Obstetric admission to intensive care units in Japan: a cohort study using the Japanese Intensive care PAtient Database

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Abstract

Purpose: This study aimed to describe the epidemiology and annual trends of obstetric patients using a multicenter intensive care database.

Methods: This multicenter, retrospective cohort study used the Japanese Intensive care PAtient Database (JIPAD). We included obstetric patients registered in the JIPAD between 2015 and 2020. We investigated the proportion of obstetric patients among all patients in the intensive care unit (ICU). We also described the characteristics, procedures, and outcomes of obstetric patients. In addition, the annual trends were examined by nonparametric tests for trends.

Results: Of the 184,705 patients enrolled in the JIPAD, 750 (0.41%) were obstetric patients from 61 facilities. The median age was 34 years, the number of post-emergency surgeries was 450 (60.0%), and the median APACHE III score was 36. Mechanical ventilation was the most common procedure performed in 247 (32.9%) patients. There were five (0.7%) in-hospital deaths. The proportion of obstetric patients in the ICU did not change between 2015 and 2020 (*P* for trend = 0.32). However, there was a trend for a significant decrease in the severity of illness and length of hospital stay on an annual basis between 2015 and 2020. Most patients were admitted to the ICU because of a pregnancy-related disorder postoperatively.

Conclusion: The proportion of obstetric patients was 0.41% of all ICU admissions. The proportion of obstetric patients admitted to the ICU did not change from 2015 to 2020, but the patients' severity of illness and length of hospital stay significantly decreased over time.

Introduction

Pregnancy results in physiological changes that may increase the risk of life-threatening obstetric conditions. The World Health Organization reported that approximately 295,000 maternal deaths occurred worldwide in 2017, with 9 critically ill obstetric patients for every maternal death [1,2]. Furthermore, the number of critically ill obstetric patients is expected to increase for the following reasons: i) an increased age at labor, ii) increased number of patients who are obese or have chronic medical conditions, iii) increased incidence of multiple pregnancies and adherent placentas resulting from assisted reproduction, and iv) increased rates of labor induction and cesarean delivery [3–9].

A national report from the Australian and New Zealand Intensive Care Society (ANZICS) and the Intensive Care National Audit & Research Centre (ICNARC) reported that the proportions of obstetric admissions among all intensive care unit (ICU) patients were 1.3% and 2.1%, respectively [10,11]. A systematic review showed that obstetric patients accounted for approximately 2.2% of all ICU admissions, with Acute Physiology and Chronic Health Evaluation (APACHE) II scores ranging from 4.8 to 40, and obstetric-related diagnoses were the most common [12]. National reports of obstetric patients admitted to the ICU are also available from the United Kingdom, France, the Netherlands, Canada, China, and Australia/New Zealand [10,11,13–16]. However, there have been no

reports on the epidemiology of critically ill obstetric patients admitted to the ICU in Japan. Japanese epidemiology may differ from that in other countries because of differences in social and medical systems surrounding obstetric care (e.g., national health insurance and the majority of deliveries being at small primary hospitals), management protocols in obstetric units, ICU admission criteria, and availability of ICU beds [17,18].

The Japanese Intensive care PAtient Database (JIPAD) was established in 2014 to obtain data on patients who are admitted to the ICU. We conducted a cohort study using this Japanese ICU database to describe the epidemiology of critically ill obstetric patients who require intensive care in Japan.

Methods

This multicenter, observational study was based on the JIPAD [19]. This study was approved by the Ethics Review Board of Hamamatsu University School of Medicine (approval number, 21-225) and the JIPAD working group. The requirement for informed consent was waived because of the anonymous nature of the data.

Data source

The JIPAD is the largest domestic database of critically ill patients in Japan, and it has been managed by the Japanese Society of Intensive Care Medicine since 2014 [19]. The

definition of ICU included in the JIPAD entails a designated unit where a minimum of one physician is present for 24 hours each day, and where the admission fee for the emergency and critical care center, the specific ICU management fee, or the pediatric specific ICU management fee is calculated. Data were collected from each facility using Filemaker Pro™ (File Maker Inc., Santa Clara, CA, USA) and anonymized upon transfer to the central department. The JIPAD collects diagnoses, admission routes, vital signs, severity scores, procedure details, complications, and discharge status under the responsibility of the clinicians involved in daily care at each facility. The JIPAD shares common codes with the Australian and New Zealand Intensive Care Society Adult Patient Database (ANZICS-APD) and the Intensive Care National Audit & Research Centre Case Mix Programme (ICNARC-CMP; a database covering the region of England, Wales, and Northern Ireland). This sharing of codes allows for comparing patient data across different regions and countries, and helps to ensure that the JIPAD adheres to global standards. A system of regular data audits has also been incorporated to maintain the quality of the JIPAD. Investigators are granted access to the dataset upon approval of their request by the JIPAD working group.

Patients' selection and outcomes

We included women aged 15–49 years among patients registered in the JIPAD between

111 the fiscal years of 2015 and 2020 on the basis of a previous study [10]. We identified
112 obstetric patients using pregnancy-related codes (pregnancy-related disorders
113 postoperatively, postpartum hemorrhage, and pre-eclampsia or pregnancy-induced
114 hypertension nephropathy) and by the diagnosis that was freely entered as Japanese
115 texts. The exclusion criteria were as follows: i) ICU re-admission, ii) admission from
116 another ICU, iii) admission to the ICU for a procedure, and iv) missing values.
117 We investigated the proportion of obstetric patients among all ICU admissions.
118 We also examined the background characteristics, procedures, and outcomes of
119 obstetric patients. Furthermore, annual trends in obstetric patients' representative
120 characteristics, procedures, and outcomes were investigated. Finally, the diagnostic
121 categories of obstetric patients were analyzed. The diagnostic categories were classified
122 using the disease names registered in the JIPAD dictionary (APACHE III compliant)
123 and were determined by selecting the most applicable disease name to the ICU
124 admission by the physician in charge at each facility.
125 **Variables**
126 The patients' characteristics included the fiscal year on admission, age, weight, height,
127 body mass index, chronic comorbidities (acquired immune deficiency syndrome,
128 congestive heart failure, respiratory failure, cirrhosis, use of immunosuppressants,

hemodialysis, acute leukemia or lymphoma, and cancer with metastases), type of ICU admission (emergency surgery, non-surgical, and planned surgery), location before ICU admission (e.g., operating room, emergency department, general ward, and other hospital), emergency response admission (none, medical emergency team/rapid response team, and code blue), cardiopulmonary resuscitation prior to ICU admission, APACHE III score, APACHE II score, Japan Risk of Death (JROD) score, and type of hospital (university, public, and private). Procedures during the ICU included mechanical ventilation, noninvasive positive pressure ventilation, high-flow nasal cannula, intra-aortic balloon pumping, extracorporeal membrane oxygenation (veno-arterial and veno-venous), and renal replacement therapy (continuous and intermittent). Outcomes consisted of the discharge status (discharge to home, discharge to other facilities, and in-hospital death), ICU mortality, length of hospital stay, and length of ICU stay. The JROD score is a variant of the APACHE III score. The JROD score shows an enhanced predictive capability for in-hospital mortality in the Japanese population, as previously reported [21].

Statistical analysis

Categorical data are shown as the number (percentage), and continuous data are shown as the median (interquartile range [IQR]). The proportion of obstetric patients was

147 calculated each year, with corresponding 95% confidence intervals (95% CIs) using the
148 Clopper–Pearson test. To assess annual trends during the study period, we used the
149 Cochrane–Armitage test for proportions and the Cuzick test for continuous variables.
150 Two-sided *P* values of < 0.05 were considered significant. All analyses were performed
151 using Stata/BE 17 (STATA Corp, College Station, TX, USA).
152
153 **Results**
154 During the study period, 184,705 patients from 70 facilities were registered in the JIPAD.
155 After applying the inclusion and exclusion criteria, 750 patients were eligible for analyses
156 (**Figure 1**). The 750 obstetric patients were registered from 61 facilities. The number of
157 obstetric patients per facility, stratified by the fiscal year of admission, is shown in **Online**
158 **Resource 1**.
159 **Table 1** shows the characteristics, procedures, and outcomes of obstetric patients
160 admitted to the ICU. The study cohort had a median age of 34 years (IQR, 30–38 years).
161 Twenty (2.7%) patients had chronic comorbidities. Emergency surgery was the most
162 frequently encountered type of admission with 450 (60.0%) patients, and the operating
163 room was the most common location before ICU admission with 525 (70.0%) patients.
164 The median APACHE III score was 36 (IQR, 28–46), the median APACHE II score was

10.5 (IQR, 8–13), and the median JROD was 0.47% (IQR, 0.23%–0.98%). University hospitals were the most common type of hospital in which patients were registered. Mechanical ventilation was the most frequently performed procedure and was carried out in 247 (32.9%) patients. There were five (0.7%) in-hospital deaths and three (0.4%) ICU deaths. The median length of the hospital stay was 10 days (IQR, 7–19 days), and the ICU stay was 1 day (IQR, 1–3 days).

Figure 2 shows the annual trends in the proportion of obstetric patients among all ICU admissions. The proportion of obstetric patients did not exhibit a significant change over time (*P* for trend = 0.32). **Table 2** shows the annual trends in the representative characteristics, procedures, and outcomes of obstetric patients. The APACHE III and the JROD scores significantly decreased during the study period (*P* for trend = 0.021 and < 0.001, respectively), although age and body mass index did not significantly change. The use of mechanical ventilation was decreased, and the length of hospital stay was decreased among the outcomes (*P* for trend = 0.013 and 0.023, respectively).

Online Resource 2 shows the diagnostic categories of obstetric patients admitted to the ICU. A pregnancy-related disorder postoperatively was the most common diagnosis at ICU admission, and postpartum hemorrhage was the second most common

183 diagnosis in all of the years.

184

185 **Discussion**

186 Using a multicenter intensive care database, we examined a cohort of obstetric patients
187 admitted to the ICU from 2015 to 2020 in Japan. A total of 750 obstetric patients from 61
188 facilities were registered, representing 0.41% of all ICU patients. There were five (0.7%)
189 in-hospital deaths. The proportion of obstetric patients admitted to the ICU did not change
190 over time. However, the severity of the patients' condition, use of mechanical ventilation,
191 and length of hospital stay significantly decreased annually over the study period. Most
192 patients were admitted to the ICU because of a pregnancy-related disorder postoperatively.

193 The proportion of obstetric admission among all ICU admissions did not
194 change over the study period. This result is consistent with earlier international studies,
195 which showed that the proportion of obstetric patients is relatively low and stable
196 [10,11,13–16]. In contrast, the proportion of obstetric admissions among all ICU
197 admissions in Japan (0.41%) is lower than that reported by the ICNARC (2.1%) and by
198 the ANZICS (1.3%) [10,11]. It is crucial to exercise caution when interpreting the
199 results of this study, owing to the variations in admission criteria across countries. The
200 relatively small proportion of obstetric patients in the present study suggests that there is

potential for optimizing ICU resource allocation.

The number of in-hospital deaths in the present study was five (0.7%) among obstetric patients admitted to ICUs in Japan. The mortality rates for obstetric ICU patients reported by the ICNARC and the ANZICS and in Canada were 2.7%, 0.7%, and 1.3%, respectively [10,11,15]. Systematic reviews have shown that the maternal mortality rate ranges from 0% to 33% among obstetric patients admitted to ICUs, with considerable variability depending on the country and year of study [12]. Notably, despite Japan's reputation for having one of the lowest maternal mortality among developed countries, this study’s interpretation of mortality should be approached with caution [21].

The mortality rate in the present study was lower than that in previous reports conducted in the same study period in Japan. The Ministry of Health, Labour and Welfare in Japan has been conducting a “Model Project on Investigation and Evaluation of Maternal Deaths” since 2006, which reported a total of 204 maternal deaths from 2015 to 2020 [22]. Additionally, the Japan Society of Obstetrics and Gynecology reported a total of 253 maternal deaths from 2015 to 2020 [23]. The reason for this discrepancy in the number of deaths between the present study and previous reports may be as follows: i) approximately half of the deliveries in Japan are performed in

219 clinics, and patients may die before reaching the ICU, and ii) the JIPAD does not cover
220 all of the ICUs, such as maternal–fetal ICUs and emergency ICUs, in Japan. We
221 acknowledge that the ICUs included in the present study were designed for intensivists
222 to deliver comprehensive care, with exclusion of maternal–fetal ICUs under the
223 management of obstetricians.

224 The severity of the patients' condition and the length of hospital stay
225 significantly decreased annually from 2015 to 2020 in the present study. To the best of
226 our knowledge, this is the first study to examine the severity of illness and treatment in
227 the ICU in Japan. Half (52%) of the maternal fatalities in Japan lacked inter-facility
228 transportation [23]. In response to this issue, the Japan Maternal Emergency Rescue
229 System Implementation Council was established in 2015 to advocate for standard
230 maternal life-saving measures, such as early maternal transportation [24]. This scheme
231 may have contributed to the reduction in the severity of obstetric ICU patients in Japan.

232 The primary reason for ICU admission was postoperative pregnancy-related
233 disorders, such as cesarean section, ectopic pregnancy, adherent placenta, and other
234 pregnancy-related surgeries, which comprised 74% of ICU admissions in this study. The
235 rate of obstetric critical hemorrhage has decreased since 2010, but there was a slight
236 increase from 2019 to 2021, possibly due to changes in underlying conditions (e.g., a

237 decrease in amniotic fluid embolism and an increase in an adherent placenta) [23,25].
238 An increase in an adherent placenta may also be associated with increased assisted
239 reproductive pregnancies [26]. Similarly, the prevalence of postpartum hemorrhage is
240 increasing in other countries because of an adherent placenta and the advancing age of
241 pregnant women [27,28]. These trends should be closely monitored in the future.
242 We acknowledge some limitations to this study, even though this is the first
243 obstetric epidemiological study in Japan to analyze the largest ICU database in Japan
244 with more than 180,000 registered patients. First, the JIPAD differs from the ANZICS-
245 APD and the ICNARC-CMP in some details. The JIPAD does not implement
246 measurement codes for pregnancy. Therefore, with non-pregnancy-related disease
247 codes, data for all obstetric patients admitted to the ICU may not be available. Second,
248 the JIPAD does not include measurements, such as blood loss, transfusion volume, and
249 the fetal status, which are specific to obstetric patients. The ICNARC-CMP collects
250 obstetric variables, such as gestational age, mode of delivery, and fetal and neonatal
251 outcomes [11]. We hope that these measurements will be added to the JIPAD in the
252 future. Third, many facilities registered in the JIPAD are university hospitals with many
253 beds and many intensivists, which may not represent ICUs in Japan. In addition, the
254 JIPAD includes ICUs representing each facility. However, if there are other units (e.g.,

maternal–fetal ICUs and emergency ICUs) at the same facility, pregnant women admitted to other units may not be registered in the JIPAD. Fourth, most national reports from other countries show ICU admission rates per 1000 deliveries. However, not all Japanese ICUs are registered in the JIPAD. Therefore, the ICU admission rate per 1000 deliveries could not be calculated. Finally, ICU admission is a helpful indicator of severe maternal morbidity, but is limited by regional variations in the availability of ICU beds and the admission criteria across different countries. To address this limitation, we intend to conduct further epidemiological research on maternal healthcare in Japan, utilizing alternative databases with more comprehensive coverage. Despite the aforementioned limitations, this present study on maternal healthcare in Japan has various advantages, including severity scores and detailed intervention information.

Conclusions

In this study, there were 750 obstetric patients from 61 facilities registered in the JIPAD, representing 0.41% of all ICU patients. The severity of the patients' condition and length of hospital stay significantly decreased annually from 2015 to 2020. Most patients were admitted to the ICU because of a pregnancy-related disorder postoperatively.

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Table 1. Characteristics, procedures, and outcomes of obstetric patients admitted to the ICU.

	Obstetric patients (n = 750)
Characteristics	
Age, years	34 [30–38]
Weight, kg	59.8 [53.7–66.8]
Height, cm	158 [154–162]
Body mass index, kg/m^2	23.9 [21.6–26.5]
Chronic comorbidities	
Acquired immune deficiency syndrome	0
Congestive heart failure	3 (0.4)
Respiratory failure	1 (0.1)
Cirrhosis	0
Use of immunosuppressants	11 (1.5)
Hemodialysis	2 (0.3)
Acute leukemia or lymphoma	0
Cancer with metastases	3 (0.4)
Type of ICU admission	
Emergency surgery	450 (60.0)
Non-surgical	184 (24.5)
Planned surgery	116 (15.5)
Location before ICU admission	
Operating room	525 (70.0)
Emergency department	121 (16.1)
General ward	93 (12.4)
Other hospital	11 (1.5)
Emergency response admission	
None	714 (95.2)
MET/RRT	26 (3.5)
Code blue	10 (1.3)
Cardiopulmonary resuscitation prior to ICU admission	3 (0.4)

APACHE III score	36 [28–46]
APACHE III risk of death, %	2.9 [1.6–5.0]
APACHE II score	10.5 [8–13]
APACHE II risk of death, %	16.1 [11.0–22.9]
JROD score, %	0.47 [0.23–0.98]
Type of hospital	
University hospital	551 (73.5)
Public hospital	100 (13.3)
Private hospital	99 (13.2)
Procedures	
Mechanical ventilation	247 (32.9)
Noninvasive positive pressure ventilation	18 (2.4)
High-flow nasal cannula	20 (2.7)
Intra-aortic balloon pumping	2 (0.3)
Veno-arterial ECMO	5 (0.7)
Veno-venous ECMO	1 (0.1)
Continuous renal replacement therapy	6 (0.8)
Intermittent renal replacement therapy	5 (0.7)
Outcomes	
Discharge status	
Discharge to home	683 (91.1)
Discharge to other facilities	62 (8.3)
In-hospital death	5 (0.7)
ICU mortality	3 (0.4)
Length of hospital stay	10 [7–19]
Length of ICU stay	1 [1–3]

354 ICU, intensive care unit; MET, medical emergency team; RRT, rapid response team; APACHE, Acute
355 Physiology and Chronic Health Evaluation; JROD, Japan Risk of Death; ECMO, extracorporeal
356 membrane oxygenation.
357 Data are shown as the number (%) or median [interquartile range].
358

Table 2. Annual trends in representative characteristics, procedures, and outcomes of obstetric patients.

	2015 (n = 18)	2016 (n = 68)	2017 (n = 97)	2018 (n = 159)	2019 (n = 184)	2020 (n = 224)	*P* for trend
Characteristics							
Age, years	32 [27–37]	34 [29.5–38]	34 [30–38]	34 [30–39]	34.5 [30.5–37.5]	34 [30–37]	0.40
Body mass index, kg/m^2	25.3 [21.9–27.5]	24.0 [21.5–27.0]	23.3 [21.2–26.2]	24.8 [22.7–27.2]	23.7 [21.6–26.3]	23.2 [21.3–26.4]	0.15
APACHE III score	36.5 [31–50]	40 [32.5–48]	36 [27–46]	36 [30–47]	36 [28–46]	35 [27–44]	0.021
APACHE III risk of death, %	3.2 [2.5–5.6]	4.3 [2.3–7.5]	2.8 [1.5–4.8]	2.9 [1.7–5.2]	2.8 [1.5–5.0]	2.7 [1.5–4.3]	0.0011
JROD score, %	0.7 [0.5–1.3]	0.7 [0.3–1.6]	0.6 [0.3–1.0]	0.5 [0.2–1.1]	0.5 [0.2–1.1]	0.4 [0.2–0.8]	< 0.001
Activation of MET/RRT	0	2 (2.9)	7 (7.2)	4 (2.5)	10 (5.4)	3 (1.3)	0.32
Procedures							
Mechanical ventilation	7 (38.9)	31 (45.6)	38 (39.2)	52 (32.7)	48 (26.1)	70 (31.7)	0.013
Outcomes							
Hospital mortality	1 (5.6)	0	0	2 (1.3)	0	2 (0.9)	0.68
ICU mortality	1 (5.6)	0	0	1 (0.6)	0	1 (0.5)	0.32
Length of hospital stay	11 [9–15]	15.5 [8–48.5]	9 [7–16]	11 [8–21]	10 [8–17]	10 [7–16]*	0.023
Length of ICU stay	1 [1–2]	2 [1–3]	1 [1–3]	1 [1–2]	2 [1–3]	1 [1–3]	0.38

APACHE, Acute Physiology and Chronic Health Evaluation; JROD, Japan Risk of Death; MET, medical emergency team; RRT, rapid response team; ICU, intensive care unit.

Data are shown as the number (%) or median [interquartile range].

*One patient with a length of hospital stay of 12,346 days was excluded as an input error.

Figure legends

Figure 1. Study flowchart.

JIPAD, Japanese Intensive care PAtient Database; ICU, intensive care unit.

Figure 2. Annual trends in the proportion of obstetric patients among all intensive care unit admissions.

Online Resources

Online Resource 1. Number of obstetric patients per facility stratified by the fiscal year of admission.

Lines in the box represent median values and box edges represent 25th to 75th percentiles.

Online Resource 2. Diagnostic categories of obstetric patients admitted to the intensive care unit.

Figure 1

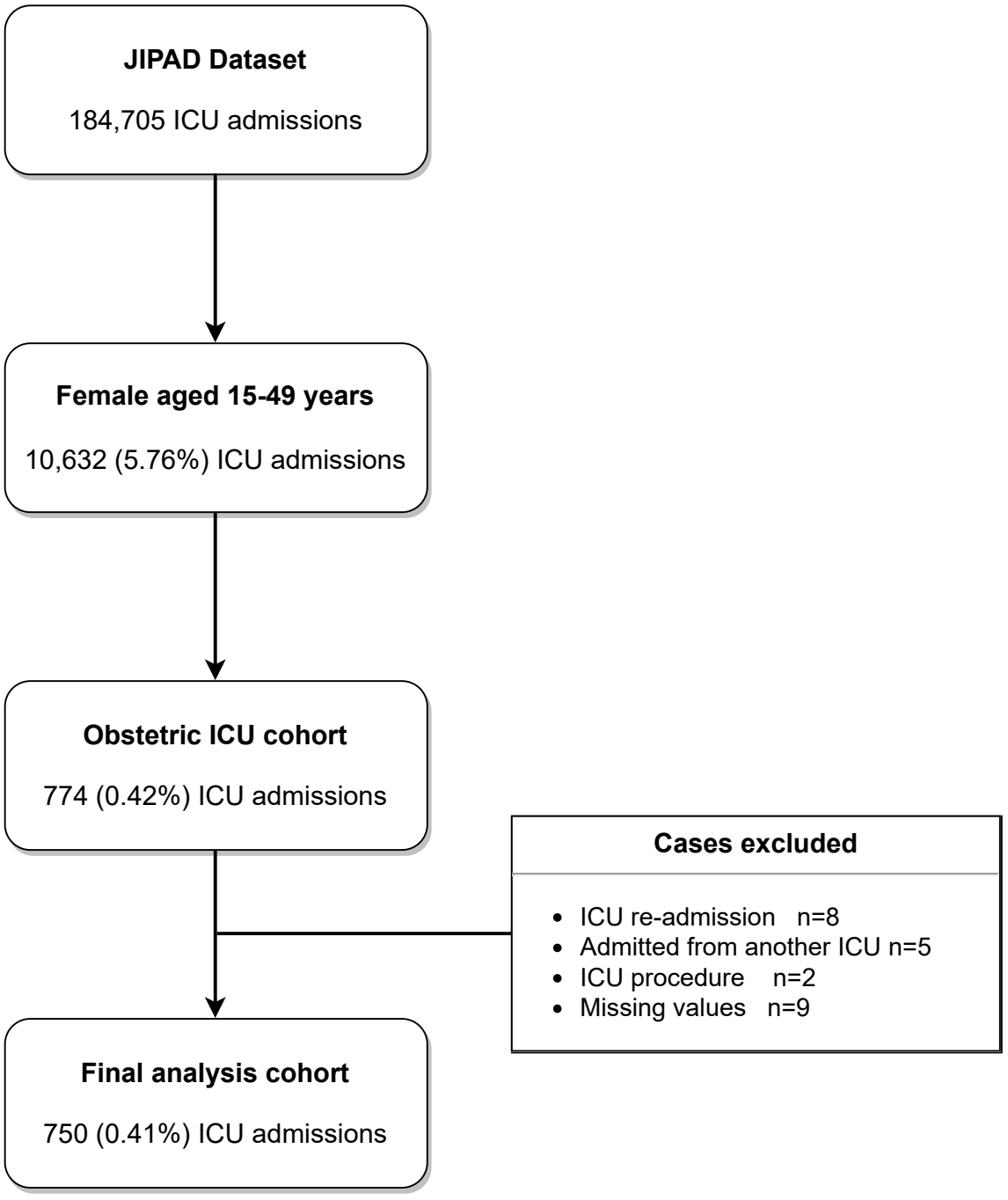
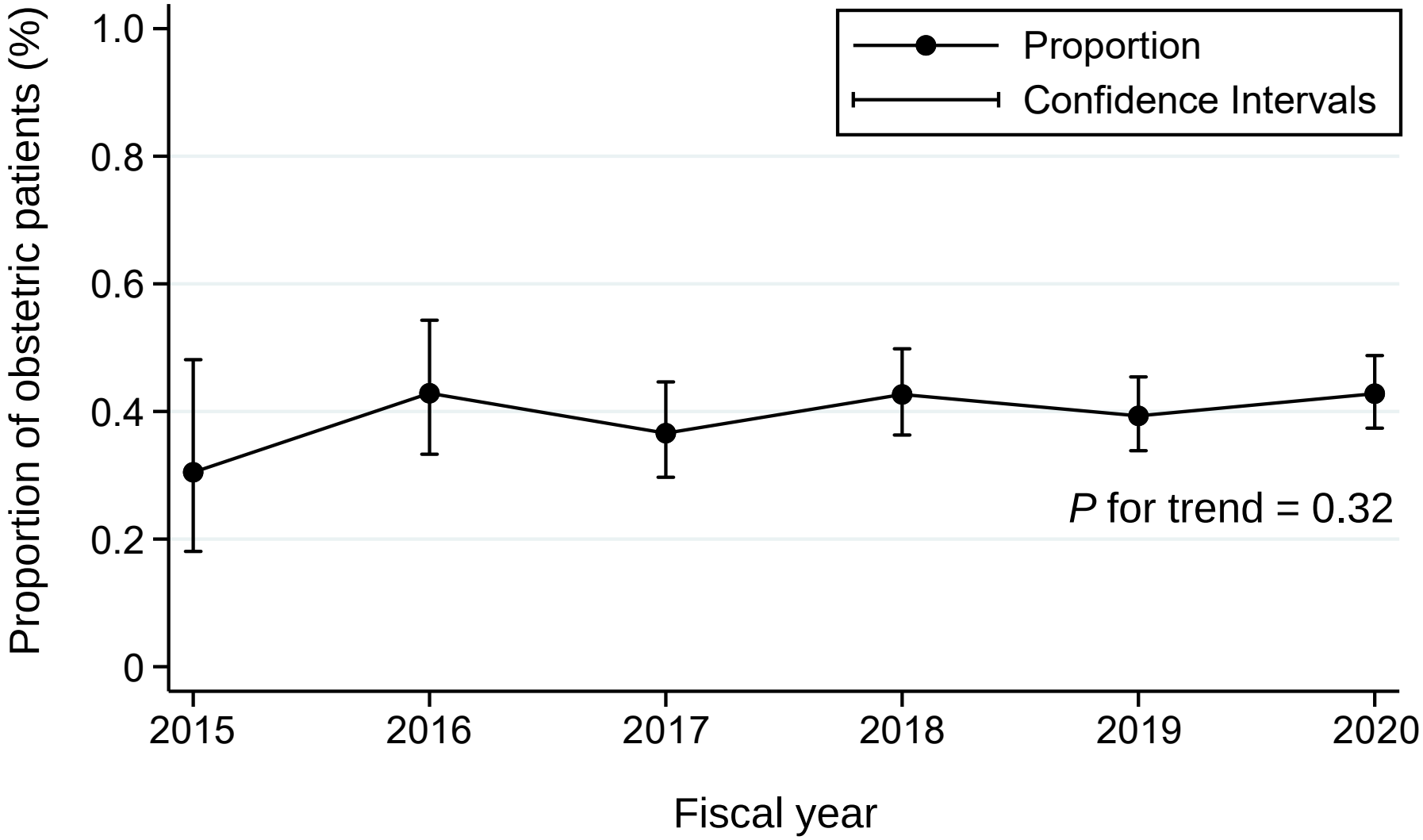
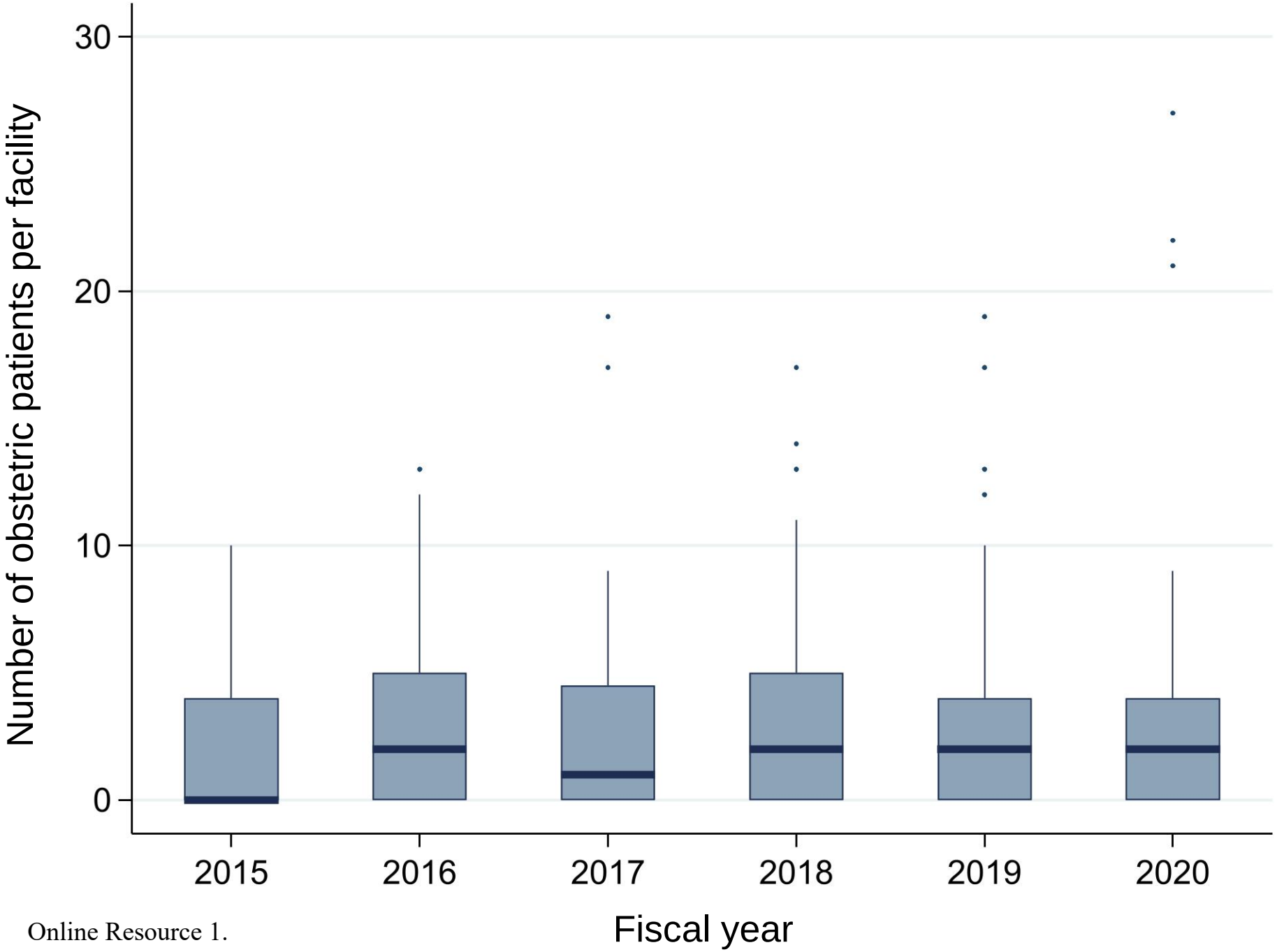

JIPAD Dataset
184,705 ICU admissions
Female aged 15-49 years
10,632 (5.76%) ICU admissions
Obstetric ICU cohort
774 (0.42%) ICU admissions
Cases excluded
ICU re-admission n=8
Admitted from another ICU n=5
ICU procedure n=2
Missing values n=9
Final analysis cohort
750 (0.41%) ICU admissions

Figure 2


Proportion
Confidence Intervals
Proportion of obstetric patients (%)
1.0
0.8
0.6
0.4
0.2
0
2015
2016
2017
2018
2019
2020
Fiscal year
P for trend = 0.32



Online Resource 1.

Online Resource 2. Diagnostic categories of obstetric patients admitted to the intensive care unit.

	2015 (N = 18)	2016 (N = 68)	2017 (N = 97)	2018 (N = 159)	2019 (N = 184)	2020 (N = 224)	Total (N = 750)
Obstetric diagnosis							
Pregnancy-related disorder postop	16 (88.9)	50 (73.5)	68 (70.1)	126 (78.3)	133 (72.3)	165 (73.7)	558 (74.4)
Postpartum hemorrhages	1 (5.6)	12 (17.7)	19 (19.6)	26 (16.4)	36 (19.6)	46 (20.5)	140 (18.7)
Pre-eclampsia or pregnancy-induced hypertension nephropathy	1 (5.6)	3 (4.4)	1 (1.0)	3 (1.9)	8 (4.4)	1 (0.5)	17 (2.3)
Non-obstetric diagnosis							
Respiratory	0	1 (1.5)	0	0	1 (0.5)	1 (0.5)	3 (0.4)
Cardiovascular	0	0	2 (2.0)	2 (1.3)	0	2 (0.9)	6 (0.8)
Sepsis	0	0	1 (1.0)	0	2 (1.1)	1 (0.5)	4 (0.5)
Neurological	0	1 (1.5)	2 (2.0)	1 (0.6)	0	1 (0.5)	5 (0.7)
Metabolic	0	0	0	0	0	3 (1.3)	3 (0.4)
Gastrointestinal	0	0	2 (2.0)	1 (0.6)	0	0	3 (0.4)
Gynecological	0	1 (1.5)	2 (2.0)	0	2 (1.1)	3 (1.3)	8 (1.0)
Renal	0	0	0	0	0	1 (0.5)	1 (0.1)
Trauma	0	0	0	0	0	0	0
Hematological	0	0	0	0	0	0	0
Musculoskeletal/Skin	0	0	0	0	1 (0.5)	0	1 (0.1)
Other/Undefined	0	0	0	0	1 (0.5)	0	1 (0.1)

The values given are number (column %).