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Ectopic pregnancy hospitalisations: A national population-based study of rates, management and outcomes

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ABSTRACT

Objective: To determine whether there were changes in the incidence, management and outcomes of ectopic pregnancy hospitalisations in Ireland during 2005–2016.
Study design: Population-based study was carried out from January 2005 to December 2016. A total of 12,098 women hospitalised due to ectopic pregnancy. All acute maternity hospital settings in the Republic of Ireland. Electronic health records were retrieved using the Hospital In-Patient Enquiry database. Rates ratios were calculated to estimate trends, risk of blood transfusion and risk of extended stay at the hospital.
Results: The rate of hospitalisation for ectopic pregnancy increased over the 12-year study period from 12.8/1,000 deliveries in 2005 to 17.7/1,000 deliveries in 2016. Risk of blood transfusion reduced over time (aIRR 0.8; 95%CI 0.6–0.9). Women aged at least 40 years had double the risk of hospitalisation and double the risk of blood transfusion. Women undergoing open surgical procedures were more likely to need a blood transfusion than those undergoing laparoscopic salpingectomy. Similar results were found for length of stay over two days. Blood transfusion was rare for patients who underwent medical management (aIRR 0.1; 95%CI 0.05–0.2).
Conclusion: Advanced maternal age increased risk of hospitalisation for ectopic pregnancy. While the overall rate of hospitalisations increased over time, there was a reduction in the risk of blood transfusion and length of stay over two days. Type of management significantly affected the risk of blood transfusion and length of stay over two days at the hospital.

Introduction

Ectopic pregnancy is one of the most serious complications in early pregnancy [1]. It is defined as the development of a fertilised fetus outside of the endometrial cavity [1]. It is estimated that 1–2% of all pregnancies end in ectopic pregnancy [2]. During the 1970s and 1980s, a considerable increase in the incidence of ectopic pregnancy was observed from several countries including Norway [3], the United Kingdom (UK) [4,5], and the United States (US) [6]. After that period of time, some countries reported a stabilisation or decrease of the rates [7,8], while other countries published an increase in rates [9,10].

The pathways of care for both ectopic pregnancy have evolved [11]. Traditionally, ectopic pregnancy was a life-threating condition which was most commonly diagnosed at the time of a surgical procedure [3]. The introduction and improvement in sensitivity of transvaginal scans (TVS) helped to diagnose asymptomatic women with an ectopic pregnancy [2]. Furthermore, medical management using methotrexate and expectant management are acceptable alternatives to surgery [12]. Nevertheless, the optimal management for ectopic pregnancy and its associated adverse effects are still being investigated [13].

Ectopic pregnancy has been associated with several complications, including blood transfusion and surgical injury [14,15]; in fact, it is one of the main causes of morbidity in early pregnancy [16]. Nonetheless, a recent study argued that non-fatal complications are not well studied at the time of an ectopic pregnancy [17]. Therefore, the aims of this study were to explore national trends in incidence rates of hospitalisation for ectopic pregnancy in the

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Republic of Ireland from 2005 to 2016 and to estimate the associated morbidity of blood transfusion and length of stay.

Material and methods

This is a population-based study of all inpatient admissions for ectopic pregnancy in all public maternity hospital settings in the Republic of Ireland (ROI) from January 1st 2005 to 31st December 2016. Data were obtained from the Hospital In-Patient Enquiry (HIPE) database. The HIPE is a computer-based system designed to collect demographic, clinical and administrative data on discharges and deaths [18]. It is an anonymous national health information system which serves as a reliable source of data from all 62 acute hospitals in the ROI; however, data from the emergency department (ED) and outpatient settings are not available [19]. It is administered and managed by the Economic and Social Research Institute on behalf of the Health Service Executive [18].

From 2005, the *10th Revision Australian modification of International Statistical Classification of Disease and Related Health Problems* (ICD-10-AM) and t*he Australian Refined Diagnosis Related Groups* (AR-DRGs) are the coding classification systems of clinical diagnosis used in the HIPE system [19]. The unit of analysis was the annual number of delivery discharges within the HIPE dataset using the diagnostic code for outcome of delivery (Z37). All ectopic pregnancies within the HIPE dataset were identified using the diagnostic codes for outcome of ectopic pregnancy (O00). HIPE data does not specify gestational age in single weeks but uses ranges between <5, 5–13, 14–19, 20–25, 26–33 and 34–36 completed weeks of gestation. Only inpatient admissions of ectopic pregnancy within 19 completed weeks of gestation were included in the analysis.

This study included blood transfusion as a complication and length of stay (LOS) as an indicator of efficiency. Diagnostic codes for blood transfusion were identified using codes within the HIPE dataset (920600 & 9206200 & 1370601–1370603). LOS was automatically obtained using the menu of the HIPE database. Hospitalisations with LOS greater than 2 days were also considered a complication for the purpose of this study.

Demographic and pregnancy-related variables within the HIPE dataset included year of discharge, maternal age (in years) and public or private health insurance. All women who are pregnant and ordinarily resident in the ROI are entitled to free maternity care, covering antenatal visits, labour and delivery and postnatal care under the Maternity and Infant Care Scheme (MICS) (38). Those inpatient admissions who were treated under the MICS were classified as public patients; whereas those who were treated using private health insurance were classified as private patients. It is important to note that in the ROI, all women who attend the maternity hospitals for ectopic pregnancy before 12 weeks of gestation have the right to be treated under the Maternity and Infant Care Scheme (MICS) as public patients. Women who held private health insurance would have had most likely a choice as to whether they were looked after publicly or privately. Therefore, this study was not able to discern if the increase in hospitalisations was due to differences between health schemes or because there was a higher proportion of women who decided to be treated under the MICS, even though they held private health insurance.

Pathways of care for patient admissions for ectopic pregnancy were categorised as: surgical, medical, other type of procedures and expectant treatment. Surgical treatment included principal procedures codes for salpingectomy, salpingotomy, and oophorectomy, with or without using laparoscopy. Medical treatment was identified using principal procedures codes for when methotrexate or other pharmacological agent to medically treat the ectopic pregnancy was administered. When neither surgical nor medical principal procedures codes were identified, then other types of procedures were considered. Finally, expectant management was considered when no procedure was identified. A more detailed description of the principal procedures codes is included in Table S1.

Statistical analysis

Hospitalisation incidence rates (IR) were calculated as the annual number of inpatient discharges for ectopic pregnancy divided by the annual number of deliveries in the ROI over the 12-year period (2005–2016). Univariate and multivariable Poisson regression was used to estimate the crude and adjusted incidence rate ratio (cIRR & aIRR respectively) of hospitalisation for ectopic with 95% confidence intervals (CIs). All analyses were adjusted by year of discharge, maternal age and public versus private patient health insurance coverage. A multivariable Poisson regression model was performed to estimate the cIRR & aIRR with 95% CIs for blood transfusion and length of stay over two days. Data analysis was performed using Stata software, version 12 (Stata Corp, 2013) and IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA).

Results

Between January 2005 and December 2016 there were 12,098 hospitalisations for ectopic pregnancy and 801,764 deliveries. Overall, the hospitalisation rate for ectopic pregnancy was 15.1/1,000 deliveries (95%CI 14.8–15.4/1,000; Table 1). Overall, 71.2% of the hospitalisations were classified as tubal ectopic pregnancy (n = 8608), followed by unspecified (n = 2541; 21.0%) and other (n = 775; 6.4%). Almost 91.9% of all women admitted to maternity hospitals were between 5–13 weeks of gestation (*n* = 11,119).

The rates for women with ectopic pregnancy increased from 12.8/1,000 deliveries in 2005 (95%CI 11.9–13.7/1,000) to 17.7/1,000 deliveries in 2016 (95%CI 16.6–18.7/1,000; Fig. 1). The incidence rate of hospitalisations for ectopic pregnancy in the ROI increased steadily with age (Table 1). Advanced maternal age (40 years or older) was associated with a double risk of hospitalisation compared to women younger than 25 years. Women hospitalised for ectopic pregnancy were more often treated as public patients compared to women hospitalised for delivery of an infant (Table 1).

Women underwent surgical treatment for ectopic pregnancy in approximately 58% (n = 6953) of cases and received medical management using methotrexate in 14.3% (n = 1726). Among those who had a surgical intervention, 45.5% (n = 5510) were managed by laparoscopy. During the 12-year study period more surgical procedures were being performed laparoscopically (Fig. 2). Open salpingotomy and laparoscopic salpingotomy were the less frequent surgical interventions over this study period (Fig. 2). Conversely, medical treatment for ectopic pregnancy increased steadily from 0.8/1,000 deliveries (95%CI 0.5–1.0/1,000) in 2005 to 3.2/1,000 deliveries (95%CI 2.7–3.6/1,000) in 2016. Expectant treatment also increased over the years (Fig. 2). The average LOS for ectopic pregnancy was 2.4 days (SD 1.9). It declined from an average of 3.4 (SD 2.2) days in 2005 to 2.0 (1.5) days in 2016. Approximately 43% (n = 5172) of inpatients for ectopic pregnancy stayed for one day, 23% (n = 2821) stayed for two days and a total of 4105 (34%) stayed for more than two days.

Among the 12,098 hospitalisations for ectopic pregnancy, 580 (4.8%) had a blood transfusion and 4105 (33.9%) had a LOS over 2 days (Table 2). After adjusting for socioeconomic factors, the risk of blood transfusion decreased over the years. Women aged 40 years or older had double the risk of blood transfusion compared to those younger than 25 years. No differences in risk were found between public and private patients. Patients undergoing open surgical

Table 1
Incidence rate and incidence rate ratio of hospitalisations for ectopic pregnancy in the Republic of Ireland.2005–2016.

		Deliveries	Ectopic pregnancy hospitalisations			
		n	n	Rate[a] (95% CI)	cIRR (95% CI)	aIRR (95% CI)
	All	801764	12098	15.1 (14.8 to 15.4)		
Year	2005-2008	257750	3411	13.2 (12.8 to 13.7)	1	1
	2009-2012	285751	4193	14.7 (14.3 to 15.1)	1.1 (1.1 to 1.2)	1.0 (1.0 to 1.1)
	2013-2016	258263	4494	17.4 (16.9 to 17.9)	1.3 (1.2 to 1.4)	1.2 (1.1 to 1.2)
Maternal Age	<25	109812	1254	11.4 (10.9 to 12.1)	1	1
	25-29	177647	2750	15.5 (14.9 to 16.1)	1.4 (1.3 to 1.5)	1.4 (1.3 to 1.5)
	30-34	281961	4300	15.3 (14.8 to 15.7)	1.3 (1.3 to 1.4)	1.6 (1.4 to 1.6)
	35-39	191970	3046	15.9 (15.3 to 16.4)	1.4 (1.3 to 1.5)	1.7 (1.6 to 1.8)
	40+	40374	748	18.5 (17.2 to 19.9)	1.6 (1.5 to 1.8)	2.0 (1.9 to 2.2)
Health insurance	Private	200014	1771	8.9 (8.4 to 9.3)	1	1
	Public	601750	10327	17.2 (16.8 to 17.5)	1.9 (1.8 to 2.0)	2.1 (2.0 to 2.2)

[a] Rate per 1000 deliveries; cIRR: crude incidence rate ratio; aIRR: adjusted incidence rate ratio from multivariable analysis including all variables in the table.

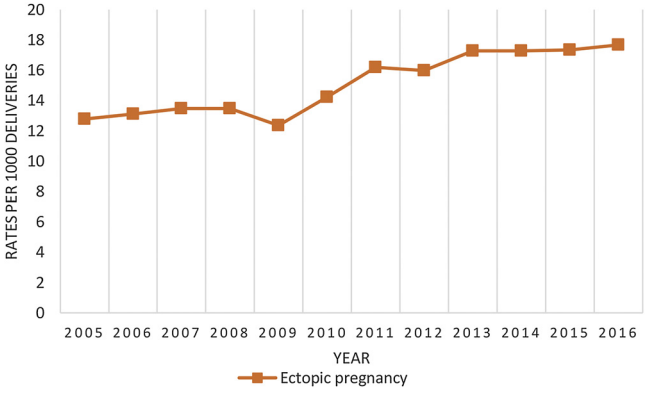

Fig. 1. National hospitalisation rates for ectopic pregnancy.

procedures were more likely to need a blood transfusion than those undergoing laparoscopic salpingectomy: open salpingectomy (aIRR 4.3; 95%CI 3.6–5.2), open salpingotomy (aIRR 2.1; 95%CI 1.2–3.5) & open oophorectomy (aIRR 6.0; 95%CI3.4–10.7). However, no differences were found when surgical treatments were performed using laparoscopy, except for laparoscopic oophorectomy (aIRR 2.1; 95%CI 1.2–3.5). Blood transfusion was rare for patients who underwent medical management (aIRR 0.1; 95%CI 0.05–0.2; Table 2).

The incidence rate ratio of experiencing an extended LOS over two days among hospitalisations for ectopic pregnancy was reduced over time (Table 2). No differences in incidence rate ratios were found for maternal age and private versus public health coverage, except for a reduction in the risk of a prolonged stay at the hospital among women aged 25–29 years old compared to women younger than 25 years old. Compared to laparoscopic salpingectomy, women who had surgical treatment without laparoscopy had an increased risk of staying longer than two days at the hospital (Table 2). No differences were found among those who had surgical treatment with laparoscopy. Those who had medical treatment and expectant treatment had less risk of staying over two days at the hospital than women who underwent laparoscopic salpingectomy (Table 2).

Discussion

This population-based study of over 12,000 hospitalisations indicates that the incidence rate of hospitalisations for ectopic pregnancy increased during 2005–2016 while the overall incidence was 15.1/1000 deliveries. Similar trends in incidence rates of ectopic pregnancy have been reported in other countries

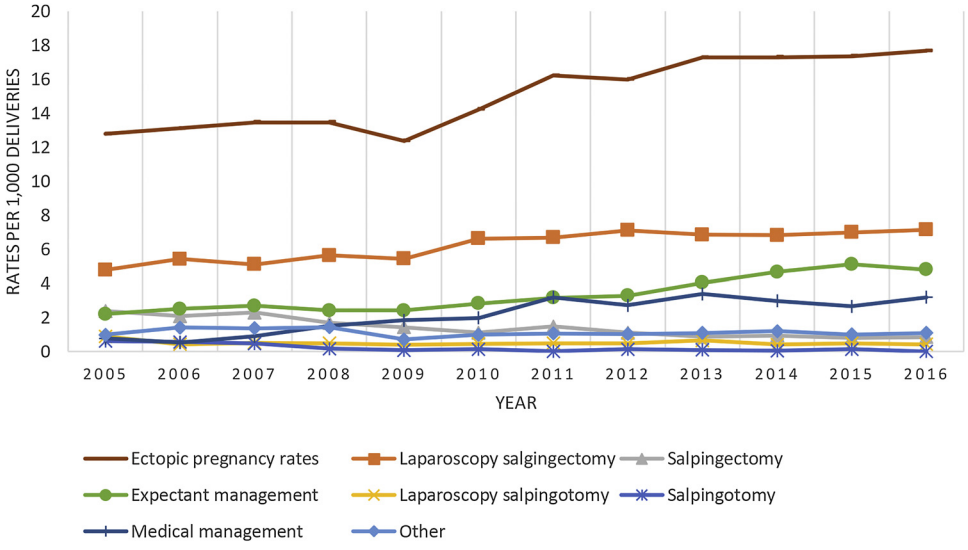

Fig. 2. Type management for hospitalisations of ectopic pregnancy.

Table 2
Blood transfusion and length of stay over 2 days of hospitalisations of ectopic pregnancy.2005–2016.

		Ectopic pregnancies	Blood transfusion				Length of stay over 2 days			
		n	n	%	cIRR (95%CI)	aIRR (95%CI)	n	%	cIRR (95%CI)	aIRR (95%CI)
	All	12098	580	4.8			4105	33.9		
Year	2005-2008	3411	200	5.9	1	1	1586	46.5	1	1
	2009-2012	4193	194	4.6	0.8 (0.7 to 0.9)	0.8 (0.7 to 0.9)	1307	31.2	0.7 (0.6 to 0.7)	0.7 (0.6 to 0.7)
	2013-2016	4494	186	4.1	0.7 (0.6 to 0.9)	0.8 (0.6 to 0.9)	1212	27.0	0.6 (0.5 to 0.6)	0.6 (0.6 to 0.7)
Maternal Age	<25	1254	45	3.6	1	1	464	37.0	1	1
	25-29	2750	124	4.5	1.3 (0.9 to 1.8)	1.2 (0.9 to 1.7)	910	33.1	0.9 (0.8 to 1.0)	0.9 (0.8 to 1.0)
	30-34	4300	202	4.7	1.3 (0.9 to 1.8)	1.3 (0.9 to 1.8)	1439	33.5	0.9 (0.8 to 1.0)	0.9 (0.8 to 1.0)
	35-39	3046	157	5.2	1.4 (1.0 to 2.0)	1.5 (1.0 to 2.0)	1029	33.8	0.9 (0.8 to 1.0)	0.9 (0.8 to 1.1)
	40+	748	52	7.0	1.9 (1.3 to 2.9)	2.1 (1.4 to 3.1)	263	35.2	1.0 (0.8 to 1.1)	1.0 (0.9 to 1.2)
Health insurance	Private	1771	96	5.4	1	1	666	37.6	1	1
	Public	10327	484	4.7	0.9 (0.8 to 1.0)	1.0 (0.9 to 1.1)	3439	33.3	0.9 (0.8 to 1.0)	1.0 (0.9 to 1.1)
Management	Laparoscopic salpingectomy	5019	242	4.8	1	1	1644	32.8	1	1
	Open Salpingectomy	1243	248	20.0	4.1 (3.5 to 4.9)	4.3 (3.6 to 5.2)	1047	84.2	2.6 (2.4 to 2.8)	2.5 (2.3 to 2.7)
	Laparoscopic salpingotomy	402	12	3.0	0.6 (0.4 to 1.1)	0.6 (0.4 to 1.1)	157	39.1	1.2 (1.0 to 1.4)	1.2 (1.0 to 1.4)
	Open Salpingotomy	160	15	9.4	1.9 (1.2 to 3.3)	2.1 (1.2 to 3.5)	130	81.3	2.5 (2.1 to 3.0)	2.3 (1.9 to 2.7)
	Laparoscopic Oophorectomy	89	9	10.1	2.1 (1.1 to 4.1)	2.1 (1.1 to 4.1)	33	37.1	1.1 (0.8 to 1.6)	1.1 (0.8 to 1.6)
	Open Oophorectomy	40	12	30.0	6.2 (3.5 to 11.1)	6.0 (3.4 to 10.7)	38	95.0	2.9 (2.1 to 4.0)	2.9 (2.1 to 4.0)
	Expectant	2667	0	0.0	[a]	[a]	444	16.6	0.5 (0.5 to 0.6)	0.5 (0.5 to 0.6)
	Medical	1726	8	0.5	0.1(0.05 to 0.2)	0.1(0.05 to 0.2)	320	18.5	0.6 (0.5 to 0.6)	0.6 (0.5 to 0.7)
	Other	752	34	4.5	0.9 (0.7 to 1.3)	0.9 (0.7 to 1.4)	292	38.8	1.2 (1.0 to 1.3)	1.2 (1.0 to 1.3)

cIRR: crude incidence rate ratio; aIRR: adjusted incidence rate ratio from multivariable analysis including all variables in the table.
[a] Excluded from multivariate model as a highly imprecise odds ratio was reported.

[3,9,10,20]. The increased rates of chlamydia is one of the suggested reasons for this. In Ireland, chlamydia is the most frequent sexually transmitted infection with 6797 notifications in 2015 [21]. Its incidence and notifications rose sharply in 2007 and have remained high since then [22]. Other factors that might influence the increase of ectopic pregnancy are pelvic surgery, pelvic inflammatory disease and current use of intrauterine contraceptive devices (IUD) [23]. In the last decades, assisted reproductive technology (ART) has also been considered a potential risk factor for ectopic pregnancy [24,25]. In Europe, an increase in the number of ART cycles has been observed since 2005 compared to previous years [26]. This trend has also been observed in Ireland, with a total of 472 deliveries achieved by ART in 2011 [27]. However, contradictory evidence can be found in the literature [28].

It is well-documented that advanced maternal age is a risk factor for adverse pregnancy outcomes [29] and this is further supported by the results in our study. The maternal and fetal loss cohort study in Denmark also found that women in their late 30 s or older had a higher risk of having ectopic pregnancy, miscarriage or stillbirth, irrespective of their reproductive history [30]. Furthermore, some risk factors for ectopic pregnancy, such as pelvic inflammatory disease, are more commonly developed at older maternal ages than in younger women [23]. With a growing trend of women getting pregnant at later maternal ages in high-income countries, several studies have warned of an increased risk of adverse pregnancy outcomes [31].

Similar trends for surgical and medical treatments for ectopic pregnancy were observed in the US and in the UK [32,33]. Although rates of laparoscopic surgery have been consistently lower in Europe and in the UK compared to the United States [34], a recent survey, which was carried out in the UK, observed an increase in minimally invasive treatments for ectopic pregnancy [33]. In addition, the same study observed that medical management increased from 1.3% in 2000 to 31% in 2014 [33]. As recommended by the Royal College of Obstetricians and Gynaecologists (RCOG), a laparoscopic approach is preferable to an open approach in haemodynamically stable patients [35]. However, unstable patients are considered a medical emergency that requires prompt surgical management [35].

The optimal treatment for women who experience an ectopic pregnancy remains a topic of debate [13]. In agreement with previous studies, our results indicated that surgical treatments without laparoscopy for ectopic pregnancy were associated with a higher risk of blood transfusion and a prolonged stay at the hospital compared to minimally invasive procedures [36,37]. However, the ESEP study, a randomised controlled trial which assessed differences between salpingotomy and salpingectomy in ectopic pregnancies, found a higher percentage of blood transfusion after salpingotomy compared to salpingectomy (7%, n = 14 versus 3% n = 7) [14]. Yet, another retrospective study found no differences between those two procedures [36]. These divergent results might be explained because: firstly, we were not able to distinguish between those women who had a salpingectomy as a primary procedure or those who had it because of further complications after a conservative approach or medical treatment. For instance, the DEMETER trial observed that 17% of women, who were initially randomised to conservative surgery, needed radical surgery because of substantial bleeding [38]. Secondly, the exclusion of women who were haemodynamically unstable in the trial might affect the results of the number of women needing a blood transfusion [14].

Strength and limitations

The use of the HIPE database was the main strength of this study. All data are standardised between maternity hospitals as the ICD-10-AM diagnosis code is integrated in the software, and the same version is used for the entry of HIPE data in all the hospitals [19]. Therefore, standardised trends in incidence rates of inpatient admissions for ectopic pregnancy were obtained at a national level, along with rates of complications and morbidity associated with hospitalisation. Ireland experienced significant change during the study period 2005–2016. Years of economic growth and population

growth, due to an increasing birth rate and inward migration, came to an end due to the financial crisis which led to economic contraction, mass emigration and a decline in the birth rate [39,40]. Consideration of the impact of these factors has not been included in this study. A limitation of the study is that only inpatient data are available from the HIPE database [19]. As a result this study will under-estimate the overall burden of ectopic pregnancy given the lack of outpatient data available nationally [3,17]. However, the majority of ectopic pregnancies in Ireland are treated in inpatient hospital settings.

Conclusion

Women of advanced maternal age had a higher risk of hospitalisations for ectopic pregnancy. This study reported an increased rate of hospitalisations for ectopic pregnancy, while an improvement in the rates for blood transfusion and length of stay over two days. Invasive surgical treatments had a higher risk of blood transfusion and LOS over two days for ectopic pregnancy compared to minimally invasive surgical treatment. Conversely, women who underwent medical management rarely had a blood transfusion. More research is needed to explore the patterns of care and clinical indications at both outpatient and inpatient settings in order to improve protocols of management and the care provided.

Disclosure of interests

None declare.

Contribution to authorship

All authors had a role in the conception of the study. P.C and I.S. L.C obtained, analysed and interpreted the data. S.M participated in data analysis. S.M and K.O.D participated in interpretation of results. All authors were involved in drafting and writing the manuscript. All authors gave final approval of this article.

Ethics statement

This study was exempt from the requirement of full ethical review as it used publicly available anonymised data.

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Data statement

Data are available with the permission of the Irish Healthcare Pricing Office.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejogrb.2018.10.054.

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