



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

the largest prospective cohort studies to investigate contraceptive use and ectopic pregnancy rates across multiple forms of contraception. Our study covers a wider range of contraceptive methods than previous studies, and the forms of contraception included in our study are more contemporary than currently included in previous literature.<sup>3–5</sup> One limitation of our work is that the incidence of ectopic pregnancy was low across all methods. This is not unexpected with more than 75% of our cohort using a highly effective method and have a low risk of contraceptive failure. In addition, recall bias is a possible limitation in defining ectopic pregnancy by using telephone call follow-up surveys and patient self-report. ■

Paige Schultheis, BA  
Department of Obstetrics and Gynecology  
Indiana University School of Medicine  
Indianapolis, IN

Melissa Natalie Montoya, MD  
Department of Obstetrics and Gynecology  
Duke University School of Medicine  
Durham, NC

Qihong Zhao, MS  
Johanna Archer, MD  
Department of Obstetrics and Gynecology  
Indiana University School of Medicine  
Indianapolis, IN

Tessa Madden, MD, MPH  
Department of Obstetrics & Gynecology  
Washington University School of Medicine  
St. Louis, MO

Jeffrey F. Peipert, MD, PhD  
Department of Obstetrics and Gynecology  
Indiana University School of Medicine  
550 N University Blvd., UH2440  
Indianapolis, IN 46208  
[JPeipert@iu.edu](mailto:JPeipert@iu.edu)

The Contraceptive CHOICE Project was funded by an anonymous donor.

J.F.P. has served as an advisory board member for Bayer and CooperSurgical and has received research support from Merck, Bayer, and CooperSurgical and Teva. T.M. serves as a data safety monitoring board member for phase 4 safety studies of Bayer contraceptive products. The remaining authors report no conflict of interest.

This work has been registered on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT00635492).

## REFERENCES

1. Peipert JF, Madden T, Allsworth JE, Secura GM. Preventing unintended pregnancies by providing no-cost contraception. *Obstet Gynecol* 2012;120:1291–7.
2. Van Den Eeden SK, Shan J, Bruce C, Glasser M. Ectopic pregnancy rate and treatment utilization in a large managed care organization. *Obstet Gynecol* 2005;105(5 Pt 1):1052–7.
3. Li C, Zhao WH, Zhu Q, et al. Risk factors for ectopic pregnancy: a multi-center case-control study. *BMC Pregnancy Childbirth* 2015;15:187.
4. Furlong LA. Ectopic pregnancy risk when contraception fails. A review. *J Reprod Med* 2002;47:881–5.
5. Li C, Zhao WH, Meng CX, et al. Contraceptive use and the risk of ectopic pregnancy: a multi-center case-control study. *PLoS One* 2014;9:e115031.

© 2020 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2020.10.013>

## Myocardial injury associated with coronavirus disease 2019 in pregnancy



**OBJECTIVE:** The coronavirus disease 2019 (COVID-19) is associated with cardiac injury<sup>1–3</sup> and bradycardia<sup>4</sup> in the nonpregnant population. The incidence of these complications in pregnancy is unknown. The objective of this study was to determine the rate of abnormal serum cardiac biomarkers or bradycardia among pregnant and immediately postpartum women admitted for treatment of severe or critical COVID-19 in a large integrated health system in New York.

**STUDY DESIGN:** This is a retrospective review of all pregnant and immediately postpartum women hospitalized for COVID-19 at 7 hospitals within Northwell Health, the largest academic health system in the state of New York, from March 1, 2020, to April 30, 2020. Women who tested positive for severe acute respiratory syndrome coronavirus 2 by polymerase chain reaction (PCR) assay and who met the

National Institute of Health criteria for severe or critical illness<sup>5</sup> were included. Women with a positive PCR test who were admitted for a reason other than treatment of COVID-19 (eg, labor) were excluded. The Northwell Health Institutional Review Board approved the study as minimal-risk research using data collected for routine clinical practice and waived the requirement for informed consent.

Clinical records were manually reviewed. Data collected included demographics, medical comorbidities, pregnancy characteristics, laboratory and imaging results, medications administered, and clinical outcomes. Laboratory and imaging studies were ordered at the discretion of the attending physician. The primary outcomes evaluated were elevated cardiac troponins (I, T, or high sensitivity), elevated brain natriuretic peptide (BNP), bradycardia (defined as <60 bpm), and maternal heart rate (HR) nadir. Descriptive statistics were used to characterize the data.

TABLE

## Characteristics of patients with normal and abnormal cardiac markers

Characteristic	Patients with normal cardiac biomarkers (n = 13)	Patients with elevated cardiac biomarkers (n = 7)
Maternal age (y)	33.0±4.4	32.0±4.5
≥35 y	2 (15.4)	3 (42.9)
Race or ethnicity		
White	5 (38.5)	2 (28.5)
African American	2 (15.4)	0
Hispanic	6 (42.8)	0
Asian	0	3 (42.8)
Other, unknown, or multiracial	0	2 (28.5)
Multiparous	9 (69.2)	7 (100)
Parity of 3 or more	3 (23.1)	2 (28.5)
BMI prepregnancy (kg/m <sup>2</sup> )	34.7±6.7	32.5±6.0
≥30 kg/m <sup>2</sup>	8 (61.5)	5 (71.4)
Medical comorbidities		
Hypertension	0	0
Diabetes	0	1 (14.3)
Asthma	1 (7.7)	1 (14.3)
Preexisting cardiac disease	0	0
Pregnancy complications		
Gestational diabetes	1 (7.7)	0
Gestational hypertension or preeclampsia	3 (23.1)	2 (28.5)
COVID-19		
Gestational age at hospitalization (wk)	33.5 (10.8)	34.5 (4.5) (1 postpartum)
Reported symptoms		
Fever, subjective or measured	9 (69.2)	6 (85.7)
Cough	8 (61.5)	6 (85.7)
Dyspnea	9 (69.2)	6 (85.7)
Nausea or diarrhea	1 (7.7)	1 (14.3)
Other	0	1 (14.3) (abdominal pain)
Medications		
Hydroxychloroquine	11 (84.6)	3 (42.8)
Corticosteroids	5 (38.5)	4 (57.1)
Remdesivir	0	2 (28.5)
Interleukin inhibitors	1 (7.7)	3 (42.8)
Convalescent plasma	0	1 (14.3)

Shetty. Myocardial injury associated with coronavirus disease 2019. *Am J Obstet Gynecol* 2021.

(continued)

**RESULTS:** A total of 31 women met the inclusion criteria; among those women, 20 (65%) had cardiac biomarkers measured during hospitalization (Table). Cardiac troponins and BNP were elevated in 4 of 18 (22%) and 3 of 10 (30%) of these

patients, respectively. Furthermore, 4 patients had transthoracic echocardiograms performed, and all were reported as normal. No patient had preexisting cardiovascular disease or hypertension. Of note, 2 maternal mortalities in this cohort

TABLE

## Characteristics of patients with normal and abnormal cardiac markers (continued)

Characteristic	Patients with normal cardiac biomarkers (n = 13)	Patients with elevated cardiac biomarkers (n = 7)
Vital signs		
Temperature, $\geq 100.4^{\circ}\text{F}$ or $38.0^{\circ}\text{C}$	6 (42.8)	5 (71.4)
Max HR, $>100$ bpm	10 (76.9)	6 (85.7)
Min HR, $<60$ bpm	6 (42.8)	3 (42.8)
Respiratory rate, $>30$ bpm	4 (30.7)	4 (57.1)
Oxygen saturation (min), %	87.8 $\pm$ 6.2	84.6 $\pm$ 10.2
$\leq 93\%$	11 (84.6)	5 (71.4)
Biomarkers		
BNP, $>300$ pg/mL	0	4 (57.1)
hs-Trop, $>6-14$ ng/L	0	1 (14.3)
Troponin T, $>0.06$ ng/mL	0	1 (14.3)
Troponin I, $>0.045$ ng/mL	0	2 (28.5)
Echocardiogram		
Number of d admitted to hospital	8 (11.0)	4 (9.0)
Intensive care unit admission	5 (38.5)	6 (85.7)
Maternal mortality	0	2 (28.5)

Data are presented as number (percentage), median (interquartile range), or mean $\pm$ standard deviation unless otherwise specified.

Reference ranges: high sensitivity cardiac troponins,  $<6-14$  ng/L; troponin T,  $0.00-0.06$  ng/mL; troponin I,  $0.000-0.045$ ; BNP,  $<300$  pg/mL.

BMI, body mass index; BNP, brain natriuretic peptide; COVID-19, coronavirus disease 2019; HR, heart rate; Max, maximum; Min, minimum.

Shetty. Myocardial injury associated with coronavirus disease 2019. *Am J Obstet Gynecol* 2021.

were previously reported<sup>6</sup>; both patients had elevated cardiac troponins, and 1 also had an elevated BNP.

The nadir HR ranged from 30 to 92 bpm, and bradycardia occurred in 10 of 31 patients (one-third). Half of the women with elevated troponin and three-fourths of the women with elevated BNP had an episode of bradycardia recorded during their hospital course.

**CONCLUSION:** Myocardial injury as demonstrated by abnormal cardiac biomarkers and bradycardia may be common among pregnant women with severe or critical COVID-19. In this study, one-fifth of the patients who had troponin levels measured were found to have elevations (one-eighth of the overall study population). Among patients who had BNP levels measured, 30% were elevated (10% of the overall study population). One-third of the women had bradycardia.

This study is limited by a small sample size. Laboratory testing and imaging were not uniform because of the retrospective nature of the study. Sampling bias was unavoidable because the decision to measure cardiac markers or perform imaging studies was made by the patient's care team, based on clinical presentation rather than a formal protocol.

Few studies have evaluated the risk of cardiac injury or arrhythmia among pregnant women with COVID-19. It is also unknown whether there are long-term sequelae that

affect maternal health or future pregnancy outcomes. This is an important area of focus for future research. ■

## ACKNOWLEDGMENTS

We would like to acknowledge the efforts of the healthcare workers caring for pregnant women during the global COVID-19 pandemic.

Sarah L. Pachtman Shetty, MD, MSE  
 Division of Maternal-Fetal Medicine  
 Department of Obstetrics and Gynecology  
 Donald and Barbara Zucker School of Medicine at Hofstra/  
 Northwell  
 Hofstra University  
 Hempstead, NY  
 Division of Maternal-Fetal Medicine  
 Department of Obstetrics and Gynecology  
 Lenox Hill Hospital  
 Northwell Health  
 New York, NY  
[spachtman@northwell.edu](mailto:spachtman@northwell.edu)

Natalie Meiorowitz, MD  
 Division of Maternal-Fetal Medicine  
 Department of Obstetrics and Gynecology  
 Donald and Barbara Zucker School of Medicine at Hofstra/  
 Northwell

Hofstra University  
Hempstead, NY  
Department of Obstetrics and Gynecology  
Long Island Jewish Medical Center  
New Hyde Park, NY 11040

Matthew J. Blitz, MD, MBA  
Division of Maternal-Fetal Medicine  
Department of Obstetrics and Gynecology  
Donald and Barbara Zucker School of Medicine at Hofstra/  
Northwell

Hofstra University  
Hempstead, NY  
Division of Maternal-Fetal Medicine  
Department of Obstetrics and Gynecology  
South Shore University Hospital  
Northwell Health  
Bay Shore, NY

Therese Gadomski, MD  
Department of Obstetrics and Gynecology  
Donald and Barbara Zucker School of Medicine at Hofstra/  
Northwell

Hofstra University  
Hempstead, NY  
Division of Maternal-Fetal Medicine  
Department of Obstetrics and Gynecology  
Lenox Hill Hospital  
Northwell Health  
New York, NY

Catherine R. Weinberg, MD  
Division of Cardiology  
Department of Internal Medicine  
Donald and Barbara Zucker School of Medicine at Hofstra/  
Northwell

Hofstra University  
Hempstead, NY  
Division of Cardiology  
Department of Internal Medicine  
Lenox Hill Hospital  
Northwell Health  
New York, NY

The authors report no conflict of interest.

## REFERENCES

1. Liu J, Virani SS, Alam M, Denktas AE, Hamzeh I, Khalid U. Coronavirus disease-19 and cardiovascular disease: a risk factor or a risk marker? *Rev Med Virol* 2020. [Epub ahead of print].
2. Ghio S, Baldi E, Vicentini A, et al. Cardiac involvement at presentation in patients hospitalized with COVID-19 and their outcome in a tertiary referral hospital in Northern Italy. *Intern Emerg Med* 2020. [Epub ahead of print].
3. López-Otero D, López-Pais J, Antúnez-Muiños PJ, Cacho-Antonio C, González-Ferrero T, González-Juanatey JR. Association between myocardial injury and prognosis of COVID-19 hospitalized patients, with or without heart disease. *CARDIOVID registry. Rev Esp Cardiol (Engl Ed)* 2020. [Epub ahead of print].
4. Capoferri G, Osthoff M, Egli A, Stoockle M, Bassetti S. Relative bradycardia in patients with COVID-19. *Clin Microbiol Infect* 2020. [Epub ahead of print].
5. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. Available at: <https://www.covid19treatmentguidelines.nih.gov/>. Accessed September 23, 2020.
6. Blitz MJ, Rochelson B, Minkoff H, et al. Maternal mortality among women with coronavirus disease 2019 admitted to the intensive care unit. *Am J Obstet Gynecol* 2020;223:595–9.e5.

© 2020 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2020.10.014>

# Declaring a gestation nonviable: when 99% certainty is not enough



**OBJECTIVE:** The modern paradigm for diagnosing early pregnancy loss, including ectopic pregnancy, is to compare 2 human chorionic gonadotropin (hCG) values with those expected for a growing intrauterine pregnancy (IUP).<sup>1</sup> Surveillance of women at risk has led to earlier diagnosis, successful medical management, and decreased morbidity and mortality.<sup>2</sup> Confirmation of nonviability is imperative because the intervention for the diagnosis or treatment with uterine evacuation or methotrexate will terminate a viable gestation or can be teratogenic. Here, we describe the hCG results and pregnancy outcome from a participant enrolled in the randomized clinical trial, ACT or NOT (NCT02152696), that evaluated the treatment of women with a persistent pregnancy of unknown location.

**STUDY DESIGN:** The definition of a persistent pregnancy of unknown location included no definitive ultrasound evidence

of intrauterine or extrauterine gestation and a plateau in hCG, defined as <30%, <50%, <75%, or <100% in 2, 3, 4, or 7 days, respectively.<sup>3</sup> Here, 2 clinicians confirmed eligibility into the trial. Serial hCG levels from the participant were compared with levels used to assess the viability of a pregnancy.

**RESULTS:** A participant was enrolled, randomized to expectant management, and later noted to have a viable gestation. A 33-year-old, G2 P1001, who conceived with use of clomiphene citrate and intrauterine insemination presented with abnormal serial hCG values of 7% in 2 days and 24% over 4 days: 86 at 4 0/7 weeks' gestation, 92 at 4 2/7 weeks' gestation, and 107 at 4 5/7 weeks' gestation. All assays were performed in the same laboratory using the Roche E170 analyzer. A transvaginal ultrasound performed at 4 5/7 weeks' gestation at an accredited academic practice