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Case Report

Lessons Learned From Three Patients Who Underwent Cesarean Section and Cardiac Valvular Surgery Simultaneously: Anesthesiologists' Perspective

Eş Zamanlı Sezaryen ve Kalp Kapak Ameliyatı Geçiren Üç Hastadan Öğrenilen Dersler: Anestezistlerin Bakış Açısı

Alpin Tamay Finci ¹ , Nevin Aydın ^{2*}

¹ Department of Anaesthesiology and Reanimation, Sait Ertürk Etimesgut Public Hospital, Ankara, Türkiye ² Department of Anaesthesiology and Reanimation, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye

Abstract

Background: Cardiac valvular disease constitutes a challenge during pregnancy. Herein, we present our experience with three patients who underwent caesarean section and cardiac valvular surgery simultaneously. The purpose of this case series was to outline the clinical characteristics and to highlight the surgical/anesthesiologic pitfalls to be considered in patients who will undergo cardiac valvular surgery and caesarean section simultaneously.

Methods: This retrospective case series was implemented using data extracted from the medical files of three patients who underwent cardiac valvular surgery and caesarean section in the obstetrics and gynecology and cardiovascular surgery departments of our tertiary care center. Demographic data, history, echocardiographic findings, surgical and anesthesiologic techniques as well as perioperative information and therapeutic outcomes were recorded.

Results: Three pregnant women with an average age of 33.67 years were diagnosed with various cardiac valvular pathologies on the 3rd trimester. Owing to their diminished cardiac reserves and clear indications for cesarean section, the patients underwent cardiac valvular surgery subsequent to the cesarean section. Procedures were completed successfully on all patients and mothers and infants were discharged after a maternal follow-up in intensive care unit.

Conclusion: We suggest that cardiac valve surgery can be performed simultaneously just after cesarean section in selected cases. Risks and benefits must be analyzed well prior to the decision making for the absolute necessity of the invasive procedure. Close collaboration between disciplines, well equipped referral centers, trained personnel and increased awareness on possible complications are the key points for successful surgical management of pregnant women with cardiac valve disease.

Keywords: Cardiac valvular disease; surgery; pregnancy; cesarean section; anesthesia

Corresponding author *: Department of Anaesthesiology and Reanimation, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye. Email: nevinaydin4334@gmail.com ORCID: 0000-0003-0189-5865 DOI: 10.46969/EZH.1377297 Received: 19.10.2023 Accepted: 16.02.2024

Öz

Amaç: Kalp kapak hastalıkları gebelik sırasında önemli bir sorundur. Burada eş zamanlı olarak sezaryen ve kalp kapağı ameliyatı geçiren üç hastayla ilgili deneyimimizi sunuyoruz. Bu vaka serisinin amacı, eş zamanlı olarak kalp kapağı cerrahisi ve sezaryen operasyonu geçirecek hastalarda klinik özelliklerin ana hatlarını çizmek ve dikkate alınması gereken cerrahi/ anesteziyolojik durumları vurgulamaktı.

Yöntem: Bu retrospektif vaka serisi, üçüncü basamak merkezimizin kadın hastalıkları ve doğum ve kalp damar cerrahisi bölümlerinde kalp kapak cerrahisi ve sezaryen operasyonu geçiren üç hastanın tıbbi dosyalarından elde edilen veriler kullanılarak uygulandı. Demografik veriler, öykü, ekokardiyografik bulgular, cerrahi ve anestezi teknikleri ile perioperatif bilgiler ve tedavi sonuçları kaydedildi.

Bulgular: Yaş ortalaması 33,67 olan üç gebeye 3. trimesterde çeşitli kalp kapak patolojileri tanısı konuldu. Kalp rezervlerinin azalması ve sezaryen endikasyonunun net olması nedeniyle hastalara sezaryen sonrası kalp kapağı ameliyatı uygulandı. Tüm hastaların işlemleri başarıyla tamamlandı ve anne ile bebekleri yoğun bakımda takibinin ardından taburcu edildi.

Sonuç: Seçilmiş olgularda sezaryen sonrası eş zamanlı olarak kalp kapak cerrahisinin yapılabileceğini düşünüyoruz. İnvaziv işlemin mutlak gerekliliği için karar vermeden önce riskler ve faydalar iyi analiz edilmelidir. Disiplinler arası yakın işbirliği, iyi donanımlı sevk merkezleri, eğitimli personel ve olası komplikasyonlar konusunda artan farkındalık, kalp kapak hastalığı olan hamile kadınların başarılı cerrahi tedavisinin kilit noktalarıdır.

Anahtar Kelimeler: Kalp kapak hastalığı; ameliyat; gebelik; sezaryen; anestezi

1. Introduction

Valvular heart disease not only represents a significant cause of cardiac disease in pregnancy, but it also poses a critical challenge to the anesthesiologist during labor and delivery. A good understanding of the pathophysiology, in conjunction with the remarkable physiologic changes associated with pregnancy, is critical for management of these patients. Therapeutic aims involve preservation of the hemodynamic and ventilatory parameters within an acceptable boundary and proper conduction of labor and postpartum period (1).

The prevalence of cardiac disease in pregnancy varies between 0.4 to 4.1% (2-4). In the developed world, congenital heart disease has become the major cause of cardiac disease; while rheumatic heart disease appears as the major cause of cardiac disease in pregnancy in developing countries (5). Counseling of women with cardiac pathologies should be performed before conception and may include a detailed history, and evaluation for invasive procedures better performed during non-pregnant state to avoid potential fetal risks. Patients with surgically correctable lesions are advised to undergo repair before pregnancy to improve maternal and fetal outcomes (1,6).

The main physiological challenges during pregnancy have anesthetic implications for pregnant women with cardiac diseases. These challenges include an increase in intravascular volume, decrease in systemic vascular resistance, fluctuations in cardiac output, hypercoagulability and diminished functional residual capacity (1). The most frequent causes of maternal death, including embolism and hemorrhage, have remained stable, but maternal mortality due to cardiac causes has increased (1). Additionally, women with cardiovascular diseases are more likely to experience abortion and give birth to children who are small for gestational age (6). Earlier cardiovascular events or arrhythmias, advanced heart failure, cyanosis and ejection fraction < 40% are predictors for cardiovascular hazards in these patients (7).

Due to the possibility of serious complications from pregnancy and cardiac disease, these patients should undergo a detailed history and a meticulous examination. Referral to higher centers with adequate monitoring facilities and well-trained personnel for peripartum and perinatal care is crucial. Close monitoring is necessary for both the mother and fetus throughout the peripartum period. The anesthesiology team should aim to avoid a decrease in systemic vascular resistance and prevent hypoxia, hypercapnia and acidosis (1).

It is clear that pregnant women with valvular disease need specialized care. Management during pregnancy involves replacement of any contraindicated medications with safer alternatives, optimization of loading conditions, careful monitoring and aggressive treatment of any exacerbating factors. In some circumstances, surgical intervention may be necessary during pregnancy. Labor a and delivery mostly require invasive hemodynamic monitoring and a multi-disciplinary approach to achieve optimal maternal and fetal outcomes (8).

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Regurgitant valve disease carries a lower risk for poor maternal and fetal outcomes than stenotic lesions. Maternal risk is dependent on the severity of the regurgitation symptoms and left ventricular function. Patients with severe disease and symptoms, or impaired left ventricular function should be advised to have surgery prior to pregnancy. During pregnancy, close follow up on a monthly basis is recommended. Medical therapy is usually sufficient to manage symptoms of fluid overload (9).

In general, vaginal delivery is the preferred method, and in symptomatic patients, epidural anesthesia and a shortened second stage is advisable. Most patients with simple congenital heart lesions tolerate pregnancy well (9). Nevertheless, for patients with complex lesions and diminished cardiac reserve, cesarean section and cardiac valvular surgery may be an alternative. For these cases, decision making should be based on assessment of efficacy and safety.

Herein, we present our experience with 3 patients who underwent cesarean section and cardiac valvular surgery simultaneously. Summarization of the principles and establishment of a practical approach for evaluation of risks in pregnant women with cardiac valvular diseases are performed. Hopefully, this case series will contribute to the follow-up and management of pregnant women with valvular heart disease and aid in selection of patients who are appropriate for cardiac valvular surgery together with cesarean section. Thereby, avoidance or minimization of complications, morbidity and mortality can be possible.

This retrospective case series was implemented using data extracted from the medical files of 3 patients who underwent cardiac valvular surgery and cesarean section in the obstetrics and gynecology and cardiovascular surgery departments of our tertiary care center. Demographic data, history, echocardiographic findings, surgical and anesthesiologic techniques as well as perioperative information and therapeutic outcomes were recorded. Approval of the institutional review board had been obtained before the study.

2. Case Presentations

All patients underwent elective conditions.

Case 1

A 39-year-old pregnant woman with a body-mass index (BMI) of 25.46 had advanced mitral stenosis and mitral insufficiency in addition to a moderate degree of tricuspid insufficiency. The

patient, whose gravity was 1 and parity 0, was 30 weeks pregnant. The patient had previously experienced a cerebrovascular event and had undergone a prosthetic aortic valve operation 4 years ago. Her complaint related to her illness was shortness of breath while lying down at night. She had been diagnosed with asthma previously and her ejection fraction (EF) was 65%. In the preoperative evaluation of the patient, the ASA score was 3. An echocardiograph performed prior to the operation revealed a mitral valvular area of 1.2 cm2, a maximum/mean gradient of 34/15 mmHg and a systolic pulmonary artery pressure of 50 mmHg. After cesarean section, the patient underwent mitral and tricuspid valvular replacements (DeVega annuloplasty). A no.29 prosthetic valve was used for replacement of the mitral valve. The total duration of operation was 4 hours. Catheterization was performed to monitor central venous pressure. Total dose of oxytocin administered prior to onset of pump was 30 U. Dobutamine DBL (Dobutamine HCL 250 mg 20 ml, Orna A.S , Turkey) was administered at a dose of 3 µg/kg/ minute for inotropic support at the end of pump. Cardioplegia was performed once during surgery using 20 cc KCl and 10 cc Mg. The patient's postoperative transthoracic echocardiography showed mild insufficiency flow in the tricuspid valve, high gradient prosthetic aortic valve (made 4 years ago), patent foramen ovale, mild mitral regurgitation , normally functioning metallic MVR, mild aortic regurgitation, and dilatation in the left atrium were observed. After staying on mechanical ventilation for 1 day, intensive care treatment continued for 6 days and she was discharged on the 14th day. Both the mother and the infant survived on 1st year postperatively.

Case 2

A 40-year-old pregnant with a BMI of 27.55 was diagnosed with aortic aneurysm and aortic insufficiency. The patient , with a gravity of 5 and parity of 4, was 36 weeks pregnant.She had been diagnosed with aortic aneurysm 1 year ago, complained of chest pain. The ASA score was 3. Echocardiography demonstrated aortic insufficiency and dilatation of aortic root and ascending aorta. Systolic pulmonary artery pressure was 214 mmHg. Following cesarean section, repair of ascending and transverse aorta with graft and aortic valve replacement were performed. The total duration of operation was 4 hours and cardioplegia was performed once during surgery. No inotropic agents were administered postoperatively but fibrinogen was applied .In the postoperative transthoracic echocardiography evaluation, pleura and pericardium were normal, an appearance compatible with non-obstructive pannus in the subvalvular area, normal left ventricularsystolic function, normofunctional AVR, high gradient aortic prosthetic valve, mild tricuspid and mitral regurgitation was detected. The patient's mechanical ventilation duration was 1 day, intensive care treatment duration was 3 days, and hospital stay was 9 days. The patient and the infant are alive and free of any complications 1 year following surgery.

Case 3

A 22-year-old pregnant woman with a BMI of 22.05 was diagnosed with mitral insufficiency, mitral stenosis, aortic insufficiency and tricuspid insufficiency. The patient with a gravidity of 1 and parity of 0 was 34 weeks pregnant. She had chronic atrial fibrillation was being followed up by the cardiology department. The patient did not mention any specific complaints. The ASA score was 4. Echocardiography was consistent with previously repaired mitral and aortic valves as well as aortic and tricuspid insufficiencies. The ejection fraction and systolic pressure of pulmonary artery were 60% and 60 mmHg, respectively. After cesarean section, replacement of mitral valve (no.29) and tricuspid valve (no.35) together with repair of aortic valve were performed .Dopamin Fresenius (Dopamin HCL,200 mg 5 ml, Fresenius Kabi, Austria) was introduced at a dose of 3 µg/kg/minute for inotropic support postperatively. After transfer to ICU, the mother and the neonate were discharged without any complications. In the patient's postoperative transthoracic echocardiography normofunctional prosthetic mitral valve, trace aortic valve insufficiency, normofunctional tricuspid ring plasty were detected. The patient was discharged in 7 days after 1 day of mechanical ventilation support and 3 days of intensive care treatment. They both are alive on the 2nd year after operation.

When the patients were brought to the operating table, priorly using 16-18G angiocath vascular access was opened priorly from the right, and left extremities, Isolyte S(PH 7.4, Eczacıbaşı-Baxter Turkey) was infused through one, and Gelofusine (gelatin, Braun, Germany) through the veins of the other extremity. Then 0.5 cc 2% Jetmonal (20 mg 10 ml, Adeka A.S, Turkey) was injected using a dental needle on the radial region, and arterial cannula was inserted under sterile conditions. After arterial monitorization, , the induction phase was performed. Induction doses of Pental (0.5 gr, Thiopental Sodium, Menarini A.S,Turkey) 3 mg/kg, Ketalar (Ketamin HCL, 500mg, Pfizer,USA) 0.5 mg/kg, Esmeron (Rocuronium Bromur, 100mg 10 ml Organon, Holland) 0.5 mg/kg were applied, and 3 minutes later, the patient was intubated.

Before cesarean section, an external pacemaker was subcutaneously implanted on the dorsal aspect of the thorax (Possible deterioration of EF towards the end of the pregnancy was detected, and anesthesiologist was warned that the pregnant patient whose 3 cardiac valves would be changed may suffer from cardiac arrest). Before proceeding with surgery transurethral catheterization was performed simultaneously with CVP catheter insertion. Disinfectant solutions were applied both to the chest, and surgical field of cesarean section, and covered with sterile drape. Priorly C-S was performed. After delivery of the baby, Sojourn(Sevofluran %100 250 ml ,Adeka A.S , Turkey) 2% and 2/2 oxygen-air mixture were delivered. All inotropic agents were kept ready. After delivery, 30 U of oxytocin Synpitan fort (oxytocin, 5 IU/mL, Deva A.S, Istanbul, Turkey) was added into Isolyte S which is used as a maintenance fluid. After delivery, until the end of the section (within 15-20 minutes) 50 µg /kg fentanyl was injected. Then, cardiac surgery was proceeded with.

During sternotomy, a combination of Demizolam (Midazolam, 15 mg 3 ml, Dem A.S, Turkey) 2 mg, Talinat (Fentanyl, 0.1 mg 2 ml ,Vem A.S ,Turkey) 100 μ g and Blok-L(Vecuronium ,10 mg, Gensenta A.S,Turkey) 2 mg was injected. At every half an hour, the same drugs were administered, and anesthesia was maintained. Nevparin (Heparin Sodium, 25000 IU ,Gentansa A.S , Turkey) was administered at a dose of 300-400 U/kg. Protamine ICN (Protamine HCL, 5000 IU 5 ml , Meda Pharma A.S, Turkey) dose was given as 1.2 times higher than the heparin dose. Off-pump patients with a normal creatinine level received Transamine (Tranexamic acid 250 mg, Actavis, Ireland) at a dose of 15mg/kg. Generally, a single session of blood cardioplegia was used intraoperatively.

The patient without aortic insufficiency received KCI, and Mg at doses of 3 mg/kg, and 1.5 mg/kg, while patients with aortic insufficiency were given KCI, and Mg at doses of 4mg/kg, and 2 mg/kg, respectively. The dose of cardioplegia solution was 10 mg/kg. Blood was used as cardioplegia solution. After the surgery the patients were intubated, and transported into ICU. An overview of baseline descriptive data, clinical data and hematologic parameters are presented in In Table 1, age, bodymass index, gestational weeks, diagnosis for valvular heart disease, type of operation performed, ejection fraction, doses of heparin and protamine administered, agents administered for induction and maintenance of general anesthesia, amount of intravenous fluids introduced and inotropic agents given are demonstrated. Preoperative and postoperative laboratory findings are shown in Table 2.

Table 1. An overview of baseline descriptives, clinical and perioperative data in our series							
	Patient 1	Patient 2	Patient 3				
Age (years)	39	40	22				
BMI (kg/m²)	25.46	27.55	22.03				
ASA Score	3	3	4				
Diagnosis	MS, MI, TI	AA, AI	MI, MS, AI, TI				
Gestasyonel Age (Weeks)	30	36	34				
Operation	CS, MVR, TVR (DE VEGA ANNULOPIASTY)	CS, AVR, AARG	CS, MVR, TVR, AVRp				
EF %	65	65	60				
Transfusion	5 U ES	3 U ES, 2 U FFP	2 U ES , 1 U FFP				
Heparin Dose (U)	25000	25000	35000				
ACT (Seconds) Before Pump	119	138	114				
ACT (Seconds) After Pump	490	100	148				
Induction of Anesthesia	Ketamine, Thiopental, Rocuronium	Ketamine, Thiopental, Rocuronium	Ketamine, Thiopental, Rocuronium				
Maintenance of Anesthesia	Sevoflurane, Fentanyl, Midazolam, Vecuronium	Sevoflurane, Fentanyl, Midazolam, Vecuronium	Sevoflurane, Fentanyl, Midazolam, Vecuronium				
Protamin (U)	45000	30000	35000				
IV Fluids (CC)	1500	1700	2200				
Urine Output (CC)	1100	300	1800				
P/O Drug	-	Fibrinogene	-				
Survival	Yes	Yes	Yes				

BMI: body-mass index; ASA: American Society of Anaesthesiologists; CS: cesarean section; AA: aortic aneurysm; AI: aortic insufficiency; MS: mitral stenosis; MI: mitral insufficiency; TI: tricuspid insufficiency; MVR: mitral valve replacement; TVR: tricuspid valve replacement; AVR: aortic valve replacement; AVRp: aortic valve repair; AARG: ascending aorta repair with graft; EF: ejection fraction; ACT: activated clotting time; IV: intravenous; PO: postoperative; U: units; ES: erythrocyte suspension; FFP: fresh frozen plasma

3. Discussion

The timing and mode of delivery should be determined by a team consistent of the obstetrician, cardiologist, and obstetric anesthesiologist. Even though vaginal delivery with appropriate anesthesia and shortening of the second stage is safer and is the choice in the majority of patients, cesarean section is reserved for obstetric indications and in the occasional patient with cardiac instability (10). Hemodynamic monitoring during labor and delivery must be performed in symptomatic patients and in cases with moderate/severe valvular stenosis, left ventricular dysfunction, and pulmonary hypertension (10,11).

Cardiac disease remains a noteworthy problem for both the obstetric care team and anesthesiologist. In spite of advances in medical technology and healthcare, there is still a substantial burden in terms of morbidity and mortality attributed to cardiac problems during pregnancy. The obstetric anesthesiologist may play an important role in the care of these patients and contribute significantly to the reduction of potential risks for both the mother and fetus. Efficient of relief of pain, prevention of pulmonary hypertension, hypoxia and myocardial depression are among the tasks to be fulfilled during administration of anesthesia in pregnant women. Furthermore, cesarean section and cardiac valvular surgery may be performed in selected patients with obstetric indications for cesarean section and with severe cardiac insufficiency (12).

Hopefully, our preliminary data extracted from this case series may be useful for determination of patients who are appropriate for cesarean section and cardiac valvular surgery simultaneously. In these procedures, the anesthesiologist will

Table 2. Preoperative and postoperative laboratory finding						
	Preoperative			Postoperative		
	Patient 1	Patient 2	Patient 3	Patient 1	Patient 2	Patient 3
WBC (x10³/µL)	9.17	7.64	12.4	6.96	12.16	16.9
Hemoglobin (gr/dL)	11	11.8	10.1	9.1	9	9.2
PLT (10 ³ /mm ³)	125	192	184	335.7	104	145.6
Glucose (mg/dL)	90	102	178	86	132	134
Na (mmol/L)	130	131	134	142	140	134
K (mmol/L)	4.1	4.8	4.6	4.7	4.3	3.8
AST (U/L)	17	22	15	14	40	16
ALT (U/L)	14	31	7	16	27	12
Fibrinogen (mg/dL)	343	337	332	271	310	321
Lactate (mmol/L)	0.90	1.36	2.39	1.57	2.31	2.33
CRP (mg/dL)	3.42	2.21	4.84	64	108.7	226
APTT (s)	25	27.7	29.1	37.7	31.5	33.4
PT (s)	11.7	11	12.8	22.1	12.4	14.3
INR	0.88	0.82	0.97	1.87	0.95	0.86
Urea (mg/dL)	14	16	14.2	17	22	26
Creatinine (mg/dL)	0.37	0.61	0.34	0.47	0.66	0.4

need to overcome hemodynamic problems attributed to both pregnancy and prosthesis. A careful anticoagulant regimen will be essential to decrease the risk of thromboembolism. Moreover, congestive heart failure, pericarditis, myocarditis, upper respiratory tract infection and anemia may occur after cesarean section and valvular surgery. The anesthetic management must be in harmony with the cardiovascular therapy of the patient.

Maintenance of hemodynamic parameters in conjunction with balance of maternal and fetal needs is the key point during simultaneous performance of cesarean section and cardiac valvular surgery. An understanding of obstetric cardiovascular pharmacology and physiology is crucial for selection of the suitable anesthetic method. Cardiac failure may occur at any time during pregnancy, but it is more commonly encountered in the third trimester. Ideally, induction of general anesthesia must keep the patient's heart rate and blood pressure within previously established limits. The onset of surgical stimulation may overcome the decrease in systemic vascular resistance and diminish the need for medical support (13). In pregnant women with valvular heart disease, the key points to achieve favorable pregnancy outcomes are accurate diagnosis for severity of valvular disease, pre-conception evaluation and counselling, and referral of the women with highest risk to centers with expertise in the management of these patients. Valvular disease must be classified with respect to its hemodynamic effects and the involvement of the valve. Normal hemodynamic changes of pregnancy can deteriorate cardiac symptoms in previously stable women or may exacerbate symptoms in those who had symptoms before pregnancy (8,14). Preconceptual planning should include counselling each woman about the risks of pregnancy, optimization of the cardiac condition, and establishment of careful monitoring and treatment. Some women are diagnosed for the first time with valvular disease due to hemodynamic decompensation during pregnancy. On the other hand, some cases with valvular disease may present for medical evaluation only after pregnancy. It is obvious that the evaluation and treatment of these patients constitute a challenge in terms of obstetric, cardiovascular and anesthetic aspects (8,15).

Hemodynamic changes during pregnancy and labour bring about a considerable demand on cardiac function in a patient with valvular disease. This change necessitates invasive hemodynamic monitoring and aggressive medical treatment in the peripartum period. If a delivery is complicated by excessive blood loss, infection, or arrhythmia, these demands will be further amplified (8).

We suggest that owing to the greater hemodynamic changes and more significant blood loss, cesarean section should be reserved for obstetric indications. Availability of intensive care unit for both the mother and the fetus and increased alertness in the occurrence of any complications are other critical issues to be remembered. Patients should be closely monitored in terms of inotropic support and adjustment of activated clotting time.

Patients with symptomatic, severe left-sided valvular obstruction are vulnerable to cardiovascular events during pregnancy (14). Invasive procedures are generally preferred if medical management fails. Thus, the second trimester may be the optimal time for surgical intervention since organogenesis is finished and the cardiac positioning is not influenced by the gravid uterus. The type of valvular disease is another important aspect fo the formulation of delivery plan and determination of the therapeutic strategy for valvular disease. Regurgitant lesions and right sided lesions are usually more tolerable in pregnancy due to the placenta-related decrease in systemic vascular resistance which alleviates the hazardous effects of increased plasma volume. Invasive monitoring with an arterial pressure line may be helpful in patients where sudden blood pressure changes may have significant hemodynamic consequences. Postpartum hemodynamic shifts associated with blood loss and placental venous return can be deleterious in the first few days postpartum and are the period with the highest risk of congestive heart failure and arrhythmia. Specifically, patients with regurgitant lesions may need diuresis or afterload reducers during this period. Right-sided heart valvular lesions are usually well tolerated in pregnancy. Symptomatic individuals with mitral regurgitation, however, are at an increased risk of developing heart failure during pregnancy and should undergo repair or replacement of the mitral valve before pregnancy (14,15).

This case series has certain limitations such as retrospective design, small sample size, and information limited to the experience of a single institution. Moreover, the influences of environmental, social and ethnic factors must be considered during the interpretation and extrapolation of our data to larger populations.

In conclusion, a comprehensive understanding of physiology of pregnancy and the pathophysiologic basis of valvular heart disease is of utmost importance for anesthesiologists, obstetricians, cardiologists and cardiovascular surgeons involved in the healthcare of pregnant women with valvular heart disease. If obstetric indications are present, cardiac valve surgery can be performed simultaneously just after cesarean section in selected cases. Risks and benefits must be analyzed well prior to the decision making for the absolute necessity of the invasive procedure. Close collaboration between disciplines, well equipped referral centers, trained personnel and increased awareness of possible complications are the key points for the successful surgical management of pregnant women with cardiac valve disease.

Author contribution

Study conception and design: NA and ATF; data collection: ATF; analysis and interpretation of results: NA and ATF; draft manuscript preparation: NA. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Kanuni Sultan Süleyman Training and Research Hospital Noninterventional Studies Ethics Committee (Protocol no. 157/05.05.2021).

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Conflict of interest

The authors declare that there is no conflict of interest.

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