

Original research

Endocarditis in pregnancy and postpartum: cases in a prospective adult cohort and literature review

Fernanda M. de Oliveira¹, Maria Theresa Fraife¹, Giovanna Ianini F. Barbosa^{2,3}, Thaissa S. Monteiro², Cristiane C. Lamas^{2,4}

¹Universidade do Grande Rio (UNIGRANRIO), Rio de Janeiro, Brazil

²Instituto Nacional de Cardiologia, Rio de Janeiro, Brazil

³Universidade do Estado do Rio de Janeiro (UERJ), Brazil

⁴Instituto Nacional de Infectologia Evandro Chagas, Fiocruz, Rio de Janeiro, Brazil

Abstract

Objective: Pregnancy and postpartum infective endocarditis (PPIE), although uncommon, is a very serious condition. To describe cases of infectious endocarditis (IE) in a cohort of adults with IE in a Brazilian center and to review data from the recent literature on the subject.

Methods: Cases of definite IE by the modified Duke criteria in adults were retrieved in a contemporary cohort of adults with IE from January 2006 to December 2020. Literature review on the topic was carried out and case reports on PPIE from 2014 to 2020 were compiled.

Results: Two cases of PPIE were found in 401 adult patients with IE, with a prevalence of 0.5% in the cohort, of 2/139 (1.4%) among women and 2/83 (2.4%) of women of reproductive age (18 -49 years) in this same cohort. The search for published case reports from 2014 to 2020 resulted in 61 episodes of PPIE; in these, 7 pregnant women (11.4%), 10 fetuses (16.4%) and 1 premature newborn (1.6%) died. There was a previous valve predisposition in 12 (19.7%) cases and intravenous drug use in 14(23%). Left-sided valves were the most frequently affected in 41 (67.2%) of the cases. The most common isolated infectious agent was methicillin sensitive *Staphylococcus aureus* in 18/61 (29.5%) patients, although as a group, oral viridans streptococci accounted for 16/61 (26.2%). Valve surgery was done for 70% of patients.

Conclusions: Intravenous drug use remained to be the main risk factor for IE. Mortality remained high for mothers and their children, despite the fact surgery was done more frequently in the recent cases. In the case of fever without an obvious focus in pregnant or post-partum women, the diagnosis of IE must be readily considered, especially in those with prosthesis and/or intravenous drug use.

Key words: infective endocarditis, pregnancy, postpartum

(Heart, Vessels Transplant 2022; 6: doi: 10.24969/hvt.2022.343)

Introduction

Cardiac disorders are the main cause of non- obstetric maternal death and approximately 1% to 4% pregnant women suffer from it, especially mitral valve disease (1-3). The majority are only diagnosed during the third trimester, with the worsening of symptoms (1-3). The incidence of infective endocarditis (IE) during pregnancy is 0.006% or 1 in 8.000 childbirths. Although rare, its occurrence is of concern, due to associated maternal and fetal death (4).

Endocarditis must be considered as a differential diagnosis each time there are signs of cardiovascular symptoms without a clear etiology in a patient, considering the urgent care required for its treatment

(5). The predisposing factors leading to IE involve congenital bicuspid aortic valve, rheumatic heart disease (RHD), intravenous drug abuse (IVDU), presence of prosthetic valves, previous IE and congenital heart disease (CHD), frequently associated with odontogenic disease responsible for triggering bacteremia (5-9).

The clinical diagnostic triad of IE is fever, heart murmurs and embolic phenomena (4, 7) . However, pregnancy itself can provoke cardiac strain due to hemodynamic changes, including increase in blood volume (this may increase by 50% in normal pregnancy), in heart rate and in cardiac output. These changes are maximal between the second and third trimester, with an additional climb in the immediate postpartum period.

Address for Correspondence: Cristiane Lamas, Cardiovascular Research Unit, 5th floor, Instituto Nacional de Cardiologia, Rua das Laranjeiras 374, Rio de Janeiro 22250-060, RJ/Brazil

Email: cristianelamas@gmail.com Phone: 5521-991628048

Received: 10.07.2022 **Revised:** 11.09.2022 **Accepted:** 12.09.2022

Copyright ©2022 Heart, Vessels and Transplantation

Furthermore, peripheral vascular resistance decreases, and a parallel decline in systemic blood pressure occurs (1-3). Due to these modifications, obstructive valve lesions - such as mitral stenosis and aortic stenosis, worsen and are associated with high rates of pregnancy and fetal complications, when compared to regurgitant lesions of the mitral and aortic valves. Likewise, significant physiological changes may happen to heart valves during pregnancy. The aortic root, the mitral and tricuspid rings enlarge. The mitral, tricuspid and pulmonary valves show some degree of insufficiency in 28%, 94% and 94% of pregnancies respectively (1, 2, 8, 9). Therefore, the presence of murmurs may result from physiological alterations that occur during pregnancy (1, 2, 8). A thorough physical examination and a high degree of suspicion are crucial to diagnose IE in pregnant women (1, 5).

Poor oral health or dental procedures may lead to bacteremia and IE, as may diagnostic or therapeutic procedures of the genitourinary and gastrointestinal tracts. Childbirth is also associated with situations that favor bacteremia, such as: membrane rupture for more than 6 hours, manual removal of the placenta, prolonged labor, and low socioeconomic status. Prophylactic measures are important in vaginal delivery and Cesarean section in order to reduce morbidity and mortality rates. Adequate antisepsis and asepsis, use of sterile instruments and correct techniques, in addition to antibiotic prophylaxis are required (10).

Although rare during pregnancy, IE can have devastating consequences for mothers and/or fetuses (4, 11). In this article, we describe cases from a Brazilian cardiology center and provide an update in the topic by doing a literature review of pregnancy and postpartum related IE.

Methods

Cases of PPIE were described retrospectively in a prospective cohort of consecutive adults with definite IE according to the modified Duke criteria (12) included in the years 2006 to 2020. Patients signed an informed consent form for inclusion in the cohort, which was approved by the Ethics Committee of Instituto Nacional de Cardiologia, under number 0171/2007. Variables included were those from the case report forms of the International Collaboration in Endocarditis (ICE) initiative (13). These cases were compared to those

obtained from reports in the literature. A literature search for clinical cases of PPIE was carried out for the period from January 2014 to June 2020. Two cases were excluded because the patients did not fit the studied profile of pregnant or postpartum women. The data were organized in tables; to complement the systematic literature review published previously (11). The Scientific Electronic Library Online (SCIELO) and National Library of Medicine (PUBMED) databases were searched. The following keywords were used: Endocarditis, Infectious endocarditis; Bacterial endocarditis; Pregnancy; Bacterial endocarditis AND pregnant women; Infectious endocarditis AND pregnancy; Clinical endocarditis; Endocarditis etiology; Endocarditis etiology AND pregnancy; Streptococcus; Streptococcus AND infection; Endocarditis diagnosis; Endocarditis treatment; Antibiotic therapy; Antibiotic therapy AND pregnant women; Heart surgery; Heart surgery AND endocarditis. Inclusion criteria were original studies describing cases or small series of cases of definite infective endocarditis according to the modified Duke criteria (12) in pregnancy or postpartum. Women 15 to 49 years of age were considered as of reproductive age, according to the World Health Organization definition (14).

Results

Two cases of IE associated with pregnancy or puerperium were found in 401 adult patients with definite IE in the study period at our institution, with a prevalence of 0.5% of the cohort, and 2/139 among women (1.4%). Considering adult women of reproductive age (18 to 49 years old) in the cohort, the prevalence of IE associated with pregnancy or puerperium was 2/83 (2.4%).

Clinical case 1

A 19-year-old black female farmer, with previous RHD, underwent a Cesarean section and presented two weeks later with fever, malaise, and pain in the left lower limb. She lived in Rio de Janeiro and denied intravenous drug use, HIV, other comorbidities, or a previous episode of IE. On the same day of symptom presentation, she sought the emergency department of a local hospital, a heart murmur was heard, and three blood culture sets were collected, which grew *Streptococcus anginosus* in all samples.

She was admitted to hospital and was started on antibiotic therapy with penicillin and gentamicin. Six days after admission, an ultrasound Doppler scan of her left leg showed a 2.5 cm diameter mycotic aneurysm of the left tibiofibular artery with a vegetation inside and a three-phase distal flow.

Computed tomography (CT) scans of the abdomen showed splenomegaly, and embolisms to the spleen and right kidney. She developed heart failure with NYHA III class and acute renal failure (creatinine 1.71 mg/dL), and was referred to our cardiac surgery hospital. A transesophageal echocardiography (TEE) was done, and it showed an aortic valve vegetation of 13x7 mm in size, prolapsing to the left ventricular outflow tract, on the non-coronary leaflet, which was ruptured; there was severe aortic insufficiency, and the mitral valve was thickened and with moderate regurgitation. She needed inotropic support before surgery, which was performed on an urgent basis, with concomitant aortic and mitral valve replacement. In the intraoperative period, a vegetation was also found on the mitral valve. She bled in the intraoperative period, and this persisted in the postoperative period. The patient also evolved with acute renal failure and had to go on hemodialysis. She died 48 hours postoperatively due to hemorrhagic shock, having undergone a total of nine days of antibiotic therapy. There was no bacterial growth of the aortic and mitral valves, but Gram-positive cocci were seen in histopathology. IE was considered hospital-acquired since the patient had undergone a Cesarean section 2 weeks before the onset of fever.

Clinical case 2

A 39-year-old white housewife, with aortic and mitral mechanical prosthesis and tricuspid valve annuloplasty 7 years before, was admitted to our cardiac hospital with a weight loss of 15 kg, associated with dizziness and worsening heart failure, with a NYHA functional class II-III. Two weeks earlier, she reported night sweats and chills. She also reported the presence of cough with intermittent whitish sputum. Past medical history included three episodes of "pneumonia" in the previous year, the last one of which was 6 months earlier, treated with levofloxacin. She referred a transient ischemic attack 3 years earlier. She had undergone mitral valvuloplasty 9 and 15 years before, due to rheumatic mitral stenosis. She was an active smoker (total was 14 pack-years). On physical examination, she presented a 4+/6+ systolic murmur in the aortic, mitral, tricuspid and pulmonary areas which radiated to the

carotid arteries. Two days after admission, a TEE was performed and showed images suggestive of vegetations on the atrial aspect of the mitral prosthesis, the lateral one measuring 1 cm and the medial one 0.9 x 0.8 cm, with mild mitral regurgitation; there was also significant stenosis of the aortic prosthesis with moderate to severe regurgitation, mild tricuspid regurgitation, with a pulmonary artery systolic pressure of 43 mmHg and the left ventricular ejection fraction was 68.5%. Blood cultures were collected and ampicillin and gentamicin started. Due to amenorrhea, a pregnancy test was requested and resulted positive; a pelvic ultrasound scan confirmed pregnancy, and a fetus estimated to be 7-weeks old was seen. She had vascular embolic events to the liver and elevated C reactive protein levels. Blood cultures taken on two different days were negative. Serologies for *Bartonella henselae* and *Coxiella burnetii* were negative. Surgery for heart failure and aortic prosthesis stenosis and regurgitation was indicated. Cardiac surgery was performed nine days after hospitalization, on an urgent basis, after the patient's consent. Vegetations on the mitral and aortic prosthesis were seen on operation, as well as pannus and thrombi. Postoperatively she developed atrioventricular block and needed a pacemaker implantation. The histopathology of the aortic mechanical prosthesis showed active endocarditis. She had several other events post-operatively: on day 4, a hypertensive acute pulmonary edema, on day 5, absence of fetal cardiac beats was noted on the obstetric ultrasonography, on day 8, a brain CT scan showed an acute right frontal ischemic lesion, on day 9 a definitive pacemaker was inserted, on day 16 uterine evacuation was performed by manual technique due to retained abortion. On day 29 postoperatively, after a repeat brain CT scan which showed a residual hypodense lesion in the left frontal cortico-subcortical area, she was discharged from hospital, asymptomatic, hemodynamically stable and without motor deficits. She completed 28 days of ceftriaxone 2g daily after surgery.

Analysis of reported cases with PPIE

Table 1 presents data from published case reports, complemented by the described 2 cases from our cohort. Data synthesis is presented on Tables 2 and 3. Overall, 61 cases reports were found on IE associated with pregnancy and puerperium, of which 55 were found related to pregnancy, and 4 to the postpartum period and in 2 cases, this was not informed (15-46).

Table 1. Clinical characteristics of reported PPIE cases									
First authour (year)	Country of publication	Patient Age in years	Gestational age	Predisposing valve condition	Risk factors (Number of cases)	Microorganism	Affected valve	Maternal death	Fetal death
Yuan et al (2014)	China	30 cases: 19-39 y average of 27 y	12-36 weeks, average of 23 weeks	- MV prolapse (2) - Rheumatic MV (1) - AVS (1) - AVR (1)	- IVDU (9) - Foreign material (3) - Urinary tract infection (3) - VSD (3) - Poor oral hygiene (1) - None (7)	MSSA (10) Viridans group streptococci (12) - <i>Streptococcus agalactiae</i> (2) - <i>H.parainfluenzae</i> (4) - <i>Salmonella typhi</i> (2) -not identified (7)	MV (13) AV (6) TV (4)	Yes (1 case)	Yes (5 cases)
Marciniak et al. (2014)	England	31 y	1 month after delivery	None	None	<i>Lactobacillus jensenii</i>	AV	No	No
Shah et al. (2015)	USA	30 y	25 weeks	None	Poor oral hygiene and IM injection of heroin	<i>Bacillus cereus</i>	TV	No	No
Connolly et al. (2015)	England	33 y	30 weeks	None	None	<i>Staphylococcus lugdunensis</i>	AV	No	No
English et al. (2015)	Australia	33 y	36 weeks	None	IV medication	MSSA	AV and TV	No	No
Saphina et al. (2015)	India	28 y	32 weeks	None	Apendectomy 2 months prior caused by <i>nonalbicans Candida</i>	<i>Non-albicans Candida</i>	MV	Yes	NI
Fu et al. (2015)	USA	23 y	31 weeks	None	IV medication and oral abscess treated with ampicillin.	<i>Candida parapsilosis</i> ,	AV	No	No
Botta et al. (2015)	Italy	39 y	14 weeks	None	None	<i>Abiotrophia defectiva</i>	MV	No	No
Benlamkadem et al. (2016)	Africa	27 y (1 st pregnancy) 29 y (2 nd pregnancy) 30 y	24 weeks (first pregnancy) 30 weeks (second pregnancy) -	None (1 st pregnancy) Mechanical AR (2 nd pregnancy) Prosthesis in mitral and aortic positions	None (1 st pregnancy) Mechanical MV (2 nd pregnancy) Prosthesis	Not described (G I) Not described (G II) <i>Staphylococcus epidermidis</i>	AV (1 st pregnancy) MV (2 nd pregnancy) AV and MV	No	No (1 st pregnancy) Yes (2 nd pregnancy) NA

Maturu et al. (2016)	India	25 y	Recent spontaneous abortion	MVS – suggestive of rheumatic valve disease	Sepsis after abortion	MSSA	MV, AV and TV	No	NA
Kastelein et al. (2016)	New Zealand	36 y	17 weeks	MVR	None	<i>Streptococcus sanguis</i>	MV	No	No
Quinn et al. (2016)	Canada	39 y	29 weeks	None	Central line 4 weeks prior for pneumonia treatment.	MSSA	TV	No	No
Khafaga et al. (2016)	Austria	35 y	24 weeks	None	Recently excised paronychia	<i>Staphylococcus lugdunensis</i>	MV	No	Yes (4 days after birth)
Birlutiu et al 2017	Romania	26 y	31 weeks	None	Fixed braces with gingival inflammation	<i>Abiotrophia defectiva</i>	MV	Yes	No
Sims et al 2017	USA	27 y	17 weeks	None	IVDU	MSSA	TV and AV	No	Yes
Kotaskova et al. (2017)	Czech Republic	NI	34 weeks	Bioprosthetic valve due to previous IE	IVDU	Not identified	TV	Yes	NI
Polewczyk et al. (2017)	Poland	29 y	28 weeks	NI	NI	Not identified	MV	No	No
Tamura M et al. (2017)	Japan	31 y	3 months after delivery	None	None	<i>Enterococcus faecalis</i>	MV	No	NA
Luo et al. (2017)	China	22 y	30 weeks	None	None	<i>Streptococcus anginosus</i>	AV	No	No
Steele et al. (2017)	USA	27 y	Not informed	None	IVDU	MRSA	TV	No	No
Garg et al. (2017)	USA	23 y	37 days after delivery	VSD	None	<i>viridans</i> group streptococcus	AV and PV	No	No
Vaideeswar et al 2017	India	23 y	36 weeks	None	None	<i>Zygomycetes</i> sp	MV	Yes	No
Piedimonte et al.(2018)	Canada	18 y	13 weeks	None	Curettage of abortion	GBS	TV	No	NI
Tamura T et al. (2018)	Japan	33 y	11 weeks	MVR	Sepsis due to pyelonephritis.	MSSA	MV	No	Yes
Ahres et al. (2018)	Hungary	30 y	29 weeks	None	IVDU	MSSA	TV	No	No
Wajih Ullah et al. (2018)	Pakistan	26 y	35 weeks	AVS	None	MSSA	AV	No	No
Khan et al.	Pakistan	25 y	NI	None	None	MSSA	AV	No	No

(2018)									
De Castro et al. (2019)	USA	34 y	30 weeks	NI	None	<i>Haemophilus parainfluenzae</i>	MV	No	No
Ramiro et al. (2019)	Philippines;	19 y	29 weeks	PDA	None	<i>viridans</i> group Streptococcus and <i>Pseudomonas putida</i>	PV	No	No
Masuda et al. (2019)	Japan	22 y	24 weeks	None	None	<i>Streptococcus gordonii</i>	MV	No	No
Wang et al. (2020)	China	30 y	26 weeks	PDA	None	<i>Group G beta-hemolytic streptococcus</i>	MV	No	No
Crofton et al (2020)	USA	24 y	13 weeks	None	None	<i>Streptobacillus sp</i>	MV	No	Yes
Clinical case 1 (unpublished)	Brazil	19 y	2 weeks after delivery	Rheumatic valve disease	Rheumatic valve disease	<i>Streptococcus anginosus</i>	AV and MV	Yes	No
Clinical case 2 (unpublished)	Brazil	39 y	7 weeks	Rheumatic valve disease, mechanical aortic and mitral prosthesis	Prosthesis	Not identified	AV	No	Yes

AV – aortic valve, AR – aortic valve regurgitation, AS – aortic valve stenosis, GBS - *group B streptococcus*, IE – infective endocarditis, IM – intramuscular, IV – intravenous, MSSA - methicillin-susceptible *Staphylococcus aureus*, MRSA - methicillin-resistant *Staphylococcus aureus*, MV – mitral valve, MR – mitral valve regurgitation, MS – mitral valve stenosis, NA – not applicable, PDA – persistent ductus arteriosus, PPIE – pregnancy and postpartum infective endocarditis, PV – pulmonary valve, TV – tricuspid valve, VSD – ventricular septal defect

Table 2. Summary of demographic and clinical characteristics of 63 patients with pregnancy-related and postpartum infective endocarditis

Clinical features	n(%)
Age, years (mean (range))	27 (19-39)
Gestational age, weeks (mean (range))	25 (7-38)
Pregnancy	57(93.4)
Puerperium	4(6.6)
Affected valves:	
Type of valve: prosthesis	4 (6.6)
Position of prosthetic valves:	
Aortic	19 (31)
Mitral	28 (45.9)
Tricuspid	13 (21.3)
Pulmonary	2 (3.3)
Not specified	1 (1.6%)
Valve replacement/repair	43/61** (70.5)
Maternal death	6 (10)
Fetal death	11 (18)
* Two cases were those described in this article and 61 from the literature review from 2014 to 2020; ** information available for 59 patients.	

Patients with PPIE had a mean age of 27 years, and the mean gestational age was 25 weeks. The most commonly affected valve was mitral (45.9%), followed by aortic (31%) and tricuspid (21.3%) valves; prostheses were affected in 6.6% of patients. Maternal death occurred in 10% of cases, and fetal death - in 18%. These results are detailed in Table 2.

Regarding responsible etiologic agents isolated in blood cultures, methicilin-sensitive *Staphylococcus aureus* was the most frequent pathogen (26%), closely followed by viridans group streptococci (23.2%); however, it is important to highlight that 17% of cases had no microorganisms identified in blood cultures. These results are presented in Table 3.

Discussion

In this present work, we sought to describe cases of pregnancy and puerperium-related IE in a cohort of adult patients with definitive IE in a reference hospital for Brazilian cardiac surgery and to make an updated

review of the literature on the subject, synthesizing the most relevant aspects.

We found that intravenous drug use remains the most frequent predisposing extracardiac risk factor for IE in pregnancy, being present in a quarter of our cases, compared to 14% in a previous literature review. Kebed et al. (11), found 90 cases in their literature review from 1988 to 2012, but only 51(56.7%) involved pregnancy, 14 were post-abortion (15.6%) and 25 (27.8%) puerperium. Although our case series is not directly comparable, we compare some features of both cohorts in Table 4. Rheumatic valve disease had a similar frequency, CHD was less frequent, and implanted prosthesis was more frequent in our series. We suppose less CHD is present in the latter period because these are being corrected at an earlier age in recent years; for this same reason, we may see more prosthesis, which are inserted in congenital and acquired valve disease. More drug use has been reported in the USA and Eastern Europe overall in more recent years, and this may be why we are seeing this predisposition in these pregnant women.

Table 3. Synthesis of microbiology data from 69 blood culture isolates from 63 patients with infective endocarditis related to pregnancy and puerperium*

Microorganisms	N=69 (100%)
MSSA	18 (26%)
MRSA	1 (1.4%)
<i>Staphylococcus lugdunensis</i>	2 (2.8%)
Viridans group streptococci	16 (23.2%)
<i>Streptococcus anginosus</i>	2 (2.8%)
<i>Beta hemolytic streptococci*</i>	2 (2.8%)
<i>Other Gram positives**</i>	2 (2.8%)
<i>Abiotrophia defectiva</i>	2 (2.8%)
<i>Streptobacillus sp</i>	1 (1.4%)
<i>H. parainfluenzae</i>	5 (7.4%)
<i>Salmonella typhi</i>	2 (2.8%)
<i>Pseudomonas putida</i>	1 (1.4%)
<i>Candida spp</i>	2 (2.8%)
<i>Zygomycetes</i>	1(1.4%)
Not identified	12 (17.4%)

* Two cases described in this article and 61 from literature review 2014-2020.
 MSSA=methicillin-sensitive *Staphylococcus aureus*; MRSA=methicillin-resistant *S.aureus* ; *Group B streptococcus in 1(1.5%) and group G streptococcus in 1 (1.5%); ***Lactobacillus jensenii* in 1 (1.5%), *Bacillus cereus* in1 (1.5%); Candida: non-albicans in 1 (1.5%), *C. parapsilosis* in 1 (1.5%)

Table 4. Comparison of selected features in a previous literature review (ref. Kebed et al., 11) and the present review

Selected features	1988-2012 cases*	2014-2020 cases**
Viridans group streptococci	17/90(18.9%)	16/61(26.2%)
Beta-hemolytic streptococci	8/90(8.9%)	2/61(3.3%)
Staphylococcal species	23/90(25.6%)	20/61(32.8%)
Intravenous drug use	13/90(14.4%)	15/61(25%)
Rheumatic valvulopathy	11/90(12.2%)	5/61(8.2%)
Congenital heart disease	11/90(12.2%)	3/61(4.9%)
Prosthetic heart valves	1/51(2%)	4/61 (6.6%)
Left-sided IE	34/51(66.7%)	43/61(70.5%)
Surgery	48(53.3%)	43/61(70.4%)
Maternal death	6/51(11%)	6/61 (10%)
Fetal death	7/51(14%)	9/61 (15%)

*Of the 90 cases described, only 51 were pregnancy-related; **Of the 61 cases described, 57 were pregnancy related

Viridans group streptococci, as well as staphylococci, became more frequent as agents of IE in our cohort, but the frequency of beta-hemolytic streps decreased, which may be due to better antenatal care and screening for *S. agalactiae*.

Valve replacement surgery in IE has improved the prognosis for patients with left-sided endocarditis, and we found more patients were offered surgery in our review, compared to a previous one (70 vs 53%). This may reflect the consensus in endocarditis published in 2015 by the American Heart Association and the European Society of Cardiology, in which the role of the Heart Team and of surgery in left sided IE are emphasized. The benefits of surgery in the acute clinical picture should always be balanced with the risk of mortality and the likelihood of the new valve recolonization in the presence of continuous bacteremia (4, 7). In the scenario of intravenous drug use, the role of surgery is even more contentious since the danger of recurrence is high (4). It must be emphasized, however, that when IE involves right-sided valves, as is often the case in intravenous drug use, surgery is most often not necessary, and mortality is lower (47). In pregnant women presenting with acute heart failure secondary to acute valve regurgitation, immediate surgery is indicated. However, there is high fetal mortality risk. During cardiopulmonary bypass, maternal outcomes remain the same as for nonpregnant but fetal mortality is high, ranging from 16% to 33% (48).

It is necessary to highlight the need for thorough prenatal monitoring, with the evaluation of the pregnant woman's valves and cardiovascular condition, so that in cases of fever with no obvious source, endocarditis is considered and expeditiously investigated, minimizing complications including maternal and fetal death.

It is also important to refer patients with left sided IE to centers with a Heart Team and have them evaluated early so that surgery may be indicated at the right moment, since heart valve surgery saves lives in left sided IE. The Heart Team in PPIE should obviously include an obstetrician and pediatrician for the best management of these patients.

Study limitations

Limitations of our study are reporting bias, as not all cases of pregnancy and postpartum related IE are published. Strengths are providing available and more recent information on this severe condition, putatively

comparing data from a previous review and possibly outlining trends.

Conclusions

Staphylococci accounted for a third of PPIE.

Intravenous drug use remains the most frequent predisposing extracardiac risk factor for IE in pregnancy, being present in a quarter of cases reviewed.

Rheumatic valve disease had a similar frequency, congenital heart disease was less frequent, and heart valve prosthesis was more frequent in this recent literature review series.

Surgery was done for over 2/3 of PPIE, a rate higher than previously reported in the literature.

Maternal and fetal mortality remain high.

Pregnancy and puerperium related to IE is a serious condition, and fever in intravenous drug users, women with previous valvular heart disease or prosthesis should prompt its diagnosis, so as to improve prognosis. Evaluation by a Heart Team with expertise in endocarditis, plus an obstetrician and pediatrician, is essential, especially in left-sided PPIE, where surgery often saves lives.

Ethics: Written patients consent form was obtained from patients before all procedures and study was approved by Ethics Committee of Instituto Nacional de Cardiologia

Peer-review: Internal and external

Conflict of interest: None to declare

Authorship: F.M.O., M.T.F., G.I.F.B., T.S.M., C.C.L. equally contributed to the patients management, study and manuscript preparation.

Acknowledgement: We acknowledge all medical and non-medical staff from Instituto Nacional de Cardiologia for their dedication and care to patients

Funding: None to declare

References

1. Martin S, Arafeh J. Cardiac disease in pregnancy. *AACN Adv Crit Care* 2018; 29: 295-302. doi: 10.4037/aacnacc2018615.
2. Anthony J, Sliwa K. Decompensated heart failure in pregnancy. *Card Fail Rev* 2016; 2: 20-6. doi: 10.15420/cfr.2015:24:2.
3. Martins LC, Freire CM, Capurucu CA, Nunes Mdo C, Rezende CA. Risk prediction of cardiovascular complications in pregnant women with heart disease. *Arq Bras Cardiol* 2016; 106: 289-96. doi: 10.5935/abc.20160028.
4. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. The 2015 ESC Guidelines for the management of infective endocarditis. *Eur Heart J* 2015; 36: 3036-7. doi: 10.1093/eurheartj/ehv488
5. Neidenbach R, Niwa K, Oto O, Oechslin E, Aboulhosn J, Celermajer D, et al. Improving medical care and prevention in adults with congenital heart disease- reflections on a global problem-part II: infective endocarditis, pulmonary hypertension, pulmonary arterial hypertension and aortopathy. *Cardiovasc Diagn Ther* 2018; 8: 716-24. doi: 10.21037/cdt.2018.10.16.
6. van Hagen IM, Roos-Hesselink JW. Pregnancy in congenital heart disease: risk prediction and counselling. *Heart* 2020; 106: 1853-61. doi: 10.1136/heartjnl-2019-314702.
7. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, et al. American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council. Infective ENDOCARDITIS IN ADULTS: DIAGNOSIS, ANTIMICROBIAL THERAPY, AND MANAGEMENT OF COMPLICATIONS: A Scientific Statement for Healthcare Professionals from the American Heart Association. *Circulation* 2015; 132: 1435-86. doi: 10.1161/CIR.0000000000000296.
8. Pessel C, Bonanno C. Valve disease in pregnancy. *Semin Perinatol* 2014; 38: 273-84. doi: 10.1053/j.semperi.2014.04.016.
9. Nanna M, Stergiopoulos K. Pregnancy complicated by valvular heart disease: an update. *J Am Heart Assoc* 2014; 3: e000712. doi: 10.1161/JAHA.113.000712.
10. van Schalkwyk J, Van Eyk N. No. 247-Antibiotic prophylaxis in obstetric procedures. *J Obstet Gynaecol Can* 2017; 39: e293-e299. doi: 10.1016/j.jogc.2017.06.007.
11. Kebed KY, Bishu K, Al Adham RI, Baddour LM, Connolly HM, Sohail MR, et al. Pregnancy and postpartum infective endocarditis: a systematic review. *Mayo Clin Proc* 2014; 89: 1143-52. doi: 10.1016/j.mayocp.2014.04.0248.
12. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000; 30: 633-8. doi: 10.1086/313753.
13. Cabell CH, Abrutyn E. Progress toward a global understanding of infective endocarditis. Early lessons from the International Collaboration on Endocarditis investigation. *Infect Dis Clin North Am* 2002; 16: 255-72, vii. doi: 10.1016/s0891-5520(01)00007-1.
14. World Health Organization. www.who.int
15. Yuan SM. Infective endocarditis during pregnancy. *J Coll Physicians Surg Pak* 2015; 25: 134-9.
16. Marciniak A, Karapanagiotidis GT, Sarsam M, Sharma R. Postpartum *Lactobacillus jensenii* endocarditis in patient with bicuspid aortic valve. *J Thorac Cardiovasc Surg* 2014; 148: e219-21. doi: 10.1016/j.jtcvs.2014.05.096.
17. Shah M, Patnaik S, Wongrakpanich S, Alhamshari Y, Alnabelsi T. Infective endocarditis due to *Bacillus cereus* in a pregnant female: A case report and literature review. *ID Cases* 2015; 2: 120-3. doi: 10.1016/j.idcr.2015.10.003
18. Connolly C, O'Donoghue K, Doran H, McCarthy FP. Infective endocarditis in pregnancy: Case report and review of the literature. *Obstet Med* 2015; 8: 102-4. doi: 10.1177/1753495X15572857
19. English N, Weston P. Multivalvular infective endocarditis in pregnancy presenting with septic pulmonary emboli. *BMJ Case Rep* 2015; 2015: bcr2014209131. doi: 10.1136/bcr-2014-209131.
20. Saphina P, Mansoor CA, Jemshad A, Musambil M. Native valve candida endocarditis complicating pregnancy after abdominal surgery. *Heart Views* 2015; 16: 111-3. doi: 10.4103/1995-705X.164459.
21. Fu J, Retherford LM, Flynn B. Preterm caesarean delivery in a parturient with *Candida parapsilosis* endocarditis. *Case Rep Anesthesiol* 2015; 2015: 897645. doi: 10.1155/2015/897645.
22. Botta L, Merati R, Vignati G, Orcese CA, De Chiara B, Cannata A, et al. Mitral valve endocarditis due to *Abiotrophia defectiva* in a 14th week pregnant woman. *Interact Cardiovasc Thorac Surg* 2016; 22: 112-4. doi: .1093/icvts/ivv289.

23. Benlamkaddem S, Berdai A, Labib S, Harandou M. A Historic case of cardiac surgery in pregnancy. *Case Rep Obstet Gynecol* 2016; 2016: 7518697. doi: 10.1155/2016/7518697.
24. Maturu MV, Devasia T, Rao MS, Kareem H. Native triple valve endocarditis as complication of post-abortal sepsis. *J Clin Diagn Res* 2016; 10: OD08-9. doi: 10.7860/JCDR/2016/20551.8147.
25. Kastelein AW, Oldenburger NY, Van Pampus M, Janszen EMW. Severe endocarditis and open-heart surgery during Pregnancy. *Case Report BMJ*; 2016: bcr2016217510. doi: 10.1136 / bcr-2016-217510.
26. Quinn KL, Osmond M, Badiwala M, Sermer M, Lapinsky SE. Severe *Staphylococcus aureus* endocarditis presenting as peripartum thrombotic thrombocytopenic purpura. *J Obstet Gynaecol Can* 2016; 38: 1028-32. doi: 10.1016/j.jogc.2016.08.008.
27. Khafaga M, Kresoja KP, Urlsberger B, Knez I, Klaritsch P, Lumenta DB, et al. *Staphylococcus lugdunensis* endocarditis in a 35-year-old woman in her 24th week of pregnancy. *Case Rep Obstet Gynecol* 2016; 2016: 7030382. doi: 10.1155/2016/7030382.
28. Birlutiu V, Birlutiu RM. Endocarditis due to *Abiotrophia defectiva*, a biofilm-related infection associated with the presence of fixed braces: A case report. *Medicine (Baltimore)* 2017; 96: e8756. doi: 10.1097/MD.00000000000008756.
29. Sims JR, Bhatia S, Anavekar NS. A 27-year-old pregnant woman with cough and scant hemoptysis. *Mayo Clin Proc* 2018; 93: 772-6. doi: 10.1016/j.mayocp.2017.05.033.
30. Kotaskova I, Nemeš P, Vanerkova M, Malisova B, Tejkalova R, Orban M, et al. First report of *Sneathia sanguinegens* together with *Mycoplasma hominis* in postpartum prosthetic valve infective endocarditis: a case report. *BMC Infect Dis* 2017; 17: 563. doi: 10.1186/s12879-017-2654-8.
31. Polewczyk A, Kurzawski J, Rokita W, Janion M. Large mass on the mitral valve in a woman in the 28th week of pregnancy. *Pol Arch Intern Med* 2017; 127: 633-4. doi: 10.20452/pamw.4109
32. Tamura M, Shoji M, Fujita K, Nakamura S, Takahashi Y, Suzuki Y, et al . Postpartum infective endocarditis with *Enterococcus faecalis* in Japan: a case report. *J Med Case Rep* 2017; 11: 324. doi: 10.1186/s13256-017-1494-x.
33. Luo L, Sun Q, Chen L, Ying D, Wu X, Chen Z. Survival of the fetus during maternal thoracotomy under cardiopulmonary bypass for infective endocarditis. *J Obstet Gynaecol Res* 2017; 43):1634-8. doi: 10.1111/jog.13414.
34. Steele JM, Seabury RW, Hale CM, Mogle BT. Unsuccessful treatment of methicillin-resistant *Staphylococcus aureus* endocarditis with dalbavancin. *J Clin Pharm Ther* 2018; 43: 101-3. doi: 10.1111/jcpt.12580
35. Garg N, Nayyar M, Khouzam RN, Salem SA, Ardeshtna D. Peri-procedural antibiotic prophylaxis in ventricular septal defect: a case study to re-visit guidelines. *Ann Transl Med* 2018; 6: 18. doi: 10.21037/atm.2017.11.11.
36. Vaideeswar P, Shah R. Zygomycotic infective endocarditis in pregnancy. *Cardiovasc Pathol* 2017; 28: 28-30. doi: 10.1016/j.carpath.2017.02.007
37. Piedimonte S, Almohammadi M, Lee TC. Group B *Streptococcus tricuspid* valve endocarditis with subsequent septic embolization to the pulmonary artery: A case report following elective abortion. *Obstet Med* 2018; 11: 39-44. doi: 10.1177/1753495X17714711
38. Tamura T, Yokota S. Mitral valve repair in infective endocarditis during pregnancy. *Ann Card Anaesth* 2018; 21: 189-91. doi: 10.4103/aca.ACA_165_17.
39. Ahres A, Ruboczky G, Somogyi P, Kapin T, Apor A, Ludwig E, et al. Pregnant intravenous drug user tricuspid valve infective endocarditis treated with a successful simultaneous valve replacement and Cesarean section. *Echocardiography* 2018; 35: 1452-5. doi: 10.1111/echo.
40. Wajih Ullah M, Lakhani S, Sham S, Ashraf F, Siddiq W, Siddiqui T. Subacute infective endocarditis of aortic valve during pregnancy. *Cureus* 2018; 10: e2748. doi: 10.7759/cureus.2748.
41. Khan F, Sattar MN, Khan S, Lashari N. Unusual presentation of infective endocarditis during pregnancy: A case report. *J Pak Med Assoc* 2018; 68: 947-9.
42. De Castro A, Abu-Hishmeh M, El Husseini I, Paul L. *Haemophilus parainfluenzae* endocarditis with multiple cerebral emboli in a pregnant woman with coronavirus. *ID Cases* 2019; 18: e00593. doi: 10.1016/j.idcr.2019.e00593.
43. Ramiro VR, Taquiso JL, Obillos SMO, Agustin CF, Magno JDA, Sison EOD. Pulmonary artery and pulmonic valve vegetations in a young pregnant Filipino with patent ductus arteriosus. *Case Rep Cardiol* 2019; 2019: 8268296. doi: 10.1155/2019/8268296.
44. Masuda Z, Miyamoto Y, Une D, Inoue Y, Tateishi A, Yokota Y, et al. Acute mitral valve endocarditis at the 24th gestational week. *Gen Thorac Cardiovasc Surg* 2020; 68: 1457-60. doi: 10.1007/s11748-019-01280-7.

45. Wang J, Wang A, Cui Y, Wang C, Zhang J. Diagnosis and treatment of infective endocarditis in pregnancy: a case report. *J Cardiothorac Surg* 2020; 15: 109. doi: 10.1186/s13019-020-01147-6.

46. Crofton KR, Ye J, Lesho EP. Severe recurrent *Streptobacillus moniliformis* endocarditis in a pregnant woman, and review of the literature. *Antimicrob Resist Infect Control* 2020; 9: 119. doi: 10.1186/s13756-020-00789-4.

47. Sinner GJ, Annabathula R, Viquez K, Alnabelsi TS, Leung SW. Infective endocarditis in pregnancy from 2009 to 2019: the consequences of injection drug use. *Infect Dis (Lond)* 2021; 53: 633-9. doi: 10.1080/23744235.2021.1912821.

48. Patel C, Akhtar H, Gupta S, Harky A. Pregnancy and cardiac interventions: What are the optimal management options? *J Card Surg* 2020; 35: 1589-96. doi: 10.1111/jocs.14637.



Issyk-Kul lake view from the operating room of the SRI of Heart, Surgery and Organ Transplantation Issyk-Kul branch, Kyrgyzstan. By Azat Turgunov, Bishkek, Kyrgyzstan