Pregnancy-related cardiac non-elective hospitalizations and pregnancy outcomes. A tertiary referral cardiac center experience

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ABSTRACT

Background: Pregnant women with cardiovascular diseases (CVD) and their offspring are at higher risk of morbidity and mortality.

Aims: To provide data on pregnancy outcomes among women with different types of CVD requiring non-elective cardiac hospitalization in a tertiary referral cardiac center.

Methods: We identified all records of non-elective hospitalizations of pregnant women hospitalized between January 2009 through March 2018, at our institution — a tertiary referral cardiac center. The incidence and types of cardiac complications during pregnancy, as well as the pregnancy and offspring outcomes, were determined.

Results: One hundred and sixty-one out of 328 pregnancy-related hospitalizations in 140 pregnancies were non-elective. Cardiac complications occurred in 62 (44%) pregnancies, with the most frequent being episodes of arrhythmia (22.1% pregnancies), followed by heart failure exacerbations (6.4% pregnancies). Maternal mortality reached 2.1% and affected only women with primary cardiomyopathies (CMP). Offspring mortality was 2.8%. Newborns of mothers with cardiac complications had significantly lower Apgar scores and gestational age at delivery, compared to mothers without cardiac complications.

Conclusions: In our series mortality and morbidity among pregnant women with CVD hospitalizations were high. An unfavorable maternal outcome mainly affected women with CMP. Offspring of mothers with cardiovascular complications are prone to have a lower gestational age and Apgar score.

Key words: cardiovascular hospitalizations, maternal outcomes, pregnancy

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INTRODUCTION

The number of pregnant women with cardiovascular disease (CVD) has increased in the last 20 years [1]. About 20%–25% of them have cardiovascular complications that may require unplanned hospitalizations [2]. Both these patients and their offspring are at increased risk of morbidity and mortality. The risk of death reaches approximately 1% and is significantly higher than in the general pregnant population [3]. The aim of the study was to analyze outcomes of pregnant women with different forms of CVD requiring non-elective cardiac hospitalizations in a tertiary referral cardiology center, as well as the outcomes of their offspring.

WHAT'S NEW?

Data on cardiac hospitalizations among women with cardiovascular diseases (CVD) is scarce. We present the experience of a single cardiac center concerning non-elective cardiac hospitalizations. The adverse maternal cardiac events rate was high and occurred in 62 (44%) pregnancies. Tachy- and bradyarrhythmias and heart failure were the most common causes of admission. The overall maternal mortality rate in the studied group was 2.1%, which is much higher than the one observed in the normal pregnant population. All maternal deaths occurred in women with cardiomyopathies (2 hypertrophic cardiomyopathies, 1 dilated cardiomyopathy). Mothers with cardiac complications gave births to neonates with significantly lower Apgar scores, as well as a lower gestational age at delivery. This analysis can help physicians in prognostication in pregnant women with CVD.

METHODS

The project was designed as a single-center retrospective registry of all pregnant women hospitalized at the National Institute of Cardiology, a tertiary referral cardiac center. We identified all records of pregnant women hospitalized from January 2009 until March 2018. Hospitalizations were defined as either elective or non-elective. Elective hospitalizations were defined as short-term hospital stays related to routine clinical control of pregnancy. Importantly, in these cases, hospitalizations, rather than outpatient visits, were dictated by administrative reasons and not by the clinical status of the patient. Non-elective hospitalizations were all hospital admissions related to new complaints or worsening of clinical status. Patients were referred by cardiologists providing ambulatory services at our center or elsewhere, general practitioners, gynecologists, and other specialists.

We limited the subsequent analysis to non-elective hospitalizations. Data on outcomes related to labor and delivery, as well as obstetric complications, were obtained from discharge records from the obstetrics and gynecology wards cooperating with our center, or directly from patients themselves (at subsequent visits or during dedicated telephone calls).

Cardiovascular events during non-elective hospitalizations were defined as any of the following: symptomatic both tachy- and bradyarrhythmia requiring treatment; any embolic event; cardiac arrest or cardiac death; decline in New York Heart Association (NYHA) class (≥1 class) compared with the baseline; or the need for an urgent invasive cardiac procedure.

We reported maternal deaths during hospitalization, until delivery, and within the following year. We excluded deaths from external causes. Neonatal events defined as fetal death (≥20 weeks gestation) or neonatal death (within 28 days after birth) were reported. The newborn's physical condition was assessed using its Apgar score. Obstetric events included: pregnancy-induced hypertension, gestational diabetes, preeclampsia/eclampsia. The follow-up was completed for all patients.

The study was approved by the local research ethics board (IK-NPIA-0021-57/1786/2019). For this type of retrospective study formal patient consent was not required.

Statistical analysis

Statistical Analysis System (SAS version 9.4, SAS Institute, Cary, NC, USA) and Statistica v.16 (StatSoft Inc., Tulsa, OK, USA) were used for statistical analyses. Each pregnancy was treated as a separate data unit. The results were expressed as count and percentages for categorical variables and mean (SD) or median and interquartile range (IQR) for continuous variables. The distribution of continuous variables was tested for normality with the Kolmogorov–Smirnov test.

Comparison between pregnancies with cardiovascular complications and those without them were performed using the chi-square test, Student's test, Fisher's exact test, and the nonparametric Mann-Whitney test as appropriate. A 2-sided *P*-value of <0.05 was considered statistically significant.

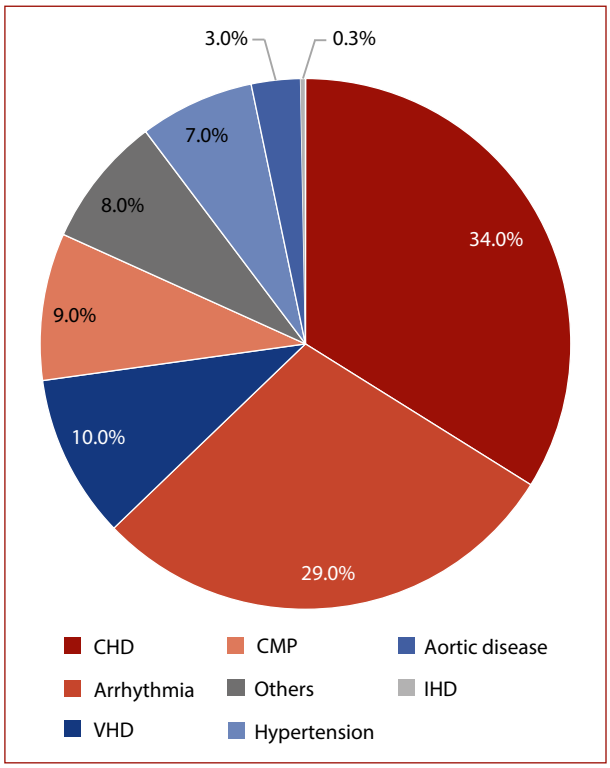
RESULTS

Between January 2009 and March 2018 (111 months), pregnant women were hospitalized in our center on 328 occasions (Figure 1). One hundred and sixty-one of them were non-elective (median 3.3 [range 0–5] pregnancy-related hospitalizations per month including median 1.5 [range 0–3] non-elective admissions per month).

One hundred and sixty-one non-elective hospitalizations occurred in 140 pregnancies (multiparity in 56 [40%] pregnancies, 2nd pregnancy in 32 [22.9%], 3rd pregnancy in 17 [12.1%], 4th pregnancy in 6 [4.3%], and 5th pregnancy in 1 [0.7%]) (Figure 2). Twenty-five pregnancies (17.8%) required more than one hospitalization. One woman was hospitalized 4 times, 7 women were hospitalized 3 times and 9 required 2 hospitalizations. The mean maternal age at hospitalization was 29.7 (5.4) years. The detailed demographic characteristics of non-electively hospitalized pregnant women are presented in Table 1.

Pregnancy-related cardiovascular events during non-elective hospitalizations

The baseline indication for non-elective hospitalizations were as follows: arrhythmia in 53 (33%), CHD in 42 (26%), CMP in 29 (18%), VHD in 14 (9%), primary arterial hypertension in 12 (7%), other (e.g. syncope, pneumothorax, myxoma) in 9 (6%), aortic disease in 1 (0.6%), and IHD in 1 (0.6%).



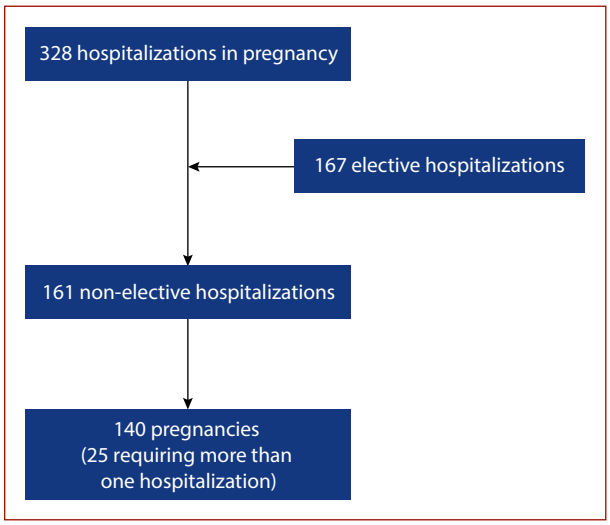


Figure 2. Flowchart of study inclusion

Figure 1. Baseline diagnosis (both elective and non-elective hospitalizations).

Abbreviations: CHD, congenital heart disease; CMP, cardiomyopathy; IHD, ischemic heart disease; VHD, valvular heart disease

Table 1. Characteristics of non-electively hospitalized pregnant women

	All (n = 140)	Without CV complications (n = 78)	With CV complications (n = 62)	*P*-value
Age, mean (SD)	29.7 (5.6)	28.7 (5.4)	30.7 (5.6)	0.83
Nulliparity, n (%)	84 (60)	53 (67.9)	31 (50)	0.06
Multiple pregnancy, n (%)	3 (2.1)	0 (0)	3 (4.8)	0.08
Diagnosis				
Congenital heart disease, n (%)	35 (25)	27 (34.6)	7 (11.2)	0.004
Aortic disease, n (%)	1 (0.7)	1 (1.3)	0 (0)	0.57
Valvular heart disease, n (%)	14 (10)	11 (14.1)	3 (4.8)	0.04
Ischemic heart disease, n (%)	1 (0.7)	1 (1.3)	0 (0)	0.51
Cardiomyopathy, n (%)	20 (14.3)	11 (14.1)	12 (19.3)	0.45
Arrhythmia, n (%)	47 (33.6)	16 (20.5)	31 (50)	0.01
Chronic hypertension, n (%)	14 (10)	8 (10.2)	6 (9.7)	0.52
Others, n (%)	8 (5.7)	4 (5.1)	3 (4.8)	0.48
NYHA class				0.004
I, n (%)	104 (74.3)	58 (74.4)	46 (74.2)	
II, n (%)	29 (20.7)	20 (25.6)	9 (14.5)	
III–IV, n (%)	7 (5)	0 (0)	7 (11.3)	
mWHO class*	n = 124	n = 74	n = 48	0.49
I, n (%)	26 (21)	13 (17.6)	11 (22.3)	
II, n (%)	44 (35.5)	25 (33.8)	19 (39.6)	
II–III, n (%)	10 (8)	8 (10.8)	2 (4.2)	
III, n (%)	39 (31.5)	26 (35.1)	13 (27)	
IV, n (%)	5 (4)	2 (2.7)	3 (6.2)	
Multiple hospitalizations, n (%)	26 (21)	15 (19.2)	11 (17.7)	0.19
Gestational age at first hospitalization (weeks), mean (SD)	19.9 (8.9)	19.9 (8.7)	19.9 (9.5)	0.35
Cardiac medications				
BB, n (%)	65 (46.4)	29 (37.1)	36 (58)	0.01
Anticoagulant, n (%)	18 (12.9)	9 (11.5)	9 (14.5)	0.67
Diuretic, n (%)	6 (4.3)	1 (1.3)	5 (8)	0.08
Other, n (%)	22 (15.7)	8 (10.3)	14 (22.5)	0.06

P-values were calculated between pregnant women without CV complications and with CV complications (independent samples t-test and chi-square test where appropriate).
*We were not able to establish mWHO class among 16 women (e.g. with hypertension before pregnancy or ischemic heart disease, as they are not included in mWHO classification).

Abbreviations: BB, β-blockers; CV, cardiovascular; mWHO, modified World Health Organization; NYHA, New York Heart Association; SD, standard deviation

Table 2. Cases of maternal death

Patient	Age	Diagnosis	Parity	NYHA before pregnancy	Events during pregnancy	Pregnancy duration, weeks	Fetal status	Timing of maternal death	Cause of death
1	30	HCM, MVR, AF parox.	1	1	AF	36	Alive	128 days after delivery	Sudden death
2	38	HCM, AF parox., ICD, HF	4	3	AF, HF	24	Death	24 weeks gestation	Cardiac arrest
3	24	DCM, HF	1	2	HF	38	Alive	87 days after delivery	Cardiogenic shock, ECMO, BIVAD

Abbreviations: AF parox., paroxysmal atrial fibrillation; BIVAD, biventricular assist device; DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenation; HCM, hypertrophic cardiomyopathy; HF, heart failure; ICD, intracardiac cardioverter defibrillator; MVR, mitral valve replacement

Cardiovascular events during non-elective hospital admission occurred in 62 pregnancies (44%), during 73 (46%) non-elective hospitalizations. In the remaining non-elective hospitalizations (88, 55%) either the initial diagnosis was not confirmed (58 admissions) or the hospitalization was uneventful (30 admissions). We did not confirm the diagnosis of suspected arrhythmia requiring treatment during 32 admissions, severe arterial hypertension during 9 admissions, pulmonary embolism during 2 admissions, arrhythmogenic right ventricular cardiomyopathy during 2 admissions, and the cardiovascular reasons of syncope during 13 admissions. The uneventful courses also concerned hospitalizations among women admitted for anticoagulation therapy change (30 admissions). The hospital stay was significantly longer in patients with cardiovascular events (median [IQR]: 4 [2–6] days vs 3 [2–5] days in patients without cardiovascular events; $P = 0.001$).

Adverse maternal cardiac events during pregnancy

Adverse maternal cardiac events occurred in 62 (44%) pregnancies. Maternal cardiac death occurred in 3 pregnancies (2.1%), all in women with CMP (the detailed data about those 3 patients are presented in Table 2. and described at the end of the section). The most frequent cardiac complications during pregnancy were arrhythmias (31, 22.1% pregnancies) and exacerbations of heart failure (9, 6.4% pregnancies). Six pregnancies (5%) were complicated by elevated blood pressure in patients with primary hypertension. Cardiovascular events during pregnancies in subsets of patients with various baseline cardiovascular diagnoses are presented in Figure 3. The following invasive procedures were required in 4 (2.8%) pregnancies: 1 cardiac surgery (cardiac myxoma operated in the 17th week of gestation), 1 radiofrequency ablation without fluoroscopy (in the 18th week of gestation), 1 needle aspiration of pneumothorax (in the 26th week of gestation), and 1 electrical cardioversion of unstable ventricular arrhythmia (in the 23rd week of gestation) were performed. The course of invasive procedures and late follow-up was uneventful.

Obstetric and fetal/neonatal outcome

The median gestational age of live births was 37.5 weeks (range: 30–40) and was significantly lower in pregnancies with cardiac complications, compared to non-complicated pregnancies (median [range] 33.5 [30–37.5] vs 39 [38–40]; $P < 0.001$). A total of 14 pregnancies (10%) were complicated by obstetric events. Pregnancy-induced hypertension occurred in 5 pregnancies (3.8%), gestational diabetes in 4 (2.9%), preeclampsia or eclampsia in 2 (1.5%), asphyxia in 2 (1.5%), and uterine rupture in 1 (0.7%). All complications were observed among women with cardiovascular complications during hospitalization, except for gestational diabetes present in women without cardiac complications.

Overall fetal/neonatal mortality reached 2.8%, and there was no difference between groups with or without cardiac problems. The Apgar score and the gestational age at delivery were significantly lower in neonates of mothers with cardiac complications, compared to mothers without complications (mean [SD] 8.5 [1.7] vs 9.98 [0.4]; $P = 0.001$ and median [range] 33.5 [30–37.5] vs 39 [38–40]; $P < 0.001$, respectively).

All women who underwent interventional procedures during pregnancy gave birth to healthy full-term children.

Cases of maternal death

Case 1 was a 30-year-old gravida 3, para 1 (G3, P1, 2 miscarriages) woman with obstructive HCM and paroxysmal atrial fibrillation (AF). Before the diagnosis of AF was established, she had suffered from a stroke, but without any significant disability. Ten years before pregnancy she underwent mitral valve replacement (mechanical) and septal myectomy. She was hospitalized twice during pregnancy, at 12 and 32 weeks of gestation. Her pregnancy was complicated by episodes of AF. Therefore, she was treated with beta-blockers and LMWH, under control of anti-Xa levels. No signs of heart failure were present during pregnancy. She delivered a healthy child by cesarean section (CS) at 36 weeks. She died at home suddenly 128 days after delivery. An autopsy was not performed.

Case 2 was a 38-year-old G4, P2 (first delivery by CS at 34 weeks) with HCM. Her past medical history included HF and intracardiac cardioverter-defibrillator implantation (ICD) for primary prevention. Her pregnancy was complicated by a threatened preterm delivery. She was admitted in the 17th week of gestation with new-onset AF (of unknown duration) and signs of severe HF (NYHA class III) causing several inappropriate ICD interventions. She received warfarin

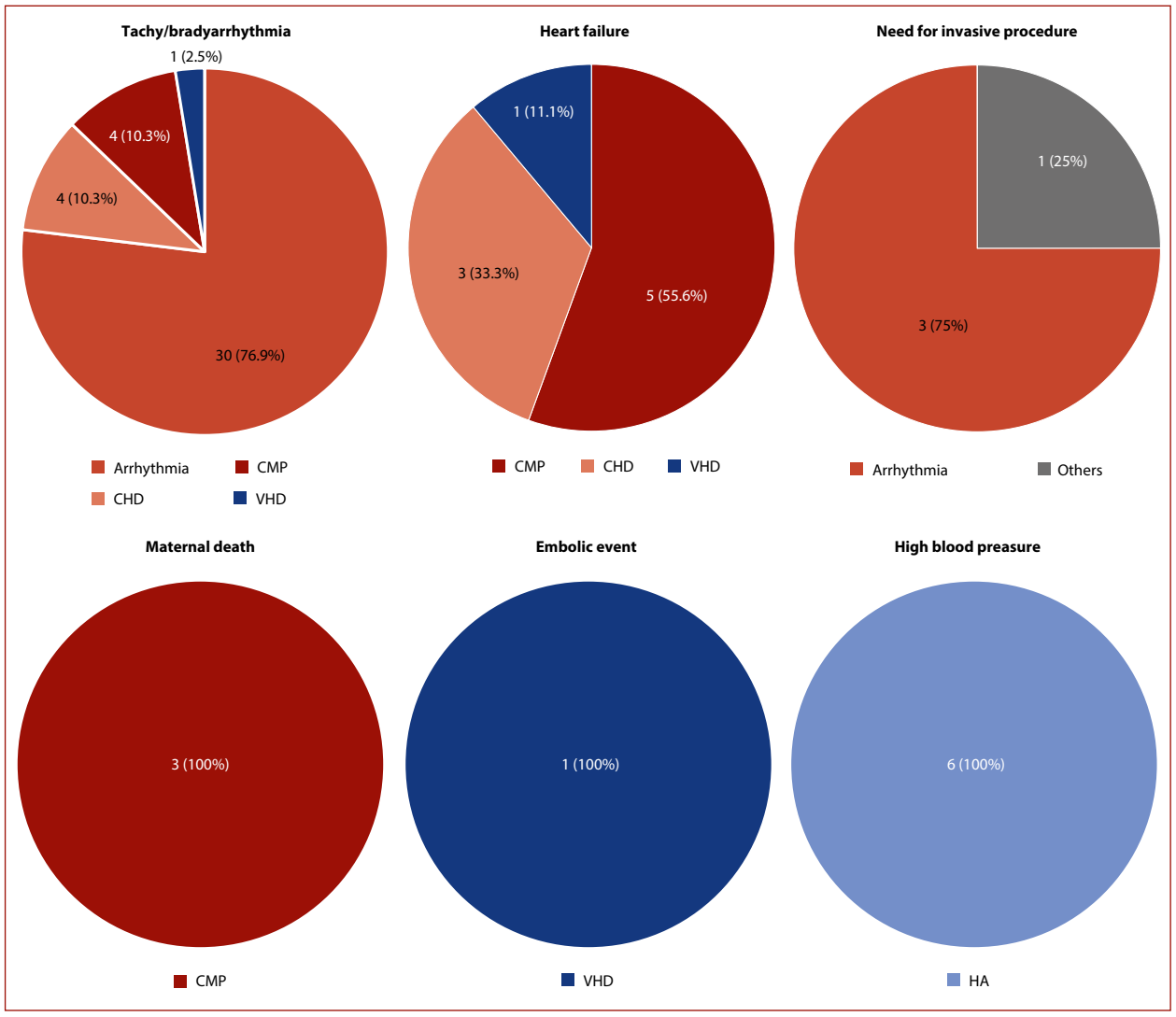


Figure 3. Maternal cardiovascular complications according to the baseline cardiovascular diagnosis in 140 pregnancies
Abbreviations: CHD, congenital heart disease; CMP, cardiomyopathy; HA, arterial hypertension; VHD, valvular heart disease

and diuretic treatment and her beta-blocker were titrated up. She was sent to the obstetric department in a stable condition. She died suddenly there at the 24th week of gestation. Her fetus died in utero. An autopsy was not performed.

Case 3 was a 24-year-old G1, P1 woman with DCM (diagnosis established in the second year of life). Before pregnancy, she was in NYHA class II, with a significantly reduced left ventricular ejection fraction (LVEF) of 35%. She was hospitalized once during pregnancy at 20 weeks of gestation to modify medical treatment, as she reported deterioration of heart failure symptoms. Echocardiographic examination revealed at least moderate mitral regurgitation. Left ventricular size and function remained stable, compared to those before pregnancy. The second time she was admitted 17 days after delivery (38 weeks of gestation, CS) with signs of severe heart failure (NYHA class IV) and a decrease of LVEF to 25%–30%. Deterioration of the clinical status required extracorporeal membrane oxygenation (ECMO) implantation, but as she developed pulmonary edema a biventricular assist device (BIVAD) was subsequently implanted. She had a cardiac arrest (pulseless electrical activity) on the 70th day after BIVAD implantation. An autopsy was not performed.

Table 2 summarizes the details of the pregnancies complicated by cardiac death.

DISCUSSION

This is an analysis of cardiovascular hospitalizations, maternal and fetal outcomes from the tertiary cardiovascular center with experience in cardiovascular care for pregnant women [4–7]. An average of 1.5 non-elective admissions of pregnant women per month translates into approximately one admission per two- to three weeks in a busy tertiary referral cardiac center, with a total number of over 13 000 hospitalizations per year.

The overall maternal cardiovascular event rate in our study was high (44%) compared to published studies, which estimated their occurrence at about 5%–15% [8–10].

This may have been due to differences in the studied populations (out-patient, hospital, both), clinical characteristics — such as types and severity of heart disease, maternal cardiac function, and the definition of cardiovascular complications.

We analyzed cases requiring non-elective hospitalization, therefore, in principle, at a greater cardiovascular risk. The frequency of cardiovascular events significantly increases with the higher modified WHO class from 4.2% in class I to 56.4% in class IV [11]. In our series, more than one-third of women were in the modified WHO class III and IV. Our results are consistent with previously published data indicating arrhythmia and heart failure as the leading cardiac complications in pregnant women with cardiovascular disease [12]. Arrhythmia was the most frequent cardiac complication found in 22.1% of pregnancies, which is much higher than approximately 10% reported by others [10, 12]. One of the potential explanations is that our center serves as an arrhythmia referral center with a special interest in the management of arrhythmia in pregnancy [13]. The second most common cardiac entity was heart failure affecting 6.4% of pregnancies. This agrees with 6.2% reported by the CAPREG investigators [12]. The overall maternal mortality rate in our study was 2.1%, which is much higher than the one observed in the normal pregnant population, and at least three times higher than reported by other researchers in women with cardiovascular diseases [3]. High mortality may be explained by the selection of non-elective hospitalizations for analysis and high proportion of high-risk women (35.5% in mWHO class III or IV). It should be emphasized that in our series one woman also had a mechanical heart valve in the mitral position and the second experienced HF in NYHA class III before pregnancy, both being important risk factors of an adverse maternal outcome.

The mean gestational age at first hospitalization was approx. 20 weeks. According to CARPREG II study, most arrhythmias occur between the 13th and the 27th week, and arrhythmia was the leading cardiac complication in our series [12].

All maternal deaths occurred in women with cardiomyopathies, which agrees with the data from other series, as well as with the current ESC guidelines that advise against pregnancy if the systemic ventricular EF is <30% [14, 15]. Data from the ROPAC registry suggest that all patients with dilated CMP, even with preserved EF, are high risk and should be counseled accordingly. In our series, two women who died had HCM. Data from ROPAC suggest that pregnant women with HCM are at lower risk than women with idiopathic pulmonary arterial hypertension or other cardiomyopathies. However, in ROPAC, major adverse cardiovascular events (MACE) defined as death, heart failure, arrhythmia, or thromboembolic events occurred in ~23% of reported pregnancies [16].

Invasive procedures are rarely performed in pregnancy. In our group, the need for any intervention was 2.8%, which is high compared to the rates reported by other authors. According to the CAPREG study, urgent cardiac interventions were required in 0.7% of pregnant women with CV disease (9 of 1315) and consisted mostly of surgical procedures (cardiac valve surgery, valvuloplasty, surgical resection of an intracardiac tumor, closure of a large secundum atrial septal defect, aortic root replacement) [17]. Cardiac tumors are the most challenging diagnoses during pregnancy requiring the most difficult therapeutic decisions [18]. Few case reports and small series of patients are available on cardiac ablation in pregnant patients, especially on the completely fluoroscopy-free procedure and cardioversion. However, based on experience from our institution and literature, with proper training, it may be considered in pregnant patients with arrhythmias refractory to medical treatment as a procedure of safety profile similar to the one reported in the nonpregnant population [19, 20]. The rate of neonatal complications is significantly increased in women with heart disease. Siu et al., in their prospective longitudinal study of pregnancy outcomes in women with heart disease, reported neonatal death in 3% of pregnancies, which is in line with our results and much higher than the 0.3% risk observed in the general population [13]. Reports comparing data in pregnant women with heart disease indicate a significantly increased rate of preterm delivery [21]. In our series, low gestational age at delivery was present only in pregnancies with cardiac complications. We also found significantly lower Apgar score among neonates of women with cardiac complications. Gestational age is one of the most important factors affecting the Apgar score. Population-based data from Sweden demonstrated that Apgar scores in range of 7–9, compared with an Apgar score of 10, were strongly associated with neonatal mortality and morbidity [22].

In 58 of 161 hospitalizations initial diagnoses of either suspected arrhythmia (in 32 cases) or cardiac syncope (in 13 cases), leading to non-elective hospitalizations, were not confirmed. The symptoms resembling palpitations and syncope in pregnant women are frequent and most arrhythmias that occur during pregnancy are benign. The advice on how to appropriately behave together with reassurance is usually sufficient [23]. The increased rate of syncope in pregnancy may be explained by physiological changes occurring during pregnancy. It may also be attributable in part to pregnant women being more likely to seek medical advice for syncope during pregnancy [24]. Physicians may be increasingly alert to these symptoms in pregnant women with cardiovascular disorders, leading to increased referrals.

Our analysis had several limitations that must be kept in mind while translating our data into the general experience of care for pregnant women with cardiovascular diseases. These are the retrospective design of the study focused on non-elective hospitalizations, as well as a selection bias related to the referral level of our center. The prospective registry of all pregnant women, also including those requiring only outpatient counselling, would be more representative.

CONCLUSIONS

This is a comprehensive analysis of non-elective hospitalizations for cardiovascular reasons among pregnant women. The latter were not infrequent and occurred every two to three weeks in a busy tertiary referral center. Most of them concerned women with congenital heart disease, arrhythmia, and valvular heart disease. Mortality and morbidity among non-electively hospitalized pregnant women were high and patients with CMP were at a particularly high risk of death. Offspring of mothers with cardiovascular complications had a lower gestational age and Apgar score.

Article information

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