


## Pregnancy in a heart transplant recipient with history of severe humoral and cellular rejection and positive donor-specific antibodies – case report

 Dubravka Šipuš\*

 Mia Dubravčić  
Došen,

 Petra Mjehović,

 Dora Fabijanović,

 Nina Jakuš,

 Ivo Planinc,

 Marijan Pašalić,

 Hrvoje Jurin,

 Jure Samardžić,

 Daniel Lovrić,

 Maja Čikeš,

 Hrvoje Gašparović,

 Renata Žunec,

 Davor Miličić,

 Vesna Elvedi

Gašparović,

 Boško Skorić

University of Zagreb School of  
Medicine, University Hospital  
Centre Zagreb, Zagreb, Croatia

**KEYWORDS:** heart transplantation, pregnancy, donor-specific antibodies.

**CITATION:** *Cardiol Croat.* 2023;18(11-12):298-9. | <https://doi.org/10.15836/ccar2023.298>

\***ADDRESS FOR CORRESPONDENCE:** Dubravka Šipuš, Klinički bolnički centar, Kišpatičeva 12, HR-10000 Zagreb, Croatia. / Phone: +385-91-7344-878 / E-mail: [dubravka.sipus@gmail.com](mailto:dubravka.sipus@gmail.com)

**ORCID:** Dubravka Šipuš, <https://orcid.org/0000-0002-5631-0353> • Mia Dubravčić Došen, <https://orcid.org/0000-0003-0441-4772>

Petra Mjehović, <https://orcid.org/0000-0003-4908-4674> • Dora Fabijanović, <https://orcid.org/0000-0003-2633-3439>

Nina Jakuš, <https://orcid.org/0000-0001-7304-1127> • Ivo Planinc, <https://orcid.org/0000-0003-0561-6704>

Marijan Pašalić, <https://orcid.org/0000-0002-3197-2190> • Hrvoje Jurin, <https://orcid.org/0000-0002-2599-553X>

Jure Samardžić, <https://orcid.org/0000-0002-9346-6402> • Daniel Lovrić, <https://orcid.org/0000-0002-5052-6559>

Maja Čikeš, <https://orcid.org/0000-0002-4772-5549> • Hrvoje Gašparović, <https://orcid.org/0000-0002-2492-3702>

Renata Žunec, <https://orcid.org/0000-0003-2607-3059> • Davor Miličić, <https://orcid.org/0000-0001-9101-1570>

Vesna Elvedi Gašparović, <https://orcid.org/0000-0002-0960-3989> • Boško Skorić, <https://orcid.org/0000-0001-5979-2346>

**Background:** Pregnancy in heart transplant (HT) recipients with episodes of rejection or positive donor specific antibodies (DSA) is discouraged by all recommendations due to higher risk of complications. Although there is paucity of data for DSA trend during pregnancy in HT recipients, there is evidence of improvement of symptoms during pregnancy in some autoimmune diseases<sup>1-3</sup>.

**Case report:** 23-year-old female who underwent HT due to post-myocarditis cardiomyopathy in June 2014, reported unplanned pregnancy in June 2022. She had a history of acute cellular (3R/3B) and humoral rejection (DSA major histocompatibility complex (HLA) class I, specificity A11, A30, B13, B35 and HLA class II, specificity DR3, DR15, DR51, DR52, DQ2, mean fluorescent intensity (MFI) 1000-13 300) in August 2017 which required mechanical circulatory support due to severe heart failure with multi-organ damage. She underwent pulse corticosteroid treatment, and 12 cycles of plasmapheresis with administration of rituximab, intravenous immunoglobulins, and thymoglobulin. After that she had persistent positive DSA, predominantly DQ2 (MFI up to 12200), and because of that was on quadruple immunosuppression (tacrolimus, mycophenolate (MMF), everolimus, prednisone) from October 2019 to July 2020 when MMF was discontinued due to gastrointestinal side effects. She had one more cellular rejection episode (2R/3A) in March 2022 which was treated with pulse corticosteroids. During pregnancy she was on tacrolimus, everolimus, and prednisone combination with closely monitoring of immunosuppressants concentrations. Echocardiography controls showed normal left ventricle function and mildly reduced right ventricle function, NT-proBNP was slightly elevated (493-823 ng/L) and DSA were in a downward trend which is shown in **Figure 1**. At 32+3 weeks of pregnancy, she was hospitalized due to early labor. The following day male baby was delivered by Caesarean section due to pathological cardiotocography (Apgar score 8/9). After delivery DSA remained weakly positive.

**Conclusion:** Although pregnancy in HT recipients with history of rejection and positive DSA is discouraged, positive outcome is possible with close monitoring of multidisciplinary team. Furthermore, we described a rare case of downward trend of positive DSA during pregnancy.

RECEIVED:

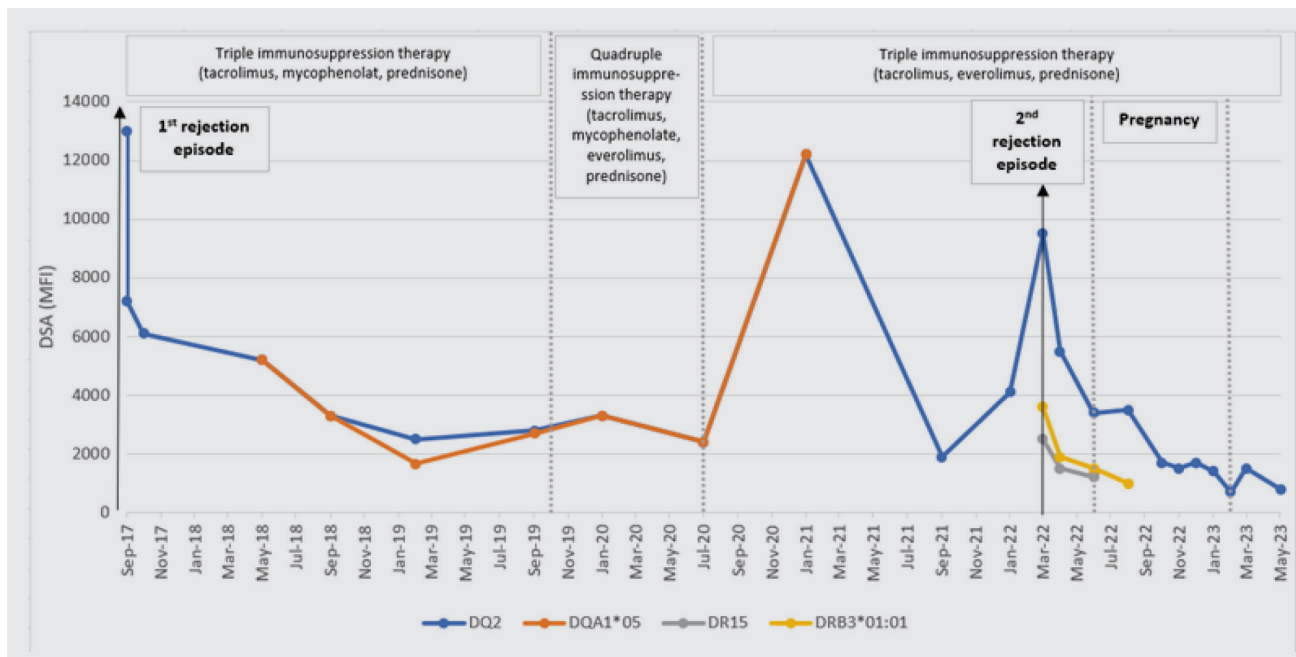
September 9, 2023

ACCEPTED:

September 27, 2023



**Pregnancy in a heart transplant recipient with history of severe humoral and cellular rejection and positive donor-specific antibodies – case report**



**FIGURE 1.** Trend in donor specific antibodies (DSA) detected by the Luminex method from September 2017 to May 2023 expressed in mean fluorescent intensity (MFI). The patient had her first episode of humoral and cellular rejection in August 2017, and the second in March 2022. She was on quadruple immunosuppression (tacrolimus, mycophenolate, everolimus, prednisone) from October 2019 to July 2020. She was pregnant from June 2022 to February 2023.

**LITERATURE**

1. Punnoose LR, Coscia LA, Armenti DP, Constantinescu S, Moritz MJ. Pregnancy outcomes in heart transplant recipients. *J Heart Lung Transplant.* 2020 May;39(5):473-480. <https://doi.org/10.1016/j.healun.2020.02.005>
2. Defilippis EM, Kittleson MM. Pregnancy after Heart Transplantation. *J Card Fail.* 2021 Feb;27(2):176-184. <https://doi.org/10.1016/j.cardfail.2020.07.011>
3. Piccinni MP, Lombardelli L, Logiodice F, Kullolli O, Parronchi P, Romagnani S. How pregnancy can affect autoimmune diseases progression? *Clin Mol Allergy.* 2016 Sep 15;14:11. <https://doi.org/10.1186/s12948-016-0048-x>