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Comprehensive analysis of current epidemiology, clinical features and Prognostic Factors of puerperal endometritis: A retrospective cohort analysis

Rafael San-Juan [a,*,1], Alba Sanz-Prieto [a], Javier Contreras-Mora [a], Iván Fojo-Suárez [a], José María Caso-Laviana [a,2], Mario Fernández-Ruiz [a,3], Francisco López-Medrano [a,4], Isabel Rodríguez-Goncer [a,5], Marina Fayos [a], Patricia Brañas [c,6], P. Barbero Casado [b], Antonio García-Burguillo [b,7], José María Aguado [a,8]

[a] Unit of Infectious Diseases, Hospital Universitario "12 de Octubre", Instituto de Investigación Sanitaria Hospital "12 de Octubre" (imas12), Madrid, Spain. Complutense University of Madrid, Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III (ISCIII), Madrid, Spain
[b] Unit of Perinatal Medicine, Obstetrics and Gynaecology Department, Hospital Universitario "12 de Octubre", Instituto de Investigación Sanitaria Hospital "12 de Octubre" (imas12), Madrid, Spain
[c] Department of Microbiology, Hospital Universitario "12 de Octubre", Instituto de Investigación Sanitaria Hospital "12 de Octubre" (imas12), Madrid, Spain

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ABSTRACT

Background: Puerperal endometritis has not been recently investigated. We aimed to describe the current dimension of the endometritis in the context of other causes of puerperal fever and investigate the microbiology and need for curettage in these patients

Methods: A retrospective cohort study was conducted based on a prospectively maintained database of patients with puerperal fever, (2014–2020) in which cases fulfilling criteria for endometritis were selected for further analysis. Description of clinical and microbiological features was performed and determination of the factors related with puerperal curettage requirement were studied using univariate and multivariate analysis through binary logistic regression.

Results: From 428 patients with puerperal fever, endometritis was the main cause of puerperal fever (233 patients, 52.7 %). Curettage was required in 96 of them (41.2 %). Culture of endometrial samples were performed in 62 (64.5 %), of which 32 (51.6 %) yielded bacterial growth. *Escherichia coli* was the most common microorganism in curettage cultures (46.9 %). Multivariate analysis identified the following predictive factors for curettage: the presence of pattern compatible with retained products of conception (RPOC) in transvaginal ultrasonography (odds ratio [OR]: 17.6 [95 % confidence interval [CI]: 8.4–36.6]; *P*-value < 0.0001), fever during the first 14 days after delivery (OR:5.1; [95 % CI: 1.57–16.5]; *P*-value 0.007), abdominal pain (OR: 2.9; [95 % CI: 1.36–6.1]; *P*-value 0.012) and malodorous lochia (OR:3.5; [95 % CI: 1.25–9.9]; *P*-value 0.017). Scheduled cesarean delivery was protective (OR: 0.11 [95 % CI 0.01–1.2]; *P*-value 0.08).

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CRP, C-reactive protein; CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; IV, intravenous; MIS, minimally invasive surgery; OR, odds ratio; RPOC, retained products of conception; VIF, variance inflation factor; WBC, white blood cell.

* Correspondence to: Unit of Infectious Diseases. Hospital Universitario "12 de Octubre", Centro de Actividades Ambulatorias, 2ª planta, bloque D. Avda. de Córdoba, s/n. Postal code 28041 Madrid, Spain.

E-mail address: rafasjg@yahoo.es (R. San-Juan).

[1] **ORCID identification number:** 0000-0003-3446-1991.
[2] **ORCID identification number:** 0000-0001-5087-0299.
[3] **ORCID identification number:** 0000-0002-0315-8001.
[4] **ORCID identification number:** 0000-0001-5333-7529.
[5] **ORCID identification number:** 0000-0003-2150-5748.
[6] **ORCID identification number:** 0000–0003-4462-1354.
[7] **ORCID identification number:** 0000-0001-7624-6478.
[8] **ORCID identification number:** 0000-0002-9520-8255.

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Conclusions: Endometritis is still the main cause of puerperal fever. Women requiring curettage typically presented with abdominal pain and foul-smelling lochia, an ultrasound image compatible with RPOC and fever in the first 14 days postpartum. Curettage culture is useful for the microbiological affiliation mostly yielding gram-negative enteric flora.

Introduction

Puerperal endometritis has been classically considered the leading cause of puerperal fever and the second cause of death in the puerperium [1,2]. Based on data from the 20th century it is assumed that this postpartum complication occurs in 1.5–7 % of deliveries [2–4]. Nevertheless, updated information regarding the causes of puerperal fever and, specifically, the contemporary incidence of endometritis is lacking. The assumed etiology of these episodes is mainly inferred from the results of studies carried out in the 1980s, in which endometrial colonization by vaginal flora -including low pathogenic microorganisms such as *Ureaplasma* sp, *Mycoplasma sp* - was assumed to cause ascending endometritis [5–8]. This previous research has conditioned current strategies of empirical antibiotic therapy [9–11]. However, there is scarce current real-world information on the micro-organisms ultimately implicated in endometritis episodes, as it is not generally recommended to attempt microbiological diagnosis due to the limitations of available sampling techniques [3].

Although the outcome of most women is favorable with antibiotic therapy, a minority of patients present clinical worsening [12] with extension into the myometrium, parametrium and abdominal cavity, and may develop peritonitis, intra-abdominal abscess or severe sepsis. Therefore, in addition to antibiotics, optimization of treatment should include in selected patients more invasive procedures, such as uterine curettage [1,2]. However, the frequency of curettage in the current practice and the clinical profile of patients with endometritis requiring this technique is not well defined.

The aims of this research are to measure the current dimension of the problem of endometritis in the context of other causes of puerperal fever and to perform a comprehensive characterization of the clinical and microbiological features of this complication in a contemporary cohort. On the other hand we tried to identify in patients with puerperal endometritis the factors which suggest they may benefit from curettage.

Materials and Methods

Study population and design

This is a retrospective analysis of a prospectively collected cohort that was conducted at the University Hospital "12 de Octubre" (Madrid, Spain). The Clinical Research Ethics Committee approved the study protocol (2022/0276) and granted a waiver of informed consent in view of the observational design. The research was performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

The study population consisted of women who had been attended for childbirth at the Hospital Universitario 12 de Octubre between January 2014 and December 2020 and were diagnosed with puerperal fever (see criteria below). Our institution is a tertiary-care center in Madrid with a reference population of ~ 450,000 inhabitants in 2019, which attends around 4000 deliveries per year.

Affiliation data and the main clinical variables of the study cohort have been prospectively collected since 2014 in a healthcare database of the Gynecology and Obstetrics Department. To confirm the cases of endometritis for the present study, the medical records of cases of puerperal fever identified during the first 42 days after delivery were retrospectively evaluated by two independent researchers (Obstetrics and Infectious Diseases specialists), applying specific criteria for puerperal fever and puerperal endometritis. Puerperal fever was defined as axillary temperature $\geq$ 38 °C during the first 42 days postpartum, excluding intrapartum fever [7]. Puerperal endometritis was defined according clinical Centers for Disease Control and Prevention (CDC) criteria: the presence of puerperal fever beginning beyond the first after 48 h or sustained for at least 3 days, and within the first 42 days postpartum, without an alternative cause [13]. Histological diagnosis of endometritis was not routinely performed.

As a first step, the different causes of puerperal fever in the overall study cohort were classified according to the following categories: (1) puerperal endometritis, (2) surgical wound infection, (3) puerperal mastitis, (4) acute pyelonephritis, (5) septic pelvic thrombophlebitis, (6) upper respiratory tract infection, and (7) other causes. This classification was carried out by two independent researchers according to the criteria proposed by the CDC for healthcare-associated infections [13].

In the subgroup of patients with puerperal endometritis, we also collected different variables related to the epidemiological and obstetric profile of the patients, as well as the clinical and microbiological characteristics of the episodes. Patients who required curettage during evolution were identified and the different clinical variables obtained on admission were compared with the remaining cohort that did not require curettage. To this end we used a standardized case report form to retrieve data from electronic medical records.

Baseline and peripartum variables included: patient age; body mass index (BMI); presence of diabetes; *Streptococcus agalactiae* colonization status; gestational age; type of gestation; form of delivery; occurrence of prelabor rupture of membranes (and duration in hours), presence of intrapartum fever, and development of postpartum anemia and transfusion requirements, among others. In addition, variables specifically collected in episodes of endometritis comprised: days from delivery to the onset of fever; temperature; maximum white blood cell (WBC) count and serum C-reactive protein (CRP) level; presence of abdominal pain or malodorous lochia; transvaginal ultrasound examination performed and ultrasound findings; requirement of uterine curettage; days of fever before and after the curettage; antibiotic therapy (agent, route of administration and duration); days of fever from the initiation of antibiotic therapy; requirement of intensive care unit (ICU) admission; and total days of fever.

Preventive measures against puerperal infection

In case of cesarean delivery, antibiotic prophylaxis consisted of a single 2 g intravenous (IV) dose of cefazolin (no additional azithromycin is administered). Neither antibiotic prophylaxis or vaginal preparation was administered in vaginal delivery. In women colonized by *S. agalactiae* or in case of prelabor rupture of membranes more than 18 h with *S. agalactiae* rectovaginal screening not performed or unknown result, Penicillin G 5 million units intravenously initial dose, then 2.5–3 million units intravenously every four hours until delivery were administered. In women with β-lactams allergy, the prophylaxis regimen was Clindamycin 900 mg intravenously every eight hours until deliver. Patients developing intrapartum fever received IV ampicillin (2 g) plus IV gentamicin (240 mg), with ampicillin being replaced by clindamycin in case of β-lactams allergy.

Management of puerperal fever

According to institutional protocols, blood and urine cultures should be obtained before the initiation of antibiotic therapy. The preferred empirical regimen was IV amoxicillin-clavulanic acid plus gentamicin,

whereas vancomycin plus gentamicin plus metronidazole or clindamycin plus gentamicin were alternatively offered in case of β-lactam allergy. In the cases of microbiological identification of causative pathogen, antimicrobial susceptibility testing directed therapy is recommended.

Curettage to remove the retained material, when necessary, is performed with sharp curettage non-aggressively.

Statistical analysis

Quantitative data were shown as the mean ± standard deviation (SD) or the median with interquartile range (IQR). Qualitative variables were expressed as absolute and relative frequencies. Categorical variables were compared using the $\chi 2$ test. Student's t-test or Mann-Whitney U test were applied for continuous variables, as appropriate.

Factors associated with the requirement of curettage in women with endometritis were investigated through univariate and multivariate analyses. Those variables with univariate *P-values* ≤ 0.1 were entered into a backward stepwise logistic regression model. Multicollinearity among explanatory variables was analyzed using the variance inflation factor (VIF), with VIF values < 3 being considered acceptable. The most parsimonious model (i.e. the highest outcome variability explained with the lowest number of variables) was selected. Results were given as odds ratios (ORs) with 95 % confidence intervals (CIs).

All the significance tests were two-tailed. The threshold for statistical significance was set at a P-value < 0.05. Statistical analysis was performed with SPSS version 21.0 (IBM Corp, Armonk, NY).

Results

Incidence and etiology of puerperal fever

As shown in Fig. 1, 27,797 deliveries were attended at our institution during the study period, 428 of which (1.54 %) met the criteria of puerperal fever. As is shown in Table 1, there were no significant changes over time in the incidence of this event, with 248 out of 16,359 deliveries in the period 2014–2017 (1.52 %) vs. 180 out of 11,438 deliveries (1.57 %) in the period 2018–2020 (*P*-value = 0.31).

The main cause of puerperal fever was endometritis (233 [54.4 %]), accounting for a cumulative incidence of 8.4 cases per 1000 deliveries. The other main causes were surgical site infection (56 [13.1 %]), puerperal mastitis (55 [12.9 %]), acute pyelonephritis (35 [8.2 %]), thrombophlebitis of pelvic vessels (10 [2.3 %]) and upper respiratory tract infection (11 [2.6 %]) (Fig. 2).

Table 1
Incidence of puerperal fever and main infectious syndromes over time.

	2014–2020	2014–2017	2018–2020	P-*value**
Puerperal fever	15.9	15.5	16.5	0.54
Puerperal endometritis	8.4	7.9	9.1	0.31
Surgical site infection.	2.0	2.3	1.7	0.34
Puerperal mastitis	2.0	2.3	1.5	0.18
Pyelonephritis	1.3	1.2	1.4	0.8

Cases per 1000 deliveries. * Comparison between both periods.

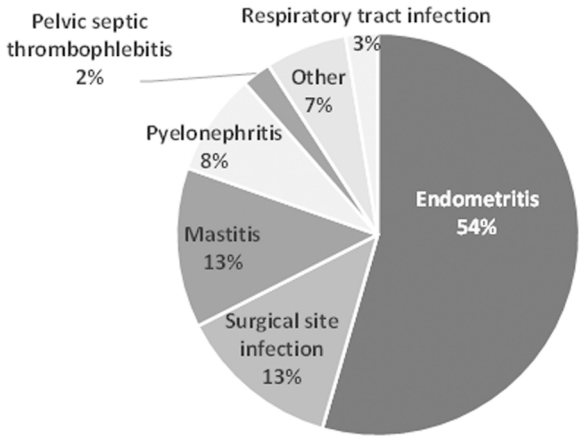

Fig. 2. Distribution of causes of puerperal fever.

Description of the endometritis cohort

The baseline and peripartum characteristics of the 233 patients that fulfilled the diagnostic criteria for puerperal endometritis are detailed in Table 2. The rate of *S. agalactiae* colonization was 13.2 % (29/233). Regarding variables related to gestation and delivery, 7 patients had a multiple pregnancy (3.0 %) and 61 patients underwent cesarean delivery (26.2 %), 46 of which (76.7 %) were emergency procedures. Cesarean delivery was performed in 61 cases (26.2 %), 14 (6.0 %) scheduled and 47 (20.2 %) emergency procedures. Finally, 122 women (52.4 %) had prelabor rupture of membranes, with a median duration of eight hours (IQR: 3–15). Twelve patients (5.2 %) had postpartum anemia (hemoglobin level < 8 g/dL), and eight of them (66.7 %) required transfusion of blood products. Forty-three patients (18.5 %) had intrapartum fever.

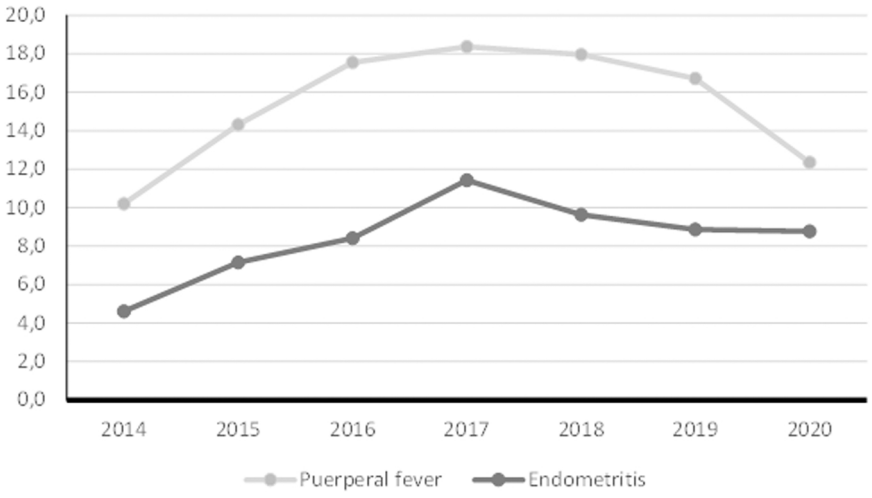

Fig. 1. Evolution of annual incidence per 1000 deliveries of puerperal fever (light grey) and puerperal endometritis (dark gray) during the study period.

Table 2
Baseline and peri-partum characteristics of 233 patients with puerperal endometritis.

Variable	
Patient age, years [mean ± SD]	29.6 ± 6.7
BMI, kg/m^2 [mean ± SD]	25.5 ± 5.7
Diabetes mellitus [n (%)]	13 (5.6)
Gestational with diet	11 (4.7)
Pregestational	2 (0.9)
Colonization with *Streptococcus agalactiae* [n (%)].	29 (12.4)
Gestational age, weeks [mean ± SD].	38.7 ± 2.6
Type of gestation [n (%)]	
Single	226 (96.9)
Multiple	7 (3.0)
Type of delivery [n (%)]	
Normal delivery	154 (66.1)
Operative	18 (7.7)
Scheduled cesarean delivery	14 (6)
Urgent cesarean delivery	47 (20.2)
Prelabor rupture of membranes [n (%)]	122 (52.4)
Hours of prelabor rupture of membranes [median (IQR)]	8 (3–15)
Intrapartum fever > 38 °C [n (%)]	43 (19.8)
Postpartum anemia [n (%)]	12 (5.2)
Blood transfusion requirements [n (%)]	8 (3.4)

BMI: body mass index; IQR: interquartile range; SD: standard deviation.

Clinical features of episodes of endometritis

Table 3 describes variables related to 233 episodes of puerperal endometritis. The median number of days from delivery to onset of fever was 8 (IQR: 4–12) and most of the episodes (188 [80.7 %]) occurred within the first 14 days. The mean maximum temperature was 38.8 ± 0.6 °C, whereas and the median number of days of fever was 2 (IQR: 1–3). As accompanying symptoms, 84 patients (36.1 %) presented with abdominal pain, and 30 (12.9 %) with foul-smelling lochia. Regarding analytical data, the mean maximum values for WBC count and CRP level were 12.15 ± 4.36 × 10^9/L and 8.4 ± 7.3 mg/dL, respectively.

Table 3
Clinical features of endometritis episodes.

Variables	
Days from delivery to onset of fever [median (IQR)]	8 (4–12)
Timing of fever onset [n (%)]	
First 7 days postpartum	112 (48.1)
Day 8–14 postpartum	76 (32.6)
Day 15–42 postpartum	45 (19.3)
Maximum axillary temperature, °C [mean ± SD]	38.8 ± 0.6
Abdominal pain [n (%)]	84 (36.1)
Foul smelling lochia [n (%)]	30 (12.9)
Maximum WBC count, × 10^9/L [mean ± SD]	12.15 ± 4.36
Maximum CRP levels, mg/L [mean ± SD]	8.4 ± 7.3
Transvaginal ultrasound performed [n (%)]	228 (97.9)
Ultrasound findings [n (%)][a]	
No pathological findings	77 (33.8)
Compatible with RPOC	100 (43.9)
Hydro/hematometra	33 (14.4)
Other	18 (7.9)
Curettage performed [n (%)]	96 (41.2)
Days of fever until curettage [median (IQR)]	1 (0–2)
Days of fever after curettage [median (IQR)]	1 (0–1)
IV antibiotic therapy [n (%)]	
Amoxicillin-clavulanic acid plus gentamicin	170 (75.6)
Gentamicin plus clindamycin	9 (4)
Amoxicillin-clavulanic acid plus gentamicin plus clindamycin	10 (4.4)
Ampicillin plus gentamicin	8 (3.6)
Ampicillin plus gentamicin plus clindamycin	14 (6.2)
Amoxicillin-clavulanic acid	8 (3.6)
Other	6 (2.7)
Days of IV antibiotic therapy [median (IQR)]	3 (2–4)
Days of oral antibiotic therapy [median (IQR)]	7 (6–9)
Total days of antibiotic therapy [median (IQR)]	10 (8–12)
Days of fever since the initiation of antibiotic therapy [median (IQR)]	1 (1–2)
Total days of puerperal fever [median (IQR)]	2 (1–3)

IQR: interquartile range; IV: intravenous; SD: standard deviation. [a]Counts over the total of 228 women with ultrasound study performed. RPOC: retained products of conception.

Transvaginal ultrasound examination was performed in 228 women (97.9 %), and a mixed echoic endometrial pattern compatible with retained products of conception (RPOC) was observed in 100 of them (43.8 %). In terms of antibiotic therapy received, the median duration was 10 days (IQR: 8–12), with 3 (IQR: 2–4) and 7 (IQR: 6–9) days of IV and oral treatment, respectively. Regarding the IV regimen, most women (170 [75.6 %]) received amoxicillin-clavulanic acid plus gentamicin. Other less frequently used regimens comprised ampicillin plus gentamicin plus clindamycin (14 [6.2 %]) and amoxicillin-clavulanic acid plus gentamycin plus clindamycin (10 [4.4 %]). On the other hand, amoxicillin-clavulanic acid was the most common oral regimen (208 [75.1 %]). Overall 96 women (41.2 %) underwent curettage after a median of 1 day from the onset of fever (IQR: 0–2).

The evolution was favorable in the majority of patients, with a median duration of fever of 2 days (IQR: 1–3). In detail, the fever abated at a median of one day (IQR: 0–1) from curettage and one day (IQR: 1–2) after the initiation of antibiotic therapy. Only two women (0.9 %) developed severe sepsis requiring ICU admission (with *Escherichia coli* identified as the causative agent in both cases), and one further patient (0.4 %) required hysterectomy. In all these complicated cases, recovery was eventually complete.

Microbiological characteristics of endometritis episodes

As is depicted in Table 4, out of the 96 curettage procedures, culture of endometrial samples was performed in 62 cases (64.5 %), 32 of which (51.6 %) yielded bacterial growth. The most frequently identified causative agent was *E. coli* (46.9 %), whereas *S. agalactiae* and *Gardnerella vaginalis* were identified in 3 cases (9.4 %) each. The majority of these isolated bacteria were susceptible to amoxicillin-clavulanate except two isolates of *E. coli,* both of them susceptible to gentamycin.

Blood cultures were processed in the overwhelming majority of episodes (233 [98.3 %]). Once presumable false positive results (i.e. pseudobacteremia) had been excluded, 7 women (3.0 %) had significant bacteremia. The microorganisms isolated were *E. coli* (four patients), *Clostridium perfringens* (two patients) and *Bacteroides fragilis* (one patient). It should be noted that in two cases *E. coli* was recovered from both blood culture and the culture of curettage sample. In these seven cases, the isolated microorganisms were finally susceptible to amoxicillin-clavulanate.

Table 4
Microbiological characteristics of endometritis episodes.

Positive curettage cultures[1] [n (%)]		N = 32
	Escherichia coli	15 (46.9)
	Gardnerella vaginalis	3 (9.4)
	Streptococcus agalactiae	3 (9.4)
	Proteus mirabilis	2 (6.3)
	Staphylococcus aureus	2 (6.3)
	Aerococcus spp.	1 (3.1)
	Enterococcus faecalis	1 (3.1)
	Mixed anaerobic flora	1 (3.1)
	Peptococcus spp.	1 (3.1)
	Prevotella spp.	1 (3.1)
	Streptococcus pyogenes	1 (3.1)
	Streptococcus anginosus	1 (3.1)
Positive blood cultures[2] [n (%)]		N = 7
	Escherichia coli	4 (57.1)
	Clostridium perfringens	2 (28.6)
	Bacteroides fragilis	1 (14.3)

[1.] Only two *E. coli* isolates were resistant to amoxicillin-clavulanate, both susceptible to gentamycin.
[2.] All of them were susceptible to amoxicillin-clavulanate.

Analysis of clinical predictors of curettage requirements

Clinical predictors of requirement of curettage

Finally, we compared the clinical characteristic at onset of fever between women that required or did not require therapeutic uterine curettage (Table 5). The presence of mixed echoic endometrial pattern (74 % vs. 17.5 %; *P*-value < 0.0001), abdominal pain (45.8 % vs. 29.2 %; *P*-value = 0.01) and malodorous lochia (18.8 % vs. 8.8 %; *P*-value = 0.04) was more common in patients requiring curettage, which also had an earlier onset of fever from delivery (7.6 ± 4.1 vs. 10.6 ± 8.7 days; *P-value* = 0.001). On the other hand, scheduled cesarean delivery was less frequent in the group of curettage (1 % vs. 9.5 %; *P*-value = 0.016). A total of 25 women (18.8 %) with ultrasound imaging compatible with RPOC did not require curettage and were successfully manage with antibiotics. Clinical picture in this subgroup was only characterized by a lower rate of abdominal pain at onset: 5/25 (20 %) vs. 34/75 (40 %) in women with RPOC compatible ultrasound findings finally undergoing curettage (*P-value* = 0.1).

On the other hand 21 out of 133 women without ultrasound findings compatible with RPOC (15.7 %) finally required curettage. Clinical picture including malodorous lochia was more frequent in patients requiring curettage (33.3 % vs. 8 %, *P-value* = 0.003) and these group of women presented higher maximum CRP serum levels (Mean: 11.1 [SD:9.4]) compared with vs. 7.8 [SD:6.6]; *P-value* = 0.06).

Univariate and multivariate analysis of the factors associated with curettage are shown in Table 6. The following variables were identified as independent risk factors: presence of mixed echoic endometrial pattern suggestive of RPOC in ultrasound examination (adjusted OR [aOR]: 17.6; 95 % CI: 8.4–36.6; *P*-value < 0.0001), fever during the first 14 days postpartum (aOR: 5.1; 95 % CI: 1.57–16.4; *P*-value = 0.007), abdominal pain at onset of fever (aOR: 2.9; 95 % CI: 1.36–6.1; *P*-value = 0.005) and malodorous lochia (aOR: 3.5; 95 % CI: 1.25–9.9; *P*-value = 0.017). Scheduled cesarean delivery exerted a protective effect (aOR: 0.11; 95 % CI: 0.01–1.2; *P*-value = 0.08).

Discussion

Principal findings

In this single center cohort with an overall incidence of 8.4 cases per 1000 deliveries of puerperal fever, more than half of episodes fulfilled the diagnostic criteria for puerperal endometritis after specific exclusion of other causes, a proportion that has remained stable over the last few years. Onset of fever close to delivery accompanied by specific symptoms as abdominal pain and foul-smelling lochia supported by ultrasound examination compatible with RPOC define the profile of women finally undergoing curettage, which was performed in more than 40 % of the patients. An additional interesting finding was the good performance of microbiological processing of curettage samples for etiological diagnosis of the episodes.

Table 5
Comparison of clinical characteristics of women with endometritis that required or did not require therapeutic uterine curettage.

	Curettage (n = 96)	No curettage (n = 137)	*P*-value
Type of gestation [n (%)]			
Single	91 (94.8)	135 (98.5)	0.2
Multiple	5 (5.2)	2 (1.5)	0.2
Type of delivery [n (%)]			
Normal delivery	73 (76.0)	81 (59.1)	0.08
Operative	4 (4.2)	14 (10.2)	0.08
Cesarean delivery	19 (19.8)	42 (30.7)	0.08
Scheduled cesarean delivery [n (%)]	1 (1)	13 (9.5)	0.01
Abdominal pain [n (%)]	44 (45.8)	40 (29.2)	0.01
Foul smelling lochia [n (%)]	18 (18.8)	12 (8.8)	0.04
Ultrasound image compatible with RPOC [n (%)]	75 (78.9)	25 (18.8)	< 0.0001
Days from delivery to onset of fever [mean ± SD]	*7.6* ± 4.1	*10.6* ± 8.7	0.001
Days of IV antibiotic therapy [mean ± SD]	3.7 ± 3.2	3 ± 1.7	0.031
Total days of antibiotic therapy [mean ± SD]	11.8 ± 4.8	10 ± 3.7	0.005

IV: intravenous; SD: standard deviation. RPOC: retained products of conception.

Table 6
Univariate and multivariate analysis of factors associated with the requirement of curettage.

	Univariate		*Multivariate*	
	OR (95 % CI)	*P*-value	OR (95 % CI)	*P*-value
Scheduled cesarean delivery	0.1 (0.01–0.78)	0.028	0.11 (0.01–1.2)	0.08
Onset of fever before 14 days postpartum	7.5 (2.8–19.8)	< 0.0001	5.1 (1.57–16.5)	0.007
Abdominal pain on debut	2.05 (1.2–3.5)	0.01	2.9 (1.36–6.1)	0.005
Foul-smelling lochia	2.38 (1.1–5.2)	0.03	3.5 (1.25–9.9)	0.017
Ultrasound image compatible with RPOC	13.4 (7.1–25.2)	< 0.0001	17.6 (8.4–36.6)	< 0.0001

RPOC: retained products of conception.

Results in the context of what is known

It is noteworthy that, despite the fact that our cohort included more than 25 % of cesarean deliveries, the incidence of endometritis was low (< 1 %) and significantly below that described in the literature [11]. Nevertheless, these usually accepted higher incidence figures are based on old cohort studies and the present experience probably better reflects the current epidemiology of this complication. On the other hand, the effort in this study to diagnose other causes of puerperal fever may have led to the reclassification of some episodes that otherwise would have been incorrectly considered as endometritis. In this sense, this study provides an updated etiological distribution of puerperal fever, incompletely analyzed to date [3].

The clinical profile of our cohort of women with puerperal endometritis was not unexpected in terms of risk factors previously described in the literature, such as emergency cesarean delivery, *S. agalactiae* colonization and prelabor rupture of membranes [2,9,14–16].

Despite the fact that patients frequently presented with high fever and significant elevation of acute phase reactants, in general the evolution was favorable with antibiotic therapy and curettage, performed in more than 40 % of the women. There is scarce information regarding the use of this invasive procedure in the therapeutic approach to puerperal endometritis and the profile of women that eventually require it [1]. Not surprisingly, the presence of an ultrasound image compatible with RPOC was the factor that most clearly prompted the indication for curettage. However, other clinical variables such as abdominal pain and foul-smelling lochia were also identified as independent predictive factors. It is likely that such a clinical presentation, which is considered relatively suggestive of endometritis [13], influenced the attending gynecologists' decision to perform curettage regardless of ultrasound examination findings. Similarly, the closer proximity between delivery and the onset of fever was another factor that could have been considered more specific of RPOC-related endometritis and also determined the therapeutic management. Markers of infection severity, such as increased acute phase reactants, were only associated to the decision of performing curettage in the subgroup of women with normal echography.

The only factor that was found to be protective was scheduled cesarean delivery which probably correlates with a procedure in which the

persistence of trophoblastic debris is less likely [17,18].

The analysis of our series also provides updated data on the microbiological etiology of endometritis. Although it is not clearly recommended to attempt a microbiological diagnosis of endometritis, given the low theoretical yield of blood cultures and the controversial role of processing endometrial samples for culture due to possible contamination by vaginal flora [19], in cases of puerperal fever blood cultures were obtained in the majority of patients of our cohort. In addition, culture was performed in more than 60 % of episodes that required curettage, returning a positive result in half of them, which allowed us to analyze microbiological data from a wide range of endometritis. Enterobacterales, and specifically *E. coli*, were the most frequently isolated causative agents and the main cause of bacteremia and sepsis. On the other hand, *S. agalactiae* was detected in less than 10 % of cases. Even considering the low rate of bacteremia (3.0 % in our cohort, in line with other series [3], blood culture is the only microbiological test with enough specificity and, therefore, therefore, it should be systematically ordered in our opinion. Although obtained through non-protected techniques, microorganisms isolated from endometrial samples were strongly correlated with the microbiologically documented colonization of the distal uterine cavity at the time of endometritis reported in previous studies [20]. In fact, the causative agents identified in our series are similar to those described in the few studies in which microbiological diagnosis of endometritis through protected uterine aspirate has been attempted [2,19]. Therefore, we believe that the processing of curettage material for culture may provide valuable information on the etiology of the episodes in order to guide the choice of antibiotic therapy. Based on our results, the empirical regimen most frequently used in our series —based on amoxicillin-clavulanic acid and gentamicin— is appropriate, since it provides good activity against Enterobacterales, *S. agalactiae* and anaerobic bacteria which were found to be the agents involved in the most severe cases of endometritis. Indeed, all the isolated microorganisms in our study were susceptible to this antibiotic combination. It should be noted that the curettage samples were not processed on media suitable for the growth of *U. urealyticum,* which has also been associated with endometritis [8]. Thus, we were unable to analyze the incidence and role of this microorganism in episodes of endometritis.

Strengths and limitations

This study has some limitations that should be noted. Its retrospective nature implies that the data used rely on the quality of the medical records available. Since it was conducted at a single center, the size of the study sample remains limited, despite the seven-year recruitment period. On the other hand, although accepted criteria were used to diagnose cases of endometritis, the specificity of these clinically-based criteria is limited. Whereas an effort has been made to assess alternative causes of puerperal fever, we cannot rule out some misclassification bias. Finally, the processing of endometrial material obtained by curettage was not protocolized, and the decision to send it for microbiological culture depended on the criteria of the attending gynecologist, raising the potential for selection bias.

Clinical implications

The present study offers a contemporary comprehensive descriptive analysis of the clinical profile of women requiring curettage in puerperal endometritis, information that could be useful to be included in the decision making algorithms for the management of this complication. In contrast to current general recommendations, our results support the inclusion of microbiological culture of endometrial samples apart from blood cultures in the work up protocols in women with suspicion of puerperal endometritis.

Research implications

Benefits of endometrial curettage in puerperal endometritis should ideally be determined through comparative clinical trials preferably focused in low risk women that could be cured with conservative treatment with antibiotics. In these regard, our study provides useful data for risk stratification in these population.

Conclusions

In conclusion, puerperal endometritis still accounts for more than half of the episodes of puerperal fever. Onset of symptoms within the first two weeks after delivery, ultrasound examination compatible with trophoblastic debris and the presence of abdominal pain and foul-smelling lochia define the profile of women that ultimately required therapeutic uterine curettage. The processing of curettage samples for culture seems to be useful for the microbiological diagnosis of a sizeable proportion of episodes. Finally, our results suggest that Enterobacterales are the most commonly involved causative agents, which should be the main target of empirical antibiotic regimens.

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Declaration of Competing Interest

All the authors declare no potential conflict of interest regarding this study.

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