italian Ministry of Health and University of Milan

Abstract

Introduction: Spontaneous hemoperitoneum in pregnancy is defined as a sudden non-traumatic intraperitoneal bleeding in pregnancy and up to 42 days postpartum. In the present study we aim to estimate the incidence and investigate the risk factors, the management and the outcomes of spontaneous hemoperitoneum in pregnancy in order to improve its clinical identification and reduce avoidable maternal deaths.

Material and methods: This is a prospective population-based cohort study, set in maternity units from nine Italian regions covering 75% of the national births. The study population comprises all women admitted for spontaneous intraperitoneal hemorrhage during pregnancy and up to 42 days postpartum between November 2017 and March 2020. Incident cases were reported by trained clinicians through electronic data collection forms. Descriptive statistics were performed. The main outcome measures included incidence rate of spontaneous hemoperitoneum in pregnancy, association with potential risk factors, clinical management and maternal and perinatal outcomes.

Results: Twenty-nine cases met the adopted definition of spontaneous hemoperitoneum in pregnancy with an estimated incidence rate of 0.04 per 1000 births. An increased risk ratio (RR) of this condition was observed in pregnancies conceived by assisted reproductive technology (RR = 6.60, 95% CI 2.52–17.29), in the case of multiple pregnancies (RR = 6.57, 95% CI 1.99–21.69) and maternal age ≥ 35 years (RR 2.10, 95% CI 1.01–4.35). In 17/29 cases the bleeding site was intra-pelvic (23.5% in the posterior uterine wall and 35.2% in the left hemipelvis). Laparotomy represented the surgical treatment in 27 cases (93%), and most women underwent a cesarean delivery (92.6%). Median blood loss was 1900 mL, one hysterectomy was necessary, and two women died. Twenty-two preterm births were recorded.

Conclusions: Spontaneous hemoperitoneum in pregnancy is a rare, life-threatening condition associated with high perinatal morbidity and mortality. Maternal age ≥ 35 years, multiple pregnancies and assisted reproductive technology were associated to a higher risk of the condition. Two women of 29 died and 70% of births occurred preterm.

Abbreviations: ART, assisted reproductive technologies; BMI, body mass index; 95% CI, 95% confidence interval; ItOSS, Italian obstetric surveillance system; RR, risk ratio; SHIP, spontaneous hemoperitoneum in pregnancy.

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KEYWORDS

assisted reproduction, endometriosis, intraperitoneal bleeding, mortality, pregnancy, preterm birth, spontaneous hemoperitoneum

1 | INTRODUCTION

Spontaneous hemoperitoneum in pregnancy (SHiP) is defined as a sudden non-traumatic intraperitoneal bleeding in pregnancy and up to 42 days postpartum. This rare and dramatic life-threatening obstetric complication has been associated with high perinatal mortality and morbidity.¹ The incidence is currently extremely difficult to estimate due to the lack of worldwide surveillance. The United Kingdom Confidential Enquiries into Maternal Deaths detected six maternal deaths due to rupture of non-aortic aneurysms between 2009 and 2012;² however, information about morbidity related to SHiP is lacking. Between 2013 and 2017, the enhanced maternal mortality surveillance system coordinated by the Italian Obstetric Surveillance System (ItOSS) reported seven cases of maternal death due to SHiP and estimated a specific MMR of 0.2 cases per 100000 live births.³ ItOSS suggested obtaining an accurate medical history of pregnant women that includes signs and symptoms attributable to endometriosis, Ehlers–Danlos syndrome or similar diseases and improving the knowledge regarding pathognomonic signs of aortic dissection.³ Although the exact etiology of SHiP is still unknown, endometriosis and assisted reproductive technologies (ART) might represent risk factors in its occurrence and severity.^{4,5}

Here we report on an observational, prospective, population-based study to improve the clinical identification of SHiP to reduce avoidable maternal deaths in Italy. The primary aim of this study was to estimate the incidence of SHiP and to analyze its associated risk factors, management and maternal and perinatal outcomes.

2 | MATERIAL AND METHODS

2.1 | Study design

The present study is part of a larger prospective population-based cohort study of obstetric near-misses conducted in Italy by ItOSS. A maternal near-miss case is defined as “a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within the 42 days of termination of pregnancy”.⁶ ItOSS collected data on women with any of the following events: sepsis, eclampsia, amniotic fluid embolism and spontaneous hemoperitoneum in pregnancy.⁷

2.2 | Setting

From November 2017 to March 2020, all women with one of these conditions delivering in public and private maternity units in the participating regions were enrolled. Nine regions participated in the study, located in the North (Piedmont, Lombardy, Friuli-Venezia

Key message

Spontaneous hemoperitoneum in pregnancy is a rare life-threatening event. This study provides valuable knowledge for the improvement of appropriate clinical treatment to avoid near-miss cases that can lead to severe maternal and perinatal outcomes.

Giulia and Emilia-Romagna), Center (Tuscany and Latium) and South (Campania, Apulia and Sicily) of Italy, covering 75% of total births in the country.

2.3 | Participants

In the present study, cases of spontaneous hemoperitoneum in pregnancy (SHiP) were defined according to the International Network of Obstetric Survey Systems (INOSS) study definition as a non-traumatic intraperitoneal hemorrhage during pregnancy and up to 42 days postpartum, requiring surgical intervention or embolization, excluding ectopic pregnancy, uterine rupture and cesarean section-associated bleeding.⁸

2.4 | Data sources

A multidisciplinary expert group of clinicians revised the data entry form and tested its online version. A reference person from each maternity unit was identified to attend a single-day training course at regional level to share the study's objectives and methodology and learn how to use the web platform for data entry. Each reference person received a monthly reminder to promote complete reporting or to confirm the nil reports.

Incident cases were reported using electronic and anonymous data collection forms including information regarding the women's sociodemographic characteristics, medical, obstetrical and gynecological history, surgical history, detailed description of the event and treatment, clinical and instrumental diagnosis, timing and mode of delivery.

2.5 | Variables

The main outcomes were maternal and perinatal mortality. The secondary outcomes were admission to intensive care unit and severe maternal morbidities, admission to neonatal intensive care unit and major neonatal complications.

2.6 | Statistical analyses

The data analysis focuses on descriptive statistics. The denominator was retrieved from the National Hospital Discharge Database, by selecting all women aged 10–55 years who gave birth in the participating maternity units, during the precise study period. The incidence rate was calculated as the number of cases of SHiP per 10 000 deliveries with a 95% confidence interval (95% CI), assuming a binomial distribution Poisson approximation. We performed a bivariate analysis to determine the association with potential risk factor (maternal age, citizenship, educational level, multiple pregnancy), which was estimated by calculating the crude risk ratio (RR) and their 95% CI, through a comparison with the denominator.

2.7 | Missing

Patient characteristics are incomplete in some cases. Data regarding body mass index (BMI) are missing in seven cases, as reported in Table 1. Since parity and ART are not available in the National Hospital Discharge Database, the prevalence rate for these variables was estimated from the 2019 National Birth Register. Due to the unavailability of microdata, it was not possible to implement a predictive model providing adjusted risks.

Data analyses were performed at the Italian National Health Institute using the Statistical Package Stata/MP 14.2.

2.8 | Ethics statement

The project was approved by the Ethics Committee of the Istituto Superiore di Sanità (Italian National Health Institute; Prot. PRE-544/17, Rome) on July 18, 2017. Data were fully anonymized before being accessed and analyzed. Thus, need for informed consent was waived by the local Ethics Committee.

3 | RESULTS

During the study period, the response rate of the participating maternity units was 94.5%, with only one region (Apulia) showing a lower rate (77.8%) than the other regions. Between November 2017 and March 2020, 741 516 women gave birth in the participating maternity units. In this period, 40 cases of SHiP were reported: of these, 11 cases were excluded because they were not consistent with the adopted definition of SHiP.⁶ The incidence rate for the remaining 29 cases was estimated as 0.04 per 1000 deliveries (95% CI 0.03–0.06 per 1000). Cases were mainly reported by the Northern Regions of the Country (19/29, 65.5%).

Sociodemographic, previous obstetric and medical history, and current pregnancy characteristics of SHiP cases are reported in Table 1. There was a high proportion of women aged ≥ 35 years (51.7%), who conceived through ART (17.2%), with multiple

TABLE 1 Sociodemographic, medical and obstetric characteristics of the studied population.

	n	%	Mean (SD)
Total	29		
Maternal Age (years)			35.2 (4.8)
<35 years	14	48.3	
≥ 35 years	15	51.7	
Preconception body mass index (kg/m ²)			23.3 (3.4)
<25	16	55	
≥ 25	5	22.7	
≥ 30	1	4.5	
Missing	7	24.1	
Weight gain (kg)			11.6 (4.0)
Citizenship			
Italian	24	82.7	
Albanian	1	3.5	
Romanian	2	6.8	
Ecuadorian	1	3.5	
Philippine	1	3.5	
Language barriers	1	3.5	
Single, unmarried	3	10.3	
Educational level			
Low < University degree	19	65.5	
High \geq University degree	6	20.7	
Missing	4	13.8	
Unemployed	6	23.1	
Nulliparous	16	55.2	
Homologous ART pregnancy	5	17.2	
Multiple pregnancy	3	10.3	
Previous surgery	19	65.5	
Previous cesarean section	6	20.7%–46%	
Previous gynecological surgery	8	27.6	
Previous appendectomy	5	17.2	
Surgery during pregnancy	2	6.9	
Endometriosis	6	20.7	
Pregnancy complications			
Preeclampsia	2	6.9	
HELLP	4	13.8	
Pregnancy outcome			
Delivery	27	93.0	
Abortion	1	3.5	
Death	1	3.5	
Mode of delivery			
Vaginal spontaneous	2	7.4	
Cesarean section	25	92.6	
Elective	3		
Emergent	22		

Abbreviation: ART, artificial reproductive technologies.

TABLE 2 Risk ratio of SHiP cases and comparison with the background population.

Total cases	SHiP		Background population		Rate (per 1000)	Risk ratio (95% CI)			P-value
	n = 29		n = 741 516		0.04				
Maternal age	n	%	n	%					
<35 years	14	48.3	490 882	66.2	0.03	1.00			
≥35 years	15	51.7	250 634	33.8	0.06	2.10	1.01	4.35	0.041
Citizenship									
Italian	24	82.8	546 020	73.6	0.04	1.00			
Not Italian	5	17.2	195 496	26.4	0.03	0.58	0.22	1.53	0.265
Educational level ^a									
High	6	20.7	155 356	21.0	0.04	1.00			
Low	19	65.5	480 678	64.8	0.04	1.02	0.41	2.56	0.961
Missing	4	13.8	105 482	14.2	0.04	0.98	0.28	3.48	0.977
Parity									
Multiparae	13	44.8	334 424 ^b	45.1	0.04	1.00			
Nulliparae	16	55.2	407 092 ^b	54.9	0.04	1.01	0.49	2.10	0.977
ART									
No	24	82.8	718 826 ^b	96.9	0.03	1.00			
Yes	5	17.2	22 690 ^b	3.1	0.22	6.60	2.52	17.29	0.000
Multiple pregnancy									
No	26	89.7	728 715	98.3	0.04	1.00			
Yes	3	10.3	12 801	1.7	0.23	6.57	1.99	21.69	0.000
Previous CS									
None	23	79.3	648 085	87.4	0.04	1.00			
At least one	6	20.7	93 431	12.6	0.06	1.81	0.74	4.44	0.189

Abbreviations: ART, artificial reproductive technologies; CS, cesarean section.

^aEducational level: high ≥ university degree, low < university degree.

^bEstimated from the 2019 National Birth Register.

pregnancies (10.3%), having a previous surgery (65.5%) and with preconception endometriosis (20.6%).

The majority of the women underwent a cesarean section (92.6%), mainly emergent during the laparotomy.

The risk ratios of SHiP cases according to maternal sociodemographic, previous and current obstetric characteristics are described in Table 2. A higher risk of SHiP was reported in pregnancies conceived by ART (RR = 6.60, 95% CI 2.52–17.29) and in multiple pregnancies (RR = 6.57, 95% CI 1.99–21.69). Advanced maternal age (≥35 years old) was also associated with a doubled RR (RR = 2.10, 95% CI 1.01–4.35) to develop SHiP.

Most cases of SHiP occurred during the third trimester (n = 19, 65.5%), and three cases were diagnosed during the first 48 hours after birth (Figure S1).

The clinical manifestation was predominantly abdominal pain (n = 26, 89.6%). Hypotensive symptoms and hypovolemic shock occurred in eight (27.6%) and seven (24.1%) women, respectively. Fetal hypovolemic signs such as fetal heart rate alterations were reported in 11 cases (37.9%).

Imaging was employed in 17 cases (58%), with ultrasound representing the preferred technique, performed alone (n = 11, 38%) or in association with tomography (n = 3, 10%). Tomography alone

was performed in three cases (10%). Magnetic resonance was never performed.

The extrapelvic bleeding sites concerned hepatic rupture in HELLP syndrome (n = 4), spontaneous splenic rupture (n = 1), splenic artery rupture (n = 3), splenic vein rupture (n = 1), ovarian artery rupture in ovarian torsion (n = 1), torsion of uterine pedunculated myoma (n = 1), and one missing site. The remaining pelvic bleeding sites are showed in Figure S2. The posterior uterine wall and the left hemipelvis were sites of bleeding respectively in four (23.5%) and six (35.2%) of the 17 pelvic SHiP cases.

The surgical treatment was almost exclusively laparotomy (n = 27, 93%), but laparoscopy was performed in a single case of miscarriage occurring during the first trimester. Laparotomy performed during pregnancy (n = 24) was associated with cesarean section in 20 cases (83.3%); only two pregnancies (8.3%) continued until term. Three laparotomies were performed postpartum.

Maternal outcomes are reported in Table 3. The median blood loss was 1900 mL (ranging from 400 to 4000 mL) and 22 (75.8%) women received blood transfusions. Hysterectomy was required in one case. Two women died due to the rupture of the splenic artery, one during postpartum without undergoing any surgery.

TABLE 3 Maternal outcomes in cases of spontaneous hemoperitoneum in pregnancy.

	n	%	Median (IQR)
Total	29		
Maternal outcomes			
Blood loss			1900 (400–4000)
Lowest Hb (g/dL)			7(4.2–11.4)
Blood transfusion	22	75.8	
ICU admission	17	58.6	
Days			3 (2–11)
Severe maternal complications			
DIC	2		
HELLP	4		
Respiratory insufficiency	1		
Renal insufficiency	1		
ACC	2		
Re-laparotomy	1		
Hysterectomy	1		
Uncontrolled hypertension	1		
Days of hospitalization			9 (4–38)
Death	2	6.90	

Abbreviations: ACC, cardio-circulatory arrest; DIC, disseminated intravascular coagulation; ICU, intensive care unit; IQR, interquartile range.

Perinatal outcomes, described in Table 4, included 22 preterm births, 4 cases of severe neonatal complications, 5 stillbirths and 1 neonatal death (1 missing outcome).

4 | DISCUSSION

In this prospective, population-based study involving nine regions, corresponding to 75% of all births in Italy, we evaluated the incidence, risk factors and management of spontaneous hemoperitoneum in pregnancy. SHiP is a rare event in Italy, with an incidence rate of 0.04 per 1000 births. This obstetrical complication is frequently associated with ART, multiple pregnancies and ≥ 35 years of age in mothers. We also observed a high prevalence of endometriosis and previous abdominal surgery in SHiP. In almost all cases, treatment was laparotomy, often combined with contemporary cesarean delivery, which led to increasing maternal and neonatal morbidity.

To our knowledge, this is the first population-based study concerning this life-threatening event and, so far, no national studies have been published that inform about a potential incidence of SHiP. The prospective population-based design, the high response rate of the maternity units through the ItOSS network, and the common and accurate SHiP definition⁸ are the main strengths of this study. The study has also limitations. The subnational design

of the study is a limitation, but results are unlikely to be biased because the participating regions are distributed over the entire country. Another potential limitation is the lack of a SHiP code in the ICD-9 Hospital Discharge database, which prevented the ascertainment of completeness of notified cases. However, the presence of a trained reference clinician in each participating hospital and the ItOSS monthly checking procedures to monitor case reporting make this limit a minor one. Moreover, the lack of individual data among women without SHiP prevented us from adjusting the estimated RRs. Co-linearity between the observed associations of SHiP with women's age ≥ 35 , having conceived by ART and likelihood of having had prior surgery (e.g. laparoscopy to determine the cause for their subfertility) is possible, but the small number of cases prevented an adjusted analysis. Finally, the absence of intraoperative biopsy data, limited the identification of the cause of bleeding as endometriosis.

Most of SHiP cases (68.9%) occurred during the third trimester, as previously reported.^{1,4,9,10} Advanced maternal age was more frequent than in the background population of women giving birth in Italy (mean maternal age 35.2 vs 32.9, respectively),¹¹ and was significantly associated with SHiP (RR 2.10, 95% CI 1.01–4.35). A total of 24 (82.7%) women were Italian, with a percentage slightly higher than that reported by the national birth register in 2018 (79%), foreign citizenship not being associated with a greater risk of SHiP.

SHiP was more likely to occur following ART (R: 6.60, 95% CI 2.52–17.29), in line with previously reported data about the occurrence of SHiP in women with endometriosis.^{4,5,12} The high hormonal levels associated with ART pregnancies have been hypothesized to potentially exacerbate the ectopic decidualization process.¹³ The prevalence of endometriosis in our cases was 20.1%, 10 times higher than the one reported in another Italian study conducted in Friuli Venezia Giulia Region, which adopted a retrospective record linkage procedure between hospital discharge database and anatomic pathology records.¹⁴ In our study, the frequency of endometriosis was lower than in previous retrospective studies,^{4,5,9,10} likely because we were more selective with the inclusion criteria regarding extrapelvic bleeding sites according to the adopted international definition of SHiP.⁷ Nonetheless, a recently published Japanese retrospective study of 31 cases of SHiP reported a prenatal diagnosis rate of endometriosis similar to our study.¹ In pelvic SHiP cases, more than half of the bleeding sites (58.7%) were located in the posterior uterine wall and in the left hemipelvis (23.5% and 35.2%, respectively), in accordance with the left lateral predisposition of endometriosis.¹² Therefore, we speculate that the bleeding sites could represent endometriosis lesions. Unfortunately, the lack of intraoperative biopsy data prevented histological confirmation.

Our study is the first to report the high frequency of a medical history of previous abdominal-pelvic surgery (65.5%) among women experiencing SHiP; this may be related to an increased intraabdominal inflammation, weakening the wall of the vessels and enhancing the peritoneal tension by adhesions. However, due to the lack of these data within the background population, we were unable to

	N	%	Median (IQR)
Perinatal outcomes			
Live births	25	80.6	
Preterm birth	18	72.00	
Extremely preterm (22–27.6 weeks)	2	11.1	
Very preterm (28–31.6 weeks)	5	27.8	
Moderate preterm (32–34.5 weeks)	8	44.4	
Late preterm (34.6–36.6 weeks)	3	16.7	
Gestational age, weeks			34.4 (24–41.5)
Birthweight, g			2320 (850–4150)
Apgar <7 at 5 minutes	7	28.0	8 (2–10)
Umbilical arterial pH ≤7.0	4	16.0	
NICU admission	17	68.0	
NICU admission days			10 (2–50)
Severe neonatal complications	4	16.0	
RDS	4		
IVH	2		
Exsanguinotransfusion	1		
Infection	1		
Neonatal death	1	4.0	
Stillbirth	5	16.1	

Abbreviations: IQR, interquartile range; IVH, intraventricular hemorrhage; NICU: Neonatal Intensive Care Unit; RDS, respiratory distress syndrome.

estimate a RR for this variable. Although higher, the RR associated with a previous cesarean section (RR 1.81, 95% CI 0.74–4.44) did not reach statistical significance.

The symptom of acute abdominal pain in pregnancy represented a diagnostic challenge. Despite European Radiology Society recommendations, imaging diagnostic techniques were rarely adopted during the management of SHiP cases (58%).¹⁵ This lack of imaging procedures usage might explain the high prevalence of laparotomy as surgical treatment (93%). This therapeutic approach often led to a cesarean section being performed during the third trimester of pregnancy (92.6%), which contributed to the high rate of preterm births (72%), adverse neonatal outcomes (16%) and one neonatal death. Considering that maternal hypovolemic shock occurred in seven of 29 cases and fetal hypovolemic signs happened in 11 of 29 cases, possibly overlapping with maternal events, we can assume that neither maternal clinical conditions nor fetal distress were the reason why second level imaging was not performed. Imaging procedures can help to reduce unnecessary laparotomies.

Stillbirths were mainly prevalent among extrapelvic SHiP (4/5), probably caused by the severity of maternal hypovolemia due to the rupture of large abdominal vessels or the liver. Likewise, two maternal deaths were caused by a SHiP due to a splenic artery rupture. The perinatal mortality reported in our study was 20%, which is lower than the 27% reported in the systematic review by Lier et al. in 2017,¹ and the same as the one described in the Japanese retrospective study.⁵

This population-based study shows for the first time the incidence of this rare catastrophic event, with a low rate of 0.04 per

TABLE 4 Perinatal outcomes in cases of spontaneous hemoperitoneum in pregnancy.

1000 live births. However, the associated high rate of preterm births (72%) highlights the need to improve the diagnostic pathway of SHiP for better surgical treatment, reducing neonatal and maternal morbidity. The causes of the seven maternal deaths due to SHiP detected by the ItOSS surveillance between 2013 and 2017¹⁶ were similar to the near-miss cases with the worst outcomes described in this study. In fact, the ItOSS Confidential Enquiries attributed maternal deaths to unrecognized Ehlers–Danlos syndromes resulting in rupture of spleen and iliac artery ($n = 2$); rupture of splenic aneurysm ($n = 2$), dissection of the aorta ($n = 2$) and unrecognized retroperitoneum endometriosis ($n = 1$).³ For each maternal death due to SHiP, we detected more cases of women who “would have died but survived” the same clinical conditions.

5 | CONCLUSION

Spontaneous hemoperitoneum in pregnancy is a rare obstetric near-miss event associated to a high risk of maternal and perinatal mortality. Advanced maternal age, multiple pregnancies and assisted reproductive technology were associated to a higher risk of the condition. Two women of 29 died and 70% of births occurred preterm. The results of our study highlight the need for educational efforts to improve clinicians' ability to recognize predisposing conditions and improve the diagnostic and therapeutic pathway of SHiP. For all these reasons, the management of high-risk cases in specialized centers is highly recommended.

AUTHOR CONTRIBUTIONS

MIM assisted with data collection, collaborated in the statistical analysis, drafted the article and edited the final version. SD conceived the study, provided overall guidance, collaborated in drafting the article and reviewed the final version. AM conducted the statistical analysis, assisted with data collection, collaborated in drafting the article and reviewed the final version. EC and EC assisted with data collection, collaborated in drafting the article, and edited and reviewed the final version. FG drafted the article and edited and reviewed the final version. IC provided scientific advice, supervised data collection, collaborated in drafting the article, and edited and reviewed the final version. All authors read and agreed to the published version of the article.

FUNDING INFORMATION

The study was supported by the Italian Ministry of Health with a CCM Grant coordinated by Regione Lombardia. The authors acknowledge support from the University of Milan through the APC initiative.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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REFERENCES

- Lier MCI, Malik RF, Ket JCF, Lambalk CB, Brosens IA, Mijatovic V. Spontaneous hemoperitoneum in pregnancy (SHiP) and endometriosis - a systematic review of the recent literature. *Eur J Obstet Gynecol Reprod Biol.* 2017;219:57-65.
- Knight M, Kenyon S, Brocklehurst P, Tuffnell D, Shakespeare J, et al. *Saving Lives, Improving Mothers' Care - Lessons Learned to Inform Future Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-12.* National Perinatal Epidemiology Unit, University of Oxford; 2014.
- Donati S, Maraschini A, Dell'Oro S, Lega I, D'Aloja P, The Regional Maternal Mortality Working Group. The way to move beyond the numbers: the lesson learnt from the Italian obstetric surveillance system. *Ann Ist Super Sanità.* 2019;55(4):363-370.
- Brosens IA, Lier MC, Mijatovic V, Habiba M, Benagiano G. Severe spontaneous hemoperitoneum in pregnancy may be linked to in vitro fertilization in patients with endometriosis: a systematic review. *Fertil Steril.* 2016;106:692-703.

- Hagimoto M, Tanaka H, Osuga Y, et al. Nationwide survey (Japan) on spontaneous hemoperitoneum in pregnancy. *J Obstet Gynaecol Res.* 2021;47:2646-2652.
- Say L, Souza JP, Pattinson RC, WHO working group on maternal mortality and morbidity classifications. Maternal near miss-towards a standard tool for monitoring quality of maternal health care. *Best Pract Res Clin Obstet Gynaecol.* 2009;23:287-296.
- Near miss ostetrici in Italia; la sepsi, l'eclampsia, l'embolia di liquid amniotico e l'emoperitoneo spontaneo in gravidanza [Near miss cases in obstetrics in Italy: sepsis, eclampsia, amniotic fluid embolism and spontaneous hemoperitoneum]. In Italian. February 2021. https://www.ccm-network.it/imgs/C_27_MAIN_progetto_544_listaFile_List11_itemName_0_file.pdf
- Schaap T, Bloemenkamp K, Deneux-Tharoux C, et al. INOSS. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. *BJOG.* 2017;126:394-401.
- Brosens IA, Fusi L, Brosens JJ. Endometriosis is a risk factor for spontaneous hemoperitoneum during pregnancy. *Fertil Steril.* 2009;92:1243-1245.
- Lier M, Malik RF, van Waesberghe J, et al. Spontaneous haemoperitoneum in pregnancy and endometriosis: a case series. *BJOG.* 2017;124:306-312.
- Boldrini R, Di Cesare M, Basili F, et al. Certificato di Assistenza al Parto (CeDAP) Analisi dell'evento nascita - Anno 2018. [Childbirth Assistance Certificate (CeDAP) Analysis of the birth event - Year 2018.]. In Italian. Direzione Generale della Digitalizzazione, del Sistema Informativo Sanitario e della Statistica - Ufficio di statistica. Ministero Della Salute.
- Al-Fozan H, Tulandi T. Left lateral predisposition of endometriosis and endometrioma. *Obstet Gynecol.* 2003;101:164-166.
- Jarvela IY, Pelkonen S, Uimari O, et al. Controlled ovarian hyperstimulation leads to high progesterone and estradiol levels during early pregnancy. *Hum Reprod.* 2014;29:2393-2401.
- Morassutto C, Monasta L, Ricci G, Barbone F, Ronfani L. Incidence and estimated prevalence of endometriosis and adenomyosis in Northeast Italy: a data linkage study. *PLoS One.* 2016;11:e0154227.
- Masselli G, Derchi L, McHugo J, et al. Acute abdominal and pelvic pain in pregnancy: ESUR recommendations. *Eur Radiol.* 2013;23:3485-3500.
- Donati S, Maraschini A, Lega I, D'Aloja P, Buoncristiano M, Manno V. Maternal mortality in Italy: results and perspectives of record-linkage analysis. *Acta Obstet Gynecol Scand.* 2018;97:1317-1324.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Mazzocco MI, Donati S, Maraschini A, et al. Spontaneous hemoperitoneum in pregnancy: Italian prospective population-based cohort study. *Acta Obstet Gynecol Scand.* 2022;00:1-7. doi: [10.1111/aogs.14431](https://doi.org/10.1111/aogs.14431)