

RESEARCH ARTICLE

Outcomes of Extracorporeal Membrane Oxygenation in Pregnant vs. Non-Pregnant Women with Cardiogenic Shock: A Nationwide Analysis

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Abstract

Introduction: Cardiovascular disease is the leading cause of pregnancy-related mortality in the U.S., with rise in heart failure and cardiogenic shock. The use of Extracorporeal Membrane Oxygenation (ECMO) in cardiogenic shock is increasing, however, data on its use in pregnancy remain limited. This study aimed to assess the utilization and outcomes of ECMO in pregnant and postpartum women admitted to the hospital with cardiogenic shock.

Methods: We conducted a nationwide retrospective study using the National Inpatient Sample (2016–2021) to evaluate ECMO utilization and outcomes in pregnant and postpartum women with cardiogenic shock. Demographic characteristics, hospital charges, complications, and clinical outcomes were compared in two groups of study population.

Results: Among 44,940 women of reproductive age with cardiogenic shock, 3,640 (8.1%) received ECMO, including 145 pregnant/postpartum women. Pregnant/postpartum women were younger (31.2 vs. 36.3 years, $p < 0.001$), had fewer cardiovascular comorbidities, and had lower mortality rates (17.2% vs. 37.05%, $p = 0.03$). Hospital charges were lower (\$661,143 vs. \$955,654, $p < 0.001$). Complication rates, including venous thromboembolism, pulmonary embolism, major bleeding, stroke, need for mechanical ventilation, and renal replacement therapy, were similar between groups.

Conclusion: ECMO remains a life-saving intervention for pregnant women with cardiogenic shock, demonstrating comparable outcomes to non-pregnant women.

Keywords: ECMO, Pregnancy, Cardiogenic shock.

Introduction

Cardiovascular disease has emerged as the leading cause of pregnancy-related mortality in the United States, responsible for over 26% of maternal mortality and morbidity [1]. The physiological changes that occur during pregnancy increases women's vulnerability to cardiopulmonary complications. These changes can exacerbate pre-existing cardiovascular conditions such as heart failure, valvular heart

diseases, and congenital heart diseases due to increased cardiac output, blood volume, altered coagulation, or even unmask previously undiagnosed issues, leading to life-threatening situations [2].

Cardiovascular diseases requiring hospitalization in both antepartum and postpartum women in the U.S. have been increasing annually by 5%, including heart failure and cardiogenic shock (3). Maternal mortality in pregnant

or postpartum women admitted to the ICU with heart failure, cardiogenic shock, severe ARDS, or cardiac arrest is approximately 40% [3,4]

With these challenges, advancements in medical technology have led to the increased use of extracorporeal life support systems, particularly extracorporeal membrane oxygenation (ECMO). ECMO has become a pivotal intervention for managing severe respiratory and cardiac failure that does not respond to conventional treatments [5]. The growing reliance on ECMO is evident in the data from the Extracorporeal Life Support Organization (ELSO), which reports that ECMO use in adults has surged more than tenfold over the past decade [6,7]

Despite the growing use of ECMO, existing literature on its use in pregnancy/postpartum is largely limited to small case series and reports, with insufficient data on safety, in-hospital outcomes, and complications [8]. Our study aims to address this gap by analyzing ECMO outcomes for cardiogenic shock in pregnant and non-pregnant women of reproductive age using a large, nationally representative database.

Material and Methods

We conducted a retrospective, observational study using the National Inpatient Sample (NIS) database from the Healthcare Cost and Utilization Project (HCUP) from the years 2016-2021. We included all women of reproductive age (18-49 years), admitted to the hospital with cardiogenic shock, for which VA-ECMO was required as shown in Figure 1. Demographic information, clinical conditions (including various comorbidities and in-hospital complications), and outcomes (mortality, hospitalization costs, and length of hospital stay) were extracted using the International Classification of Diseases, 10th Revision (ICD-10) codes. Ethics committee approval was not required as this database is exempt from institutional review board approval. The datasets are publicly available at <https://www.hcup-us.ahrq.gov/databases.jsp>.

All women of reproductive age admitted with cardiogenic shock (ICD-10 code: R57.0) who received VA- ECMO (ICD-10 procedure codes: 5A1522F, 5A1522G, 5A15223, 5A15A2F, 5A15A2G) were included in the study. The study population was divided into two groups based on pregnancy/postpartum status, and outcomes were compared between these two groups. Details of ICD-10 diagnosis and procedure codes for various diagnoses and comorbidities, along with descriptions of demographic variables, are provided in the supplemental table.

Primary and Secondary Variables

The primary outcome is mortality and the secondary hospital outcomes are hospital length of stay (LOS), total hospital charges, and various in-hospital complications such as bleeding, stroke, venous thromboembolism, acute kidney

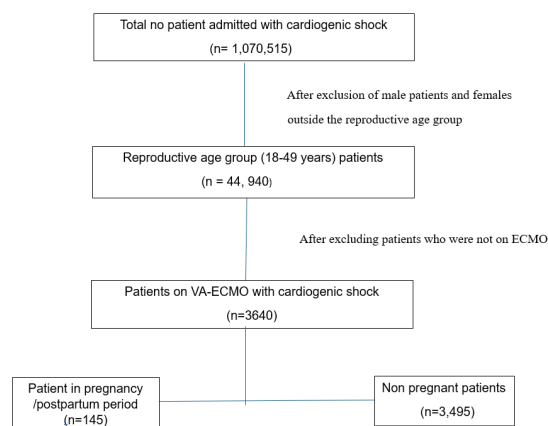


Figure 1: Study flow diagram

injury (AKI), the requirement of mechanical ventilation, and renal replacement therapy (RRT).

Statistical Analyses

Data analysis was performed using Stata version 17. Chi-square and Student's t-tests were used to compare categorical and continuous variables, respectively. Frequencies, confidence intervals, and p-values were reported for all outcomes, with statistical significance set at a p-value <0.05. Univariate and multivariate regression analyses were conducted to estimate the risk of various complications. The desired outcomes were analyzed individually across various clinical and demographic characteristics, and variables found to be significant in univariate analysis were included in the multivariate analysis.

Results

A total of 44,940 women of reproductive age were admitted with cardiogenic shock during the study period, of which 3,640 received VA- ECMO. This included 145 pregnant/postpartum women and 3,495 non-pregnant women. Pregnant/postpartum women who required ECMO were younger than non-pregnant women (31.2 vs. 36.3 years, $p < 0.001$).

Pregnant/postpartum women had a significantly lower mortality rate compared to non-pregnant women (17.2% vs. 37.05%, $p = 0.03$). They also had lower hospital charges (\$661,143 vs. \$955,654, $p < 0.001$). There was no statistically significant difference in the mean duration of hospital stay (22 vs. 25 days, $p = 0.4$).

Pregnant/postpartum women had significantly lower rates of comorbidities such as atrial fibrillation/flutter, diabetes, and history of cardiovascular disease (stroke, MI, cardiac arrest, CABG, presence of ICD). Pregnant and postpartum women had a lower risk of acute kidney injury (AKI) after adjusting for age, race and Charlson comorbidity index (aOR: 0.21, 95% CI 0.09-0.46). The risks of venous thromboembolism (VTE) and pulmonary embolism (PE),

major bleeding, stroke, mechanical ventilation, and renal replacement therapy (RRT) were similar between the two groups. The main results of our study are summarized in Table 1-6

Discussion

The use of ECMO in pregnant patients presents a complex scenario where the life-saving benefits must be weighed against the risk of serious complications. Our study identified several important findings regarding the utilization and outcomes of ECMO in this population. Similar to the rising utilization of ECMO in other adult population, we found an increasing trend in ECMO use among pregnant and postpartum women with cardiogenic shock as shown in Figure 1, particularly following the Corona virus Disease-19 (COVID-19) pandemic [6].

We found a lower in-hospital mortality rate among pregnant/postpartum patients (17.2% vs. 37.2%) and a higher survival rate in Kaplan-Meier survival analysis (Cox regression hazard ratio: 0.51, $p=0.04$) as shown in Figure 3. This reduced mortality rate could be attributed to several factors, including younger age and potentially fewer comorbidities in the pregnant and post-partum cohort as we observed in our study. The survival rate of pregnant/postpartum women on ECMO varies significantly across different studies, with systematic reviews and analyses of large administrative data sets reporting survival rates between 69.5% and 79.3% when considering all etiologies for ECMO use during pregnancy or the peripartum period [7-10]. This variation could be due to the complexity of ECMO outcomes in this population, which may depend on factors such as the underlying indication for ECMO, the timing of the intervention, and the presence of pregnancy-related comorbidities.

Table 1: Demographic characteristics of study population

<i>Variables</i>	<i>Pregnant and postpartum women (n = 145)</i>	<i>Non-Pregnant reproductive age women (n = 3495)</i>	<i>p-value</i>
Age, mean $\pm$ SD (years)	31.2($\pm$ 5.9)	36.3 ($\pm$ 9.04)	<0.001
Race, n (%)			
White	75(51.72)	1695(52.7)	0.2
Black	25(17.24)	805(25.04)	
Hispanic	35(24.1)	380(11.8)	
Asian	0	125(3.8)	
Native American	5(3.4)	25(0.78)	
Other	5(3.4)	185(5.75)	
Location/Teaching, n (%)			
Rural nonteaching	0	15(4.3)	0.14
Urban nonteaching	10(6.9)	65(1.86)	
Urban teaching	135(93.1)	3415(97.71)	
Household Income, n (%)			
0-25th percentile	40(27.5)	1065(30.78)	0.48
25th –50th percentile	45(31.03)	910(26.3)	
50th –75th percentile	20(13.79)	825(23.84)	
75th –100th percentile	40(27.59)	660(19.08)	
Hosp Bed Size, n (%)			
Small	5(3.45)	155(4.43)	0.94
Medium	15(10.34)	315(9.01)	
Big	125(86.21)	3025(86.55)	
Hospital Region, n (%)			
Northeast	25(17.24)	700(20.03)	0.21
Midwest	55(37.93)	915(26.18)	
south	30(20.69)	1305(37.34)	
West	35(24.14)	575(16.45)	

Table 2: Comorbidities in the study population

Comorbidities, (n (%))	Pregnant and postpartum women(n=145)	Non-Pregnant reproductive age women (n=3495)	p-value
Atrial fibrillation/flutter	0	545(15.6)	0.01
Cardiomyopathy	870(24.8)	25(17.24)	0.35
Peripheral Vascular Disease	15(10.34)	405(11.59)	0.83
COPD	30(20.6)	640(18.3)	0.73
Rheumatoid disease	0(0)	195(5.58)	0.19
Diabetes	0(0)	445(12.7)	0.04
Diabetes+ complications	0(0)	230(6.5)	0.15
Cancer	0(0)	105(3)	0.33
Metastatic cancer	10(6.9)	25(0.7)	<0.001
Peripartum Cardiomyopathy (PPCM)	40(27.5)	110(3.15)	<0.001
History of cardiac arrest	0	125(3.58)	0.29
History of MI	0	80(2.29)	0.42
History of stroke	0	65(1.86)	0.46
Presence of pacemaker	0	15(0.43)	0.72
Presence of ICD	0	80(2.29)	0.4
Presence of prosthetics or other heart valves	0	70(2)	0.43
History of CABG	0	60(1.72)	0.44

Table 3: Complications of ECMO

Variables	Pregnant and postpartum women(n=145)	Non-Pregnant reproductive age women (n=3495)	p-value
Complications, n (%)			
Intraoperative cardiac abnormalities	0(0)	95(2.7)	0.34
Pericardial effusion	10(6.9)	440(12.5)	0.36
Renal Replacement Therapy (RRT)	5(3.45)	665(19.03)	0.03
Mechanical Ventilation	96(65.5)	2520(72.1)	0.44
Venous Thromboembolism (VTE)	35(24.14)	1105(31.62)	0.37
Pulmonary embolism	20(13.79)	585(16.74)	0.67
Bleeding (other than PPH)	15(10.34)	640(18.31)	0.27
Post Partum Hemorrhage (PPH)	65(44.83)	-	-
Stroke	25(17.24)	545(15.5)	0.8
Acute Kidney Injury (AKI)	50(34.48)	2495(71.39)	<0.001

Despite the potential risks of thromboembolic events in pregnant/postpartum women, our findings did not indicate a significant difference in these outcomes. Around a quarter of the peripartum patients on ECMO in our study experienced VTE, but the risk of VTE did not differ significantly between the two groups. The reported incidence of thromboembolic events in pregnant patients on ECMO ranges from 2.8% to 33.0% [7,11-13]. A recent study among pregnant and postpartum women receiving ECMO for COVID-19 infection showed a slightly higher rate of VTE

(40%) [14]. We did not find any cases of acute limb ischemia in either study group. In a meta-analysis, limb ischemia was reported in 10% of VA-ECMO cases, but none were reported in VV-ECMO cases [15].

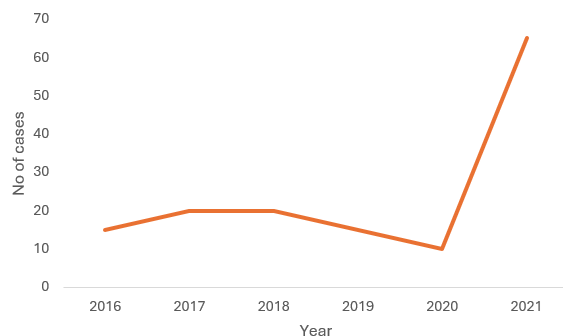
Similarly, other complications such as bleeding, septic shock, acute kidney injury (AKI), and stroke were lower in pregnant and postpartum patients compared to non-pregnant women, although these differences were not statistically significant. A 15-year longitudinal study reported that AKI occurred in up to 42% of patients post-ECMO, with

Table 4: Risk of complications of ECMO in pregnant and postpartum females

Complications of ECMO in pregnant and postpartum females	Odds Ratio (OR) (95% CI)	p-value
Mortality	a OR 0.36 (0.13-0.99)	0.04
AKI	a OR 0.21(0.09-0.47)	<0.001
VTE	0.68(0.28-1.58)	0.37
Bleeding	0.47(0.14-1.61)	0.23
Cardiac tamponade	1.07(0.24-4.7)	0.92
RRT	0.15(0.02-1.14)	0.06
Mechanical ventilation	0.73(0.33-1.63)	0.4
Pericardial effusion	0.51(0.11-2.23)	0.37

Table 5: Outcomes of ECMO

Variables	Pregnant and postpartum women(n=145)	Non-Pregnant reproductive age women (n=3495)	p -value
Mortality, n (%)	25(17.2)	1295(37.05)	0.03
LOS, days, mean (95% CI)	22 (13.9-30.9)	25 (23.4-27.9)	0.4
Total Charges, \$, mean (95% CI)	661143(433583-888704)	955654 (857070-1054239)	<0.001

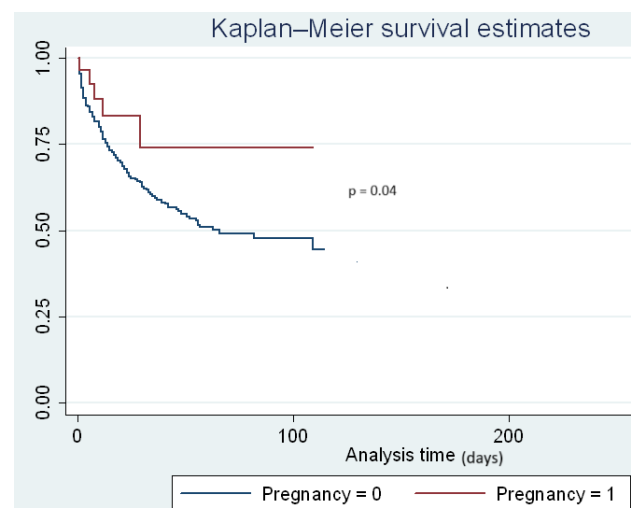
**Figure 2:** Trend of ECMO use in cardiogenic shock in pregnant/postpartum men

the incidence of post-ECMO AKI requiring RRT varying from 26.6% to 74.5% in such studies [16-18]. The incidence of bleeding, which includes major intracranial bleeding, GI bleeding, hemoptysis, and hematuria was lower among pregnant and postpartum patients (10% vs. 18%), although this difference was not statistically significant. The incidence of bleeding in our study was lower compared to other studies. A meta-analysis found an incidence of mild to moderate bleeding of 24% and severe bleeding of 26% in postpartum patients [7]. The incidence of bleeding in the general adult population has been reported to be as high as 30-40% [19-21]. Additionally, the incidence of postpartum hemorrhage (PPH) is higher among postpartum patients who were on ECMO. In our study, 45% of postpartum patients experienced PPH. A 19-year longitudinal study in the United States found that 3% of delivery hospitalizations were complicated by PPH [22].

Cost of hospitalization (mean cost \$661,143 vs \$955,654, $p < 0.001$) was lower among pregnant and postpartum

Table 6: Maternal/fetal comorbidities and outcomes

Gestational Diabetes, n (%)	10(6.9)
Gestation Hypertension, n (%)	45(31.03)
Eclampsia/preeclampsia, n (%)	40(27.59)
Intrauterine fetal death, n (%)	15(10.34)
Cesarian section, n (%)	70(48.28)

**Figure 3:** Kaplan meier survival curve

patients compared to the non-pregnant group. There was no significant difference in the mean length of hospital stays (22 days vs 25, $p=0.4$). A six-yearlong study using the National Readmission Database (NRD) from the United States found that ECMO use in pregnancy was associated with lower hospitalization cost and shorter length of stay [11].

Our study has several limitations. First, the diagnoses in the NIS database are based on billing codes rather than direct chart reviews, which means that any errors or limitations in provider documentation and coding could have influenced our findings. Additionally, the sequence of events cannot be accurately determined using this data. The NIS also lacks essential details about medical management, such as ECMO and ventilator settings, medication details, lab values, and the timing of interventions. These details are critical for a comprehensive understanding of patient care and could affect the interpretation of our results.

Conclusion

In conclusion, our study provides valuable insights into the outcomes of ECMO in pregnant/postpartum versus non-pregnant women with cardiogenic shock. The findings indicate that pregnant women have a significantly lower mortality rate and incur lower hospital charges compared to their non-pregnant counterparts. Despite the physiological challenges and complexities associated with pregnancy, ECMO appears to be a viable and effective intervention for managing cardiogenic shock in this population. The take-home message from this study is that ECMO can be a life-saving intervention for pregnant women experiencing cardiogenic shock, with outcomes that are comparable, if not superior, to those in non-pregnant women. These results underscore the importance of considering ECMO as a treatment option in this high-risk group and highlight the need for further research to optimize ECMO protocols and improve patient outcomes in this population.

Author Contributions

Manoj Ghimire: Conceptualization, Writing – review & editing, Writing – original draft, Formal analysis

Sajana Poudel: Writing – review & editing, Writing – original draft, Formal analysis

Kalpna Ghimire: Writing – review & editing, Writing – original draft, Formal analysis

Karun Shrestha: Writing – review & editing, Writing – original draft

Prakriti Subedi: Writing – review & editing, Writing – original draft

Salomon Chamay: Writing – review & editing, Writing – original draft

Suleman Celaj: Writing – review & editing, Writing – original draft, Supervision

Dinesh Kadariya: Writing – review & editing, Writing – original draft, Supervision

Paolo C. Colombo: Writing – review & editing, Writing – original draft, Supervision

Sanjay Chaudhary: Writing – review & editing, Writing – original draft, Supervision

Availability of Data

The datasets are publicly available at <https://www.hcup-us.ahrq.gov/databases.jsp>.

Ethical Approval

Ethics committee approval was not required as NIS database is exempt from institutional review board approval.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Source of Funding

None.

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