



Successful Pregnancy after a Heart Transplant in Iran: A Case Report

Fateme Mehri, MD^{1,2}, Kianoush Saberi, MD³, Mehrdad Salehi, MD⁴, Fahimeh Ghotbizadeh Vahdani, MD⁵, Farnoosh Larti, MD⁶, Alireza Bakhshandeh, MD⁴, Shahrzad Sheikhhasani, MD^{1,2*}

¹Department of Gynecology and Obstetrics, Vali-e-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran.

²Vali-e-Asr Reproductive Health Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran.

³Department of Anesthesiology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.

⁴Department of Cardiac Surgery, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.

⁵Maternal, Fetal and Neonatal Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran.

⁶Department of Cardiology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Received 07 April 2023; Accepted 25 July 2023

Abstract

Pregnancy after a heart transplant is a concern for many female recipients, and it remains a medical challenge that raises many questions. A 24-year-old woman, gravida 3, para 0, contacted us for obstetric care in the first trimester of gestation, about 3 years after an orthotopic cardiac transplant. She was a known case of dextrocardia with congenitally corrected transposition of the great arteries. The transplant had been performed for severe retractable heart failure, manifesting during her previous lost pregnancy. The course of the current gestation was uneventful. The patient's cardiovascular function was good throughout the pregnancy. She was admitted to the hospital for dyspnea at 35 weeks and 4 days of gestational age. A cardiovascular consult and echocardiography were performed. The results were within the normal range, and labor pains explained the patient's dyspnea. Because of labor pain, a repeat Cesarean section was performed at 35 weeks and 4 days of gestational age. A male baby weighing 2700 g, with an Apgar score of 7/9, was delivered. The patient was discharged after delivery with enoxaparin (40 mg), prednisolone (5 mg), levothyroxine, and mycophenolate mofetil (500 mg) without any complications. Follow-up was carried out at 1 month, and no abnormality was found. Here, we report a case of a successful pregnancy in a young woman after a heart transplant.

J Teh Univ Heart Ctr 2023;18(4):294-297

This paper should be cited as: Mehri F, Saberi K, Salehi M, Ghotbizadeh Vahdani F, Larti F, Bakhshandeh A, et al. Successful Pregnancy after a Heart Transplant in Iran: A Case Report. *J Teh Univ Heart Ctr* 2023;18(4):294-297.

Keywords: Heart transplantation; Pregnancy; Delivery; Obstetric; Immunocompromised host

*Corresponding Author: **Shahrzad Sheikhhasani**, Associate Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, School of Medicine, Department of Obstetrics and Gynecology, School of Medicine, Vali-E-Asr Hospital, Tehran, Iran. Tel: +98 21 61192240. Fax: +98 21 66904848. E-mail: dr_sh1356@yahoo.com.





Introduction

Heart transplants have been used in recent decades as a treatment for severe heart failure.¹ A comprehensive single-center experience of pregnancy in cardiac transplant recipients over 29 years showed encouraging maternal and fetal outcomes with a higher live birth rate (91%) than that reported by the National Transplantation Pregnancy Registry (NTPR) in 2010 (62%).^{2,3} According to the International Heart and Lung Transplant Association (ISHLT) registry report in 2019, the 1-year survival of adults after transplant is approximately 90%, with a conditional half-life of more than 13 years.⁴ With this description, survival after a heart transplant is improving, and many transplant recipients are of childbearing age or survive until then.⁵

These women frequently regain fertility following transplant and may wish to consider pregnancy.⁶ Nonetheless, pregnancy in heart transplant recipients is a common challenge for physicians and poses significant risks to the mother, transplant, and fetus.⁷ Such pregnancies are considered high-risk because they are associated with the risk of several common complications, including preeclampsia, spontaneous abortion, low birth weight, and intrauterine growth restriction.^{8,9}

Herein, we report the first case of successful pregnancy after repeated abortions in a young patient who had undergone a heart transplant due to severe retractable heart failure in the setting of congenitally corrected transposition of the great arteries in Iran.

Case Report

A 24-year-old woman with a history of heart transplant was admitted to the Obstetrics Clinic at Imam Khomeini Hospital, Tehran, Iran, at the gestational age of 35 weeks for delivery. She had been previously diagnosed with congenitally corrected transposition of the great arteries. She had dextrocardia with abdominal situs inversus. In May 2018, at the age of 19 and in the 28th week of her first pregnancy, she was admitted to Imam Khomeini Hospital, Tehran, Iran, due to aggravation of shortness of breath and increased coughs. Transthoracic echocardiography revealed evidence of a moderately reduced systemic ventricle and moderate systemic atrioventricular valve regurgitation. During this hospitalization, she experienced cardiopulmonary arrest and was resuscitated and transferred to the ICU. Afterward, she underwent a hysterotomy in May 2018 due to intrauterine fetal death.

In July 2018, she was referred to the hospital again due to shortness of breath. According to her clinical condition and echocardiographic findings, a severely reduced systemic ventricle with an ejection fraction of 10–15% was reported. A possible diagnosis of postpartum cardiomyopathy

superimposed on previous systemic (subaortic ventricle) dysfunction was proposed. The patient became a candidate for a heart transplant. In July 2018, she underwent right heart catheterization. During this period, she was treated with methotrexate, sildenafil, and furosemide. Finally, in October 2018, she underwent a heart transplant. As the patient had situs inversus, the surgical technique was demanding. The donor's inferior vena cava was anastomosed to the recipient's left-sided inferior vena cava directly, such that the heart was slightly rotated, resulting in the altered geometry of the transplanted heart in the chest. Her echocardiographic views, albeit inadequate, showed satisfactory results with the preserved function of the ventricles. Six months after the heart transplant surgery, in April 2019, she underwent curettage due to a missed pregnancy in the 5th week. Subsequently, her condition remained stable (left ventricular ejection fraction=50–55%, normal left ventricular and right ventricular size, and pulmonary artery pressure=20 mm Hg). Under cardiac supervision and prenatal care, she became pregnant in August 2021. We kept her in an immunosuppressed and controlled state by treating her with tacrolimus (1 cap/d), Aspirin (80 mg/d), enoxaparin (40 mg/d), levothyroxine (0.1 mg/d) and prednisolone (5 mg/d). During pregnancy, antenatal care was performed promptly, and no obstetrical complication was found. She was also hospitalized in March 2022 due to a COVID-19 infection, and she was treated with dexamethasone and remdesivir and was discharged after 5 days in stable condition. During her pregnancy, a perinatologist and cardiologist visited her every 2 weeks. In April 2022, she was admitted again due to dyspnea and labor pain. The patient underwent a Cesarean section at 35 weeks and 5 days of gestational age. She gave birth to a baby with a birth weight of 2700 g. The newborn was in good general condition with an Apgar score of 7 and without signs of growth restriction. The mother was discharged after delivery with enoxaparin (40 mg), prednisolone (5 mg), levothyroxine, and mycophenolate mofetil (500 mg) without any complications. Follow-up was carried out at 1 month, and no abnormality was found.

Discussion

Post-heart transplant pregnancy has been performed safely in selected patients.^{8,9} According to the ISHLT guidelines, a multidisciplinary approach to reproductive health after a heart transplant should be considered.¹⁰ Maternal comorbidities in the heart transplant population underscore the importance of a multidisciplinary approach to counseling and management. A history of peripartum cardiomyopathy may warrant closer attention to pregnancy's increased hemodynamic load and graft dysfunction monitoring.¹¹ Here, we reported another successful pregnancy following a heart transplant in a young woman with a history of previous abortion.

Still, there is limited information about pregnancy in heart transplant recipients. Pregnancy management in women after vital organ transplant is mostly based on expert recommendations, and there are no guidelines based on randomized controlled trials.^{9,12} Heart transplant women can give birth to healthy children through natural childbirth and Cesarean section. However, heart transplant recipients have been advised to avoid pregnancy in the first year after transplant, when the risk of rejection is higher and immunosuppressive therapy is the most aggressive.¹³ A recent systematic review and meta-analysis of 385 pregnancies in 272 cardiac transplant recipients reported a mean transplant-to-pregnancy interval of 81.4 months for heart transplant recipients with an average maternal age of 28 years.⁴ Nevertheless, it is still challenging to pinpoint the safest time for fertilization. Immunosuppressive drugs should be prescribed during pregnancy. According to the Food and Drug Administration (FDA), these drugs are Class C in terms of safety for use in pregnant women.¹⁴ Currently, however, no standard immunosuppressive protocol exists for transplant recipients during pregnancy. Heart transplant recipients wishing to become pregnant should be aware of the potential effects of immunosuppressive drugs on fetal growth and the complications associated with pregnancy and transplant.^{10,15} The ISHLT recommends that women who plan to become pregnant have a complete cardiac evaluation (coronary angiography, echocardiography, and electrocardiography) 6 months before pregnancy. Mycophenolate mofetil and sirolimus should be discontinued approximately 6 weeks before scheduled pregnancy due to the risk of fatal birth defects. Statins are also contraindicated and should be discontinued.^{16,17} Generally accepted guidelines recommend other treatments, such as tacrolimus or cyclosporine and folic acid supplementation, during the first trimester.⁷ After delivery, levels of immunosuppressive drugs should be adjusted to maintain adequate immunosuppression.

Experts in this field have not recommended breastfeeding to women undergoing treatment for chronic immunosuppression,⁹ although the infant is exposed only to approximately 0.5% of the tacrolimus concentration in the mother's blood.¹⁸ On the other hand, the American Transplant Association states that breastfeeding should not be contraindicated.⁷ Some studies have also shown that breastfeeding in these individuals has no particular complication in the infant.⁹ It may be necessary to document decisions related to breastfeeding by obtaining a written consent form.

Conclusion

Little information is available to healthcare professionals to be able to recommend breastfeeding for mothers receiving immunosuppressive therapy confidently. Based on recent

review advice, a healthcare professional should take a 3-pronged approach when assessing whether these mothers should breastfeed. First, if the mother is taking drugs of known toxicity without a safety threshold (eg, MPA drugs), the mother should probably be advised not to breastfeed. Second, if the mother is taking drugs that appear safe at low or unmeasurable levels (eg, cyclosporine and tacrolimus) or are thought to be safe (eg, corticosteroids and azathioprine), the infant's serum should be monitored for measurable drug levels after the first week or 2 of breastfeeding. Third, caution must be advised for drugs of unknown safety (eg, sirolimus, everolimus, and belatacept).

The successful outcome of the case presented herein, similar to several previous reports, can be attributed to the participation of an interdisciplinary team and the cooperation of the patient.

References

1. Crespo-Leiro MG, Barge-Caballero E. Advanced Heart Failure: Definition, Epidemiology, and Clinical Course. *Heart Fail Clin* 2021;17:533-545.
2. Bhagra CJ, Bhagra SK, Donado A, Butt T, Forrest L, MacGowan GA, Parry G. Pregnancy in cardiac transplant recipients. *Clin Transplant* 2016;30:1059-1065.
3. Coscia LA, Constantinescu S, Moritz MJ, Frank AM, Ramirez CB, Maley WR, Doria C, McGrory CH, Armenti VT. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. *Clin Transpl* 2010:65-85.
4. DeFilippis EM, Haythe J, Farr MA, Kobashigawa J, Kittleson MM. Practice Patterns Surrounding Pregnancy After Heart Transplantation. *Circ Heart Fail* 2020;13:e006811.
5. Hasan A, Kittleson MM. Heart Transplantation in Women. *Heart Fail Clin* 2019;15:127-135.
6. Bhagra CJ, Bhagra SK, Donado A, Butt T, Forrest L, MacGowan GA, Parry G. Pregnancy in cardiac transplant recipients. *Clin Transplant* 2016;30:1059-1065.
7. McKay DB, Josephson MA, Armenti VT, August P, Coscia LA, Davis CL, Davison JM, Easterling T, Friedman JE, Hou S, Karlx J, Lake KD, Lindheimer M, Matas AJ, Moritz MJ, Riely CA, Ross LF, Scott JR, Wagoner LE, Wrenshall L, Adams PL, Bumgardner GL, Fine RN, Goral S, Krams SM, Martinez OM, Tolkoff-Rubin N, Pavlakis M, Scantlebury V; Women's Health Committee of the American Society of Transplantation. Reproduction and transplantation: report on the AST Consensus Conference on Reproductive Issues and Transplantation. *Am J Transplant* 2005;5:1592-1599.
8. AlRaffa A, AlJubairy S, Alwatban SJ. A successful pregnancy and delivery after heart transplantation: The first case report in Saudi Arabia. *Saudi J Anaesth* 2023;17:97-100.
9. Kalinka J, Szubert M, Zdziennicki A, Chojnowski K, Maciejewski M, Piestrzeniewicz K, Zakliczyński M, Drożdż J. A second delivery after heart transplantation - a case study. *Kardiolog Pol* 2014;11:339-342.
10. Costanzo MR, Dipchand A, Starling R, Anderson A, Chan M, Desai S, Fedson S, Fisher P, Gonzales-Stawinski G, Martinelli L, McGiffin D, Smith J, Taylor D, Meiser B, Webber S, Baran D, Carboni M, Dengler T, Feldman D, Frigerio M, Kfoury A, Kim D, Kobashigawa J, Shullo M, Stehlik J, Teuteberg J, Uber P, Zuckermann A, Hunt S, Burch M, Bhat G, Canter C, Chinnock R, Crespo-Leiro M, Delgado R, Dobbels F, Grady K, Kao W, Lamour J, Parry G, Patel J, Pini D, Towbin J, Wolfel G, Delgado D, Eisen H, Goldberg L, Hosenpud J, Johnson M, Keogh A, Lewis C, O'Connell J, Rogers



- J, Ross H, Russell S, Vanhaecke J; International Society of Heart and Lung Transplantation Guidelines. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Transplant* 2010;29:914-956.
11. Acuna S, Zaffar N, Dong S, Ross H, D'Souza R. Pregnancy outcomes in women with cardiothoracic transplants: A Systematic review and meta-analysis. *J Heart Lung Transplant* 2020;39:93-102.
 12. Svangaard SM, Løgstrup BB, Eiskjær H, Fuglsang J. [Pregnancy after heart transplantation]. *Ugeskr Laeger* 2022;184:V01220016.
 13. Lee HY, Jeon ES, Kang SM, Kim JJ. Initial Report of the Korean Organ Transplant Registry (KOTRY): Heart Transplantation. *Korean Circ J* 2017;47:868-876.
 14. Abdalla M, Mancini DM. Management of pregnancy in the post-cardiac transplant patient. *Semin Perinatol* 2014;38:318-325.
 15. Miniero R, Tardivo I, Centofanti P, Goggi C, Mammana C, Parisi F, Dall'Omo AM. Pregnancy in heart transplant recipients. *J Heart Lung Transplant* 2004;23:898-901.
 16. Bateman BT, Hernandez-Diaz S, Fischer MA, Seely EW, Ecker JL, Franklin JM, Desai RJ, Allen-Coleman C, Mogun H, Avorn J, Huybrechts KF. Statins and congenital malformations: cohort study. *BMJ* 2015;350:h1035.
 17. Schoner K, Steinhard J, Figiel J, Rehder H. Severe facial clefts in acrofacial dysostosis: a consequence of prenatal exposure to mycophenolate mofetil? *Obstet Gynecol* 2008;111(2 Pt 2):483-486.
 18. Gardiner SJ, Begg EJ. Breastfeeding during tacrolimus therapy. *Obstet Gynecol* 2006;107(2 Pt 2):453-455.