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Antenatal Hospitalizations Among Pregnancies Conceived With and Without Assisted Reproductive Technology

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Abstract

OBJECTIVE: To describe the prevalence of antenatal hospitalizations, compare characteristics of women with and without antenatal hospitalizations, and compare timing, length of stay, and reason for hospitalization among pregnancies conceived with and without assisted reproductive technology (ART).

METHODS: We performed a retrospective cohort analysis using linked ART surveillance, vital records, and hospital discharge data from Michigan to calculate the hospitalization ratio as the number of antenatal admissions per 100 live birth deliveries for ART and non-ART deliveries during 2004–2012 and compare trends by ART status. We then restricted analysis to 2008–2012 and used logistic, multinomial, and Poisson regression analysis to model antenatal admissions, trimester of admission, and length of stay, respectively, for ART compared with non-ART deliveries. We examined reason for hospitalization by ART status.

RESULTS: Between 2004 and 2012, the hospitalization ratio for ART deliveries decreased from 14.6 to 12.3 per 100 deliveries ($P<.001$). Of 557,708 live deliveries during 2008–2012, 22,763 (4.1%) had an antenatal hospitalization. Assisted reproductive technology was a risk factor for

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having any antenatal admission (singletons adjusted risk ratio [RR] 1.63, 95% confidence interval [CI] 1.43–1.83; multiples adjusted RR 1.24, 95% CI 1.12–1.38) and two or more admissions (singletons adjusted RR 1.86, 95% CI 1.25–2.75; multiples adjusted RR 1.33, 95% CI 1.14–1.54). The percent of time (days) hospitalized during the antenatal period was greater for ART deliveries than non-ART deliveries (singleton adjusted RR 1.28, 95% CI 1.09–1.51; multiples adjusted RR 1.14, 95% CI 1.01–1.29). The most common reason for antenatal admission was preterm labor among all non-ART and multiple gestation deliveries and vaginal bleeding among ART singleton gestations.

CONCLUSION: Deliveries after ART were associated with increased risk of antenatal admissions and longer hospitalizations compared with non-ART deliveries.

Antenatal hospitalization is an important marker of maternal morbidity. A study from a national managed care organization found an antenatal hospitalization ratio of 10.1 hospitalizations per 100 deliveries in 1997,¹ whereas data from the National Hospital Discharge Survey showed a ratio of 10.5 hospitalizations per 100 deliveries from 1999 through 2000.² Little has since been published on antenatal hospitalizations. It is important to understand factors associated with antenatal hospitalizations to develop and implement preventive approaches that can help reduce maternal morbidity and health care burden.

We have recently shown that pregnancies conceived with assisted reproductive technology (ART) are at increased risk of intrapartum or postpartum severe maternal morbidity.³ Many studies suggest ART pregnancies are at increased risk of antenatal and perinatal morbidity. Assisted reproductive technology pregnancies have been associated with antepartum hemorrhage,^{4–6} gestational diabetes,^{4,5,7} pregnancy-induced hypertension,^{5,6,8} and preterm birth.^{9,10} The occurrence and frequency of antenatal hospitalization have not been evaluated in this potentially high-risk population.

Our objective was to describe the prevalence of antenatal hospitalizations, characteristics of women with and without antenatal hospitalizations, and differences in timing, length of stay, and reason for antenatal hospitalization among deliveries to women who conceived with and without ART. We hypothesized that characteristics of women with live birth deliveries would differ between those with compared with without antenatal admission and, among those with antenatal admission, would differ between those who conceived with compared with without ART. Furthermore, we hypothesized that deliveries of pregnancies conceived with ART would have increased risk of antenatal admissions and prolonged admissions compared with deliveries of non-ART pregnancies.

MATERIALS AND METHODS

We performed a retrospective cohort analysis using data from the States Monitoring ART collaborative database.¹¹ Briefly, the States Monitoring ART collaborative was formed by the Centers for Disease Control and Prevention and health departments of Massachusetts, Michigan, Florida, and Connecticut to examine ART-related health outcomes. Data from the National ART Surveillance System are linked to states' vital records with a probabilistic linkage methodology using mother's date of birth, neonate's date of birth, plurality, gravidity, and zip code. This method has been validated and found to be accurate.¹¹ We

performed this analysis using only Michigan data, because it was the only state with the required hospital discharge variables available at the study time. The linkage rate for Michigan data was 91.8%. Our study was approved by the institutional review boards of the Michigan Department of Health and Human Services and the Centers for Disease Control and Prevention.

Liveborn deliveries at greater than 20 weeks of gestation were identified using Michigan birth certificates between 2004 and 2012. Any delivery that occurred within the state of Michigan was included, even if the ART occurred outside of the state. Maternal hospital discharge data were directly linked to birth certificate data using a unique identifier assigned to each delivery. Any delivery that could not be linked was excluded. Deliveries were also excluded if International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes for molar pregnancy (630), spontaneous abortion or termination (631, 632, 634.x–638.x, 69.01, 69.51, 74.91, 75.0, or Diagnosis-Related Group codes 380, 381 for version 24 or earlier and 770, 779 for version 25 or later, or Current Procedural Terminology codes 59840, 59841, 59850–59852, 59855–59857), or ectopic pregnancy (633.x, Diagnosis-Related Group code 378 for version 24 or earlier and 777 for version 25 or later) were found in the linked hospital data.

Antenatal hospitalization before delivery was defined as any hospitalization with a date of admission within 260 days (37 weeks of gestation) and more than 4 days before the date of delivery. Any admission that occurred within 4 days of delivery was classified as a delivery admission to avoid classifying admissions intended for delivery with prolonged intrapartum courses as antenatal hospitalizations. This 4-day interval between admission and delivery has been used previously when examining antenatal hospitalizations.¹ A delivery was identified as conceived with ART by a specific variable that indicated the birth certificate data were linked to the National ART Surveillance System. Information from the National ART Surveillance System including type of ART cycle (fresh or frozen), if intracytoplasmic sperm injection was performed, and stage of embryo transfer was obtained to calculate the rate of hospitalization among subgroups of ART pregnancies.

Characteristics for deliveries were identified using birth certificates and hospital discharge ICD-9-CM codes and included maternal age, prior number of live births, history of preterm birth, plurality, estimated gestational age and birth weight at delivery, maternal education, marital status, race–ethnicity, smoking status during pregnancy, maternal body mass index (BMI calculated as weight (kg)/[height (m)]²), and the presence of comorbid conditions including chronic hypertension, renal disease, seizure disorder, pregestational diabetes, cardiac or cardiovascular disease, and chronic lung disease. The characteristic or condition was considered to be present if identified using either birth certificate or hospital discharge data. International Classification of Diseases, 9th Revision, Clinical Modification codes used include 305.1, 649.0, V15.82 for tobacco use; 401.0, 401.1, 401.9, 402.00–405.99, 642.0, 642.1, 642.2 for chronic hypertension; 250.4, 403, 404, 405.01, 405.11, 405.91, 585.1–585.6, 585.9 for renal disease; 649.43, 345.0, 345.1, 345.4–345.9 for seizure disorder; 250–250.93, 648.00–648.04 for pregestational diabetes; 412, 414.0, 414.8, 414.9, 429.2 for cardiac or cardiovascular disease; and 490–496 for chronic lung disease. Characteristics were compared between those with no antenatal admission and those with at least one

antenatal hospitalization before delivery and between non-ART and ART deliveries among those with an antenatal hospitalization using χ^2 and Fisher exact tests. Only deliveries between 2008 and 2012 were included for this part of the analysis as a result of the collection of more accurate birth certificate data after fall 2007 when Michigan adopted a new birth certificate format.

Hospitalization ratio was defined as the number of antenatal hospitalizations per 100 deliveries and was calculated for ART and non-ART deliveries between 2004 and 2012 overall and stratified by plurality. Trend analysis was performed for the hospitalization ratio using linear models setting year as a continuous variable. For deliveries between 2008 and 2012, we performed logistic regression, controlling for maternal characteristics, to estimate the risk of having any antenatal admission (one or more admissions) and multiple antenatal admissions (two or more admissions) among ART deliveries compared with non-ART deliveries. Among those with at least one antenatal hospitalization, we used multinomial logistic regression to model trimester of the first antenatal admission in ART compared with non-ART deliveries. Poisson regression was used to compare the number of days spent hospitalized in the antenatal period between ART and non-ART deliveries with at least one antenatal admission accounting for length of gestation. We used generalized estimating equations with an independent working correlation matrix to address the correlation between multiple deliveries to the same mother during the study period.¹² Adjusted risk ratios (RRs) and confidence intervals (CIs) were produced by computing the ratios of conditional marginal proportions (ie, model-adjusted RR) for all regression analyses after controlling for maternal characteristics. All missing or unknown values were excluded in the model fitting.

Finally, we reviewed the primary ICD-9-CM code associated with antenatal admissions for 2004–2012 to determine the reason for admission for ART and non-ART singleton and multiple deliveries. Differences in proportions of deliveries reporting a specific reason for admission between ART and non-ART were compared using a χ^2 test. For each reason of admission, the mean and median lengths of stay were calculated and differences in length of stay between ART and non-ART deliveries were compared using a Wilcoxon rank sum test. *P* values <.05 were considered statistically significant. Data analysis was performed using SAS 9.3 and SUDAAN 11.

RESULTS

There were 1,038,311 live birth deliveries during 2004–2012, of which 42,876 (4.1%) had an antenatal hospitalization. The hospitalization ratio for all live birth deliveries (singleton and multiples) is shown in Figure 1 stratified by ART status. The overall hospitalization ratio decreased from 2004 to 2012 for both ART and non-ART pregnancies (*P*<.001). Overall hospitalization among ART conceptions ranged from 14.6 antenatal admissions per 100 deliveries in 2004 to 12.3 antenatal admissions per 100 deliveries in 2012 with the nadir in 2011 at 10.5 per 100 deliveries. The hospitalization ratio among all non-ART deliveries ranged between 3.6 and 4.4 antenatal admissions per 100 deliveries. Hospitalization ratio stratified by plurality is shown in Figure 2. Multiple gestations had higher hospitalization ratios for both ART and non-ART deliveries when compared with singletons. The hospitalization ratio decreased for both ART and non-ART multiple

gestations over time with a peak for ART multiples of 30.6 antenatal admissions per 100 deliveries in 2006 and for non-ART multiples with 24.3 antenatal admissions per 100 deliveries in 2005. Hospitalization ratio for singleton gestations ranged from 5.2 to 7.0 antenatal hospitalizations per 100 deliveries for ART and 3.4 to 4.2 antenatal hospitalizations per 100 deliveries for non-ART pregnancies. Trend analysis showed that the hospitalization ratio decreased for both non-ART and ART multiple gestations but only for non-ART singleton gestations ($P<.001$). The hospitalization ratio was significantly higher for pregnancies conceived with ART among all deliveries and when stratified by plurality ($P<.001$).

Among 557,708 live deliveries between 2008 and 2012, 22,763 (4.1%) had at least one antenatal admission. Deliveries with at least one antenatal admission were more likely among women who conceived with ART (2.7% compared with 0.8%), were 35 years old or older (14.0% compared with 12.6%), had a history of preterm birth (5.0% compared with 1.8%), had a multiple gestation (9.3% compared with 1.5%), delivered preterm (43.5% compared with 7.6%), were non-Hispanic black (31.8% compared with 18.5%), smoked (26.3% compared with 21.9%), were obese (29.2% compared with 24.1%), and had a comorbid condition (26.2% compared with 11.0%). These and other differences (all statistically significant) among those with and without an antenatal admission are presented in Table 1.

Characteristics of deliveries with at least one antenatal admission stratified by ART status are shown in Table 2. The mean and median lengths of stay were significantly longer for ART pregnancies (mean 8.8 days, median 3.0 days) compared with non-ART pregnancies (mean 4.5 days, median 2.0 days). A higher percentage of the deliveries for pregnancies conceived with ART compared with without ART occurred among women who were older (42.0% 35 years or older compared with 13.4%), nulliparous (46.9% compared with 40.9%), had a multiple gestation (64.6% compared with 7.8%), delivered preterm (77.3% compared with 42.7%), had some graduate-level education (63.7% compared with 17.8%), were non-Hispanic white (86.7% compared with 57.8%), and were nonsmokers (92.8% compared with 72.3%). Statistically significant differences were also observed for marital status and BMI. As a requirement of the Michigan Department of Health and Human Services institutional review board, we were not allowed to report any cell with $n<20$. We therefore performed complementary suppression to protect the patient's identity in Table 2.

Overall, deliveries of ART pregnancies were preceded by more antenatal admissions than deliveries of non-ART pregnancies, and deliveries of multiple gestations had more antenatal admissions than deliveries of singletons (Table 3). Among singletons, 6.2% of ART deliveries had at least one antenatal admission compared with only 3.8% of non-ART deliveries. Among multiples, 24.3% and 19.8% of ART and non-ART deliveries experienced at least one antenatal admission, respectively. After controlling for maternal factors, ART was associated with significantly more pregnancies experiencing at least one antenatal admission (singletons adjusted RR 1.63, 95% CI 1.43–1.83; multiples adjusted RR 1.24, 95% CI 1.12–1.38) and multiple antenatal admissions (singletons adjusted RR 1.86, 95% CI 1.25–2.75; multiples adjusted RR 1.33, 95% CI 1.14–1.54). Assisted reproductive technology pregnancies were less likely than non-ART pregnancies to be admitted for the

first time in the third trimester (singletons adjusted RR 0.86, 95% CI 0.74–0.98; multiples adjusted RR 0.83, 95% CI 0.73–0.95). Rates of hospitalization among ART treatment subgroups of fresh and frozen embryo transfers (6.2% and 6.1%, respectively), cycles where intracytoplasmic sperm injection was used (6.0%), and cleavage compared with blastocyst embryo transfer (6.3% and 7.0%, respectively) did not vary markedly.

The percent of gestational days hospitalized in the antepartum period for singleton ART deliveries was 5.2% compared with 3.5% for non-ART singleton deliveries (Table 3). After adjusting for characteristics including maternal age, history of prior live birth, education, marital status, race, BMI, and history of prior preterm birth, the adjusted RR for percent of gestational days hospitalized in the antepartum period was 1.28 (95% CI 1.09–1.51) for ART singletons. Among multiples, the percent of gestational days hospitalized in the antepartum period for ART deliveries was 8.2% compared with 6.4% for non-ART deliveries with an adjusted RR of 1.14 (95% CI 1.01–1.29) after adjusting for maternal age, history of prior live birth, education, marital status, race, and BMI.

The most common reasons for antenatal admission and average length of stay for each reason are listed in Table 4. Among singleton gestations, preterm labor and hypertensive disorders were the two most common specified reasons for antenatal admissions of non-ART pregnancies with genitourinary complications as the third most common reason. Vaginal bleeding and preterm labor were the most common reasons specified for admission among ART singleton gestations followed by hypertensive disorders. The frequency of admissions for vaginal bleeding was significantly higher among ART as compared with non-ART, singleton gestations (15.6% compared with 3.7%, $P<.001$). There was no statistically significant difference in length of stay for any reason of admission between ART and non-ART singletons. Among multiple gestations, preterm labor followed by hypertensive disorders and cervical insufficiency were the most common specified reasons for antenatal admission regardless of ART status. Of these three reasons, comparing frequencies among ART and non-ART multiples, significant differences were detected for hypertensive disorders (11.5% compared with 6.6%, $P<.001$) and cervical insufficiency (9.9% compared with 6.0%, $P=.001$). Assisted reproductive technology multiples had significantly longer lengths of stay when admitted for preterm labor compared with non-ART multiples (ART mean 8.8 days, median 4.0 days compared with non-ART mean 6.3 days, median 3.0 days, $P<.001$). Any cell with $n<20$ was suppressed in Table 4 to protect the patient's identity as required by the Michigan Department of Health and Human Services institutional review board.

DISCUSSION

In 2013, 1.5% of all neonates born in the United States were conceived using ART and the number of ART pregnancies continues to rise.¹³ We found ART to be a risk factor for having antenatal admissions with a nearly twofold increase in the average length of stay (8.8 days) compared with non-ART deliveries (4.5 days). These findings have important implications for the individual patient who conceived with ART and the health care system.

Deliveries with an antenatal admission after ART were more likely to be preterm, which may be attributable in part to the increase in multiple gestations with ART¹⁴; however, it has been shown that ART singletons have an increased risk of preterm birth compared with spontaneously conceived singletons.^{9,10} Pregnancy outcomes associated with ART such as antepartum hemorrhage⁴⁻⁶ and pregnancy-induced hypertension^{5,6,8} may increase antenatal admissions. Consistent with these findings, there were significantly more admissions for vaginal bleeding among singleton ART deliveries and hypertensive disorders among multiple gestation ART deliveries compared with their non-ART counterparts.

An important question to ask is whether the increase in antenatal hospitalizations among ART pregnancies is the result of maternal characteristics and underlying infertility of women seeking treatments or the ART procedures. Among singleton and multiple gestations, we found ART was associated with a significant increase of having any antenatal admission, multiple admissions, and longer hospital stays after controlling for important maternal characteristics and comorbidities. Although many of the admissions may be the result of the pregnancy complications mentioned (preterm labor, antenatal hemorrhage, and pregnancy-induced hypertension), it is possible patients and clinicians are more sensitive to potential pregnancy complications after conceiving with ART. To further address this question, our study should be performed in a subfertile population among women with infertility who ultimately conceived spontaneously. We were unable to identify a subfertile population using our database.

Among non-ART deliveries in Michigan, the antenatal hospitalization ratio ranged from 3.6 to 4.4 per 100 deliveries, which is lower than what has been reported in previous literature.^{1,2} This difference could be attributable, in part, to advances in prenatal care such as fetal fibronectin and cervical length measurement as prediction tools for preterm birth.^{15,16} Differences in study populations and definitions of antenatal hospitalization likely also contributed.

Women with an antenatal hospitalization (regardless of ART status) were more likely to be non-Hispanic black, single, less educated, to smoke during pregnancy, and to have BMIs greater than 30 compared with women who were only admitted for delivery. Non-Hispanic black race, educational status, and single marital status are all correlated with an increased risk for preterm birth^{17,18}; obese women are at increased risk of several pregnancy complications, including hypertensive disorders and preterm delivery¹⁹; smoking is associated with preterm birth, preterm rupture of membranes, and placental pathology,²⁰ all of which were common reasons for admission in our population.

This study addresses an important marker for maternal morbidity, antenatal hospitalizations among a high-risk group of ART-conceived pregnancies. The strengths of this study include the use of a comprehensive database that includes state vital records, the National ART Surveillance System, and hospital discharge data.

Our findings are subject to several limitations. Although the accuracy and completeness of data collected from birth certificates and hospital discharge are variable, studies have shown that identifying cases from more than one source, as was done for the current study,

increases ascertainment without significantly increasing false-positives.^{21,22} However, as a result of the nature of our database and limitations inherent to retrospective cohort studies, residual confounding may be present from unknown, poorly measured, or unmeasured factors and may explain the observed associations. One unmeasurable factor is chorionicity of twin gestations, which is important because monochorionic twins have increased complications compared with dichorionic twins,¹⁴ which could lead to increased antenatal hospitalizations. We excluded women with a hospital admission date 37 weeks before the delivery date in an attempt to prevent inclusion of nonpregnancy admissions; however, a nonpregnancy admission before a pregnancy ending preterm may have still been classified as an antenatal hospitalization. Finally, our study was conducted using data from one state and may not be generalizable to populations outside of Michigan.

Antenatal hospitalizations continue to be an important marker of maternal morbidity and health care burden. Pregnancies conceived with ART are a high-risk group for antenatal admission. As the number of pregnancies conceived with ART continues to increase, it is important to identify and implement approaches to reduce modifiable factors associated with risk of antenatal hospitalizations, both for the individual patient and the larger health care system. Efforts toward risk factor modification, expanded patient education, and improved screening should be made to ultimately reduce maternal morbidity and thus antenatal hospitalizations.

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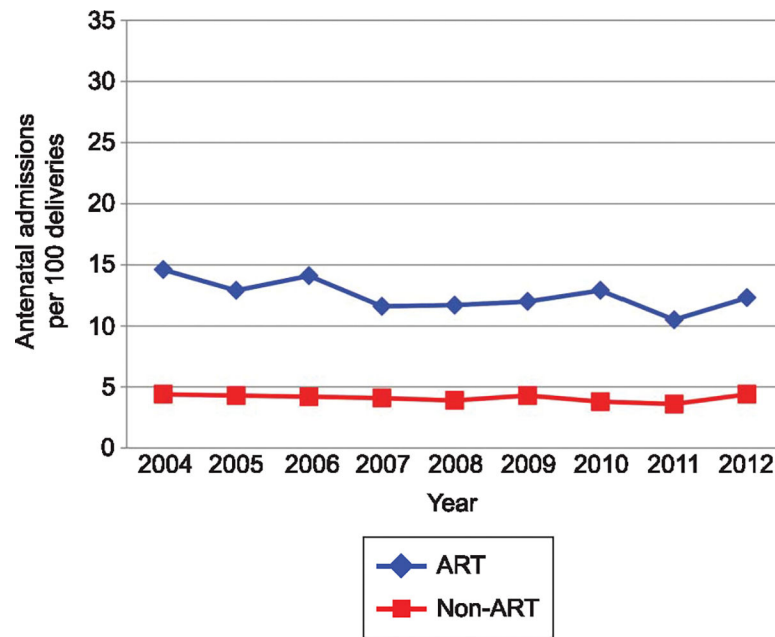


Fig. 1.

Hospitalization ratio for all deliveries by assisted reproductive technology (ART) status in Michigan, 2004–2012. Chi square test $P < .001$ between ART and non-ART deliveries.

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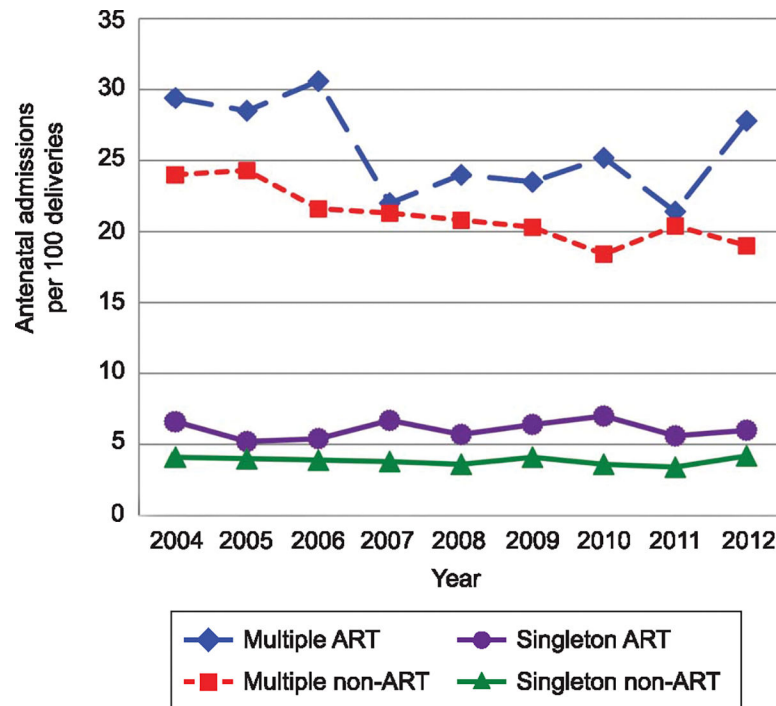


Fig. 2.

Hospitalization ratio for singleton and multiple gestation deliveries by assisted reproductive technology (ART) status in Michigan, 2004–2012. Chi square test $P < .001$ between ART and non-ART for both singleton and multiple deliveries. *Martin. Antenatal Hospitalizations After ART. Obstet Gynecol 2016.*

Table 1.
Characteristics of Deliveries With and Without Antenatal Admissions in Michigan, 2008–2012

Maternal Characteristics	No Admission Before Delivery (n=534,945)*	1 or More Admissions Before Delivery (n = 22,763)*	P
ART status			
Non-ART	530,445 (99.2)	22,155 (97.3)	<.001
ART	4,500 (0.8)	608 (2.7)	
Age (y) at the time of delivery			
Younger than 30	338,955 (63.4)	14,723 (64.7)	<.001
30–34	128,426 (24.0)	4,824 (21.2)	
35–39	54,960 (10.3)	2,514 (11.0)	
40–44	11,865 (2.2)	646 (2.8)	
45 or older	739 (0.1)	56 (0.2)	
Prior no. of live births			
0	216,934 (40.6)	9,351 (41.1)	<.001
1	169,784 (31.7)	6,471 (28.4)	
2 or more	147,813 (27.6)	6,913 (30.4)	
History of prior preterm birth			
Yes	9,794 (1.8)	1,148 (5.0)	<.001
No	520,037 (97.2)	21,302 (93.6)	
Plurality			
Singleton	526,765 (98.5)	20,656 (90.7)	<.001
Twin	8,007 (1.5)	1,950 (8.6)	
Triplet or higher	173 (<0.1)	157 (0.7)	
EGA at delivery (wk)			
Term (37 wk or greater)	493,979 (92.3)	12,836 (56.4)	<.001
Late preterm (34–36.6)	31,700 (5.9)	4,905 (21.5)	
Early preterm (28–33.3)	6,946 (1.3)	3,668 (16.1)	
Extremely preterm (less than 28)	2,320 (0.4)	1,354 (5.9)	
Birth weight (g)	3,323.7 (3,345.0)	2,711.6 (2,851.0)	<.01
Education			
Less than high school	80,392 (15.0)	4,157 (18.3)	<.001

Maternal Characteristics	No Admission Before Delivery (n=534,945) [*]	1 or More Admissions Before Delivery (n = 22,763) [*]	P
High school	140,347 (26.2)	6,745 (29.6)	
Some college	168,533 (31.5)	7,346 (32.3)	
Some graduate	142,518 (26.6)	4,320 (19.0)	
Marital status			
Single	224,491 (42.0)	12,115 (53.2)	<.001
Married	310,284 (58.0)	10,640 (46.7)	
Race-ethnicity			
Non-Hispanic white	372,465 (69.9)	13,334 (58.6)	<.001
Non-Hispanic black	98,974 (18.5)	7,240 (31.8)	
Hispanic or Latina	38,290 (7.2)	1,427 (6.3)	
Asian or Pacific Islander	4,930 (0.9)	179 (0.8)	
Other	18,697 (3.5)	533 (2.3)	
Smoking during pregnancy			
Yes	116,947 (21.9)	5,987 (26.3)	<.001
No	414,020 (77.4)	16,579 (72.8)	
Maternal BMI (kg/m ²)			
Less than 18.5	18,110 (3.4)	945 (4.2)	<.001
18.5–24.9	235,440 (44.0)	8,687 (38.2)	
25–29.9	131,035 (24.5)	5,161 (22.7)	
30 or greater	128,862 (24.1)	6,656 (29.2)	
Unknown or missing	21,498 (4.0)	1,314 (5.8)	
Comorbid condition [†]			
No	471,320 (88.1)	16,542 (72.7)	<.001
Yes	58,834 (11.0)	5,973 (26.2)	

APT, assisted reproductive technology; EGA, estimated gestational age; BMI, body mass index.

Data are n (%) or mean (median) unless otherwise specified.

^{*} Percent may not equal 100 for each variable as a result of missing data (less than 2% missing if not reported).

[†] Chronic hypertension, renal disease, seizure disorder, pregestational diabetes, cardiac or cardiovascular disease, chronic lung disease.

Characteristics of Deliveries With One or More Antenatal Hospitalizations by Assisted Reproductive Technology Status in Michigan, 2008–2012

Table 2.

Maternal Characteristics	Non-ART (n=22,155)*	ART (n=608)*	P †
Length of stay (d)	4.5 (2.0)	8.8 (3.0)	<.001
Age (y) at time of delivery			
Younger than 30	14,600 (65.9)	123 (20.2)	<.001
30–34	4,594 (20.7)	230 (37.8)	
35–39	2,350 (10.6)	164 (27.0)	
40–44	576 (2.6)	70 (11.5)	
45 or older	35 (0.2)	21 (3.5)	
Prior no. of live births			
0	9,066 (40.9)	285 (46.9)	<.001
1	6,260 (28.3)	211 (34.7)	
2 or more	6,801 (30.7)	112 (18.4)	
History of prior preterm birth			
Yes	1,121 (5.1)	27 (4.4)	.444
No	20,726 (93.6)	576 (94.7)	
Plurality			
Singleton	20,441 (92.3)	215 (35.4)	<.001
Twin	1,613 (7.3)	337 (55.4)	
Triplet or higher	101 (0.5)	56 (9.2)	
EGA at delivery (wk)			
Term (37 wk or greater)	12,698 (57.3)	138 (22.7)	<.001
Late preterm (34–36.6)	4,701 (21.2)	204 (33.6)	
Early preterm (28–33.6)	3,458 (15.6)	210 (34.5)	
Extremely preterm (less than 28)	1,298 (5.9)	56 (9.2)	
Birth weight (g)	3,301.6 (3,345.0)	2,992.4 (3,080.0)	<.01
Education			
Less than high school	4,146 (18.7)	<20‡	<.001
High school	6,693 (30.2)	>50‡	
Some college	7,190 (32.5)	156 (25.7)	

Maternal Characteristics	Non-ART (n=22,155)*	ART (n=608)*	P †
Some graduate	3,933 (17.8)	387 (63.7)	
Marital status			
Single	12,099 (54.6)	<20 ‡	<.001
Married	10,048 (45.4)	>500 ‡	
Race-ethnicity			
Non-Hispanic white	12,807 (57.8)	527 (86.7)	<.001
Non-Hispanic black	7,208 (32.5)	32 (5.3)	
Hispanic or Latina	1,410 (6.4)	<20 ‡	
Asian or Pacific Islander	177 (0.8)	<20 ‡	
Other	503 (2.3)	28 (4.6)	
Smoking status			
Yes	5,949 (26.9)	38 (6.3)	<.001
No	16,015 (72.3)	564 (92.8)	
Maternal BMI (kg/m ²)			
Less than 18.5	936 (4.2)	<20 ‡	<.001
18.5–24.9	8,391 (37.9)	296 (48.7)	
25–29.9	5,006 (22.6)	155 (25.5)	
30 or greater	6,531 (29.5)	125 (20.6)	
Unknown or missing	1,291 (5.8)	<30 ‡	
Comorbid condition §			
No	16,085 (72.6)	457 (75.2)	.181
Yes	5,827 (26.3)	146 (24.0)	

ART, assisted reproductive technology; EGA, estimated gestational age; BMI, body mass index.

Data are mean (median) or n (%) unless otherwise specified.

* Percentage may not equal 100 for each variable as a result of missing data (less than 2% missing if not reported).

† χ^2 P-value except length of stay, which was calculated with a Wilcoxon rank-sum test.

‡ Not reported to protect patient confidentiality as requested by the Michigan Department of Health and Human Services institutional review board.

§ Chronic hypertension, renal disease, seizure disorder, pregestational diabetes, cardiac or cardiovascular disease, chronic lung disease.

Table 3.

Risk of Any Antenatal Hospitalization, More than One Antenatal Hospitalization, Trimester of Hospitalization, and Risk of Increased Days Hospitalized After Assisted Reproductive Technology in Michigan, 2008–2012

Antenatal Hospitalization	Non-ART	ART	Crude RR (95% CI)	Adjusted RR* (95% CI)
Singleton birth				
All deliveries				
1 or more admission	20,441 (3.8)	215 (6.2)	1.64 (1.44–1.86)	1.63 (1.43–1.83)
2 or more admissions	2,660 (0.5)	28 (0.8)	1.64 (1.13–2.38)	1.86 (1.25–2.75)
Deliveries with 1 or more admission				
Trimester of first hospitalization				
1st	2,033 (9.9)	22 (10.2)	1.03 (0.69–1.53)	1.38 (0.91–2.10)
2nd	6,091 (29.8)	70 (32.6)	1.09 (0.90–1.33)	1.17 (0.96–1.43)
3rd	12,317 (60.3)	123 (57.2)	0.95 (0.85–1.07)	0.86 (0.74–0.98)
Antenatal days hospitalized [†]	180,780 (3.5)	2,698 (5.2)	1.49 (1.28–1.73)	1.28 (1.09–1.51)
Multiple birth				
All deliveries				
1 or more admission	1,714 (19.8)	393 (24.3)	1.23 (1.12–1.36)	1.24 (1.12–1.38)
2 or more admissions	844 (9.7)	220 (13.6)	1.40 (1.22–1.61)	1.33 (1.14–1.54)
Deliveries with 1 or more admission				
Trimester of first hospitalization				
1st	62 (3.6)	12 (3.1)	0.84 (0.46–1.55)	1.28 (0.63–2.59)
2nd	671 (39.1)	180 (45.8)	1.17 (1.03–1.32)	1.24 (1.07–1.43)
3rd	981 (57.2)	201 (51.1)	0.89 (0.80–0.99)	0.83 (0.73–0.95)
Antenatal days hospitalized [†]	25,079 (6.4)	7,395 (8.2)	1.27 (1.14–1.42)	1.14 (1.01–1.29)

ART, assisted reproductive technology; RR, risk ratio; CI, confidence interval.

Data are n (%) unless otherwise specified.

Bold indicates statistically significant RR.

* Adjusted for maternal age, history of prior live birth, education, marital status, race-ethnicity, and body mass index. In addition, number of days hospitalized among singleton gestations adjusted for prior preterm birth; trimester of first hospitalization among singleton and multiple gestations also adjusted for smoking status; and risk of one or more and two or more admissions among singleton and multiple gestations also adjusted for estimated gestational age at delivery, smoking status, history of prior preterm birth, and comorbid conditions.

$$\% = \frac{\text{number of days hospitalized in the antenatal period}}{\text{total number of days hospitalized in the antenatal period}} \times 100.$$

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Most Common Reason for Antenatal Hospitalization and Mean (Median) Length of Stay by Assisted Reproductive Technology Status and Plurality in Michigan, 2008–2012

Table 4.

Reason for Hospitalization	N (%)			Mean (Median) Length of Stay (d)		
	Non-ART	ART	P *	Non-ART	ART	P *
Singleton gestations						
Preterm labor †	5,926 (13.8)	60 (15.3)	.444	3.6 (2.0)	5.7 (3.0)	.108
HTN (chronic and pregnancy-related)	3,952 (9.2)	32 (8.2)	.505	5.4 (3.0)	7.7 (3.0)	.306
Genitourinary complications (UTI, pyelonephritis, renal failure)	2,920 (6.8)	<20 ‡	<.001	2.9 (2.0)	3.4 (2.0)	.988
Preterm PROM	2,099 (4.9)	27 (6.9)	.138	10.6 (7.0)	10.6 (8.0)	.104
Fetal abnormality (distress, arrhythmia, IUGR, macrosomia, anomaly, aneuploidy)	2,048 (4.8)	20 (5.1)	.771	4.6 (2.0)	8.0 (3.0)	.841
Diabetes (pregestational and gestational)	1,678 (3.9)	<20 ‡	.039	4.0 (3.0)	4.0 (3.0)	.939
Vaginal bleeding (including previa and abruptio)	1,582 (3.7)	61 (15.6)	<.001	6.2 (3.0)	7.3 (3.0)	.456
Hyperemesis	1,381 (3.2)	<20 ‡	.030	3.0 (2.0)	2.0 (2.0)	.972
Cerclage or cervical insufficiency	1,221 (2.8)	20 (5.1)	.058	8.8 (3.0)	19.4 (5.0)	.102
Psychologic disorders and drug dependence or abuse	649 (1.5)	<20 ‡	.097	5.1 (3.0)	2.7 (1.0)	.250
Not otherwise specified	4,463 (10.4)	28 (7.2)	.026	3.2 (2.0)	2.5 (2.0)	.922
Multiple gestations						
Preterm labor †	1,124 (30.5)	250 (31.3)	0.690	6.3 (3.0)	8.8 (4.0)	<.001
HTN (chronic and pregnancy-related)	242 (6.6)	92 (11.5)	<.001	8.4 (6.0)	10.1 (9.0)	.551
Cerclage or cervical insufficiency	222 (6.0)	79 (9.9)	.001	12.7 (6.0)	18.7 (8.0)	.090
Fetal abnormality (distress, arrhythmia, IUGR, macrosomia, anomaly, aneuploidy)	186 (5.1)	20 (2.5)	<.001	9.6 (4.0)	6.7 (3.0)	.475
Preterm PROM	154 (4.2)	40 (5.0)	.331	11.8 (7.0)	14.5 (8.0)	.685
Vaginal bleeding (including previa and abruptio)	88 (2.4)	28 (3.5)	.157	6.2 (3.0)	7.3 (3.0)	.700
Hyperemesis	58 (1.6)	0 (0.0)	<.001	3.8 (2.5)		
Genitourinary complications (UTI, pyelonephritis, renal failure)	53 (1.4)	<20 ‡	.024	4.9 (2.0)	2.2 (2.0)	.566
Hematologic disorders (anemia, thrombocytopenia, ITP, TTP)	44 (1.2)	<20 ‡	.128	7.0 (6.0)	4.0 (4.0)	.097
Diabetes (pregestational and gestational)	24 (0.7)	<20 ‡	.282	12.0 (7.0)	6.0 (7.0)	.146
Not otherwise specified	111 (3.0)	23 (2.9)	.836	4.9 (3.0)	5.1 (2.0)	.602

ART, assisted reproductive technology; HTN, hypertension; UTI, urinary tract infection; PROM, premature rupture of membranes; IUGR, intrauterine growth restriction; TTP, idiopathic thrombocytopenic purpura; TTP, thrombotic thrombocytopenic purpura.

Bold indicates statistically significant risk ratio.

* χ^2 P-value for n (%) and Wilcoxon rank-sum test P value for length of stay.

[†]Preterm labor as the primary reason for antenatal hospitalization does not necessarily indicate a preterm birth.

[‡]Not reported to protect patient confidentiality as requested by the Michigan Department of Health and Human Services institutional review board.