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Ventilatory Parameters in Obstetric Patients with COVID-19 and Impact of Delivery: A Multicenter Prospective Cohort Study

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Ventilatory Parameters in Obstetric Patients with COVID-19 and Impact of Delivery: A Multicenter Prospective Cohort Study

Daniela N. Vasquez, MD[1], Roberto Giannoni, MD[2], Adriana Salvatierra, MD[3], Karina Cisneros, MD[4], Diego Lafosse, MD [5], Fernanda Escobar, MD[6], Martín Montenegro, MD [7], Paula Juárez, MD[8], Lucía Visani, MD[9], Verónica Mandich, MD[10], Erika Barrozo, MD[11], Mariana Kirschbaum, MD[12], Andrea V. Das Neves, MD[13], María F. Valenti, MD[14], María C. Canseco, MD[15], Ignacio Romero, MD[16], Pedro Macharé, MD[17], Ana K. Marquez, MD[18], Eva Rodriguez, MD[19], Cristina Palacio, MD[20], Laura Rapela,RT[21], José M. Amillategui Scenna, MD [22], Rossana Nuñez [23], Sebastián Torres, MD[24], Miguel A. González, MD[3] , Lorena Franconieri, MD[4] , Daniela Nasner, MD[6] , Patricia Okurzaty, MD[7] ,Gustavo A. Plotnikow,RT[1], Dante Intile, MD [1].

1. Sanatorio Anchorena, City of Buenos Aires, Argentina
2. Hospital Regional Ramón Carrillo, Santiago del Estero; Argentina
3. Hospital del Este "Eva Perón", San Miguel de Tucumán, Tucumán, Argentina
4. Sanatorio Antártida, City of Buenos Aires, Argentina
5. Hospital Materno Infantil Dr. F Escardó, Tigre, Buenos Aires, Argentina
6. Fundación Valle del Lili, Cali, Colombia
7. Hospital Materno Infantil Ramón Sardá, City of Buenos Aires, Argentina
8. Hospital de la Madre y el Niño, La Rioja, Argentina
9. Hospital Cuenca Alta Néstor Kirchner, Cañuelas, Buenos Aires, Argentina

10. Hospital Santojanni, City of Buenos Aires, Argentina
11. Maternidad Provincial Teresita Baigorria, San Luis, Argentina
12. Sanatorio Finochietto, City of Buenos Aires, Argentina
13. Hospital Interzonal General de Agudos Gral. San Martín, La Plata, Buenos Aires
14. Argentine Society of Critical Care Medicine, City of Buenos Aires, Argentina
15. Instituto de Maternidad y Ginecología nuestra Señora de las Mercedes, San Miguel de Tucumán, Tucumán, Argentina
16. Sanatorio Güemes, City of Buenos Aires¸ Argentina
17. Hospital Mi Pueblo, Florencio Varela, Buenos Aires, Argentina
18. Hospital Municipal de Morón, Morón, Buenos Aires, Argentina
19. Hospital Simplemente Evita, González Catán, Buenos Aires, Argentina
20. Sanatorio Itoiz, Avellaneda, Buenos Aires, Argentina
21. Hospital Municipal del Carmen, Chacabuco, Buenos Aires, Argentina
22. Hospital Provincial del Centenario, Rosario, Santa Fé, Argentina
23. Hospital Mariano y Luciano de la Vega, Moreno, Buenos Aires, Argentina
24. Sanatorio Anchorena San Martín, San Martín, Buenos Aires, Argentina

Running head: Ventilation and delivery in COVID-19 obstetric patients

Corresponding Author:

Daniela N. Vasquez, MD

Intensive Care Unit, Sanatorio Anchorena, Ciudad de Buenos Aires, Argentina.

Address: 25# 1977, Villa Elisa, La Plata, Buenos Aires, Argentina CP 1894

Phone number: 542214733200

Fax number: 542214733200

Email address: daniela.vasquez@alumni.utoronto.ca

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Abbreviations list:

IMV: invasive mechanical ventilation

HFNC: high flow nasal cannula

NIMV: non-invasive mechanical ventilation

$SOFA_{24}$: Sequential organ failure assessment during the first24h

NP: nasal prongs

NRM: non-rebreathing masks

PEEP: positive-end expiratory pressure

PP: plateau pressure

DP: driving pressure

SC: static compliance

PE: pulmonary embolism

DVT: deep vein thrombosis

BMI: body mass index

ABSTRACT

Background: Current evidence on obstetric patients requiring advanced ventilatory support and impact of delivery on ventilatory parameters is retrospective, scarce and controversial.

Research Question: What are the ventilatory parameters for COVID-19 obstetric patients and how does delivery impact them? And what are the risk factors for invasive mechanical ventilation (IMV) and for maternal/fetal/neonatal mortality?

Study Design and Methods: Prospective, multicenter, cohort study including pregnant/postpartum patients with COVID-19 requiring advanced ventilatory support in ICU.

Results: 91 patients were admitted to 21 ICUs at 29.2±4.9 weeks-63(69%) antepartum. Maximal ventilatory support: IMV (69;76%), high flow nasal cannula (20;22%) and non-invasive mechanical ventilation (2;2%). $SOFA_{24}$ was the only risk factor for IMV (OR 1.97[1.29-2.99]p0.001). Respiratory parameters at IMV onset for pregnant patients were: plateau pressure (PP) 24.3±4.5, driving pressure (DP) 12.5±3.3, static compliance (SC) 31[26-40] and PaO_2/FiO_2 142[110-176]. Respiratory parameters before (<2h) and after delivery (≤2h and 24h), respectively: PP (25.6±6.6, 24±6.7 and 24.6±5.2; p0.59); DP (13.6±4.2, 12.9±3.9 and 13±4.4; p0.69); SC (28[22.5-39], 30[24.5-44] and 30[24.5-44]; p0.058) and PaO_2/FiO_2 (134[100-230], 168[136-185] and 192[132-232.5], p0.022). Reasons for induced delivery: maternal (43/71; 60.5%), maternal and fetal (21/71; 29.5%) and fetal (7/71; 9.9%). Fourteen patients (22.2%) continued pregnancy after ICU discharge. Risk factors for maternal mortality: BMI (OR 1.10[1.006-1.204];p0.037) and comorbidities (OR

4.15[1.212- 14.20];p0.023). Risk factors for fetal/neonatal mortality: gestational age at delivery (OR 0.67[0.52-0.86]p0.002) and $SOFA_{24}$ (OR 1.53[1.13-2.08]p0.006).

Interpretation: Contrary to expectations, pregnant patient lung mechanics were similar to the general COVID-19 ICU population. Delivery was mainly induced for maternal reasons but did not change ventilatory parameters other than PaO_2/FiO_2. $SOFA_{24}$ was the only risk factor for IMV. Maternal mortality was independently associated with BMI and comorbidities. Risk factors for fetal/neonatal mortality were $SOFA_{24}$ and gestational age at delivery.

Evidence on obstetric patients requiring invasive mechanical ventilation (IMV) and the impact of delivery on maternal respiratory mechanics and oxygenation is scarce, controversial and limited to retrospective studies.[1-11] Before the COVID-19 pandemic, most studies included myriad causes of respiratory failure leading to IMV, either obstetric (preeclampsia, hemorrhage, etc.) or non-obstetric (pneumonia, sepsis, etc.), with only 10 to 71 patients.[5-7,10] Effects on respiratory parameters after delivery proved different in these two categories preventing us from generalizing conclusions for specific diseases, such as pneumonia. Evidence supporting use of other respiratory support, e.g. high flow nasal cannula (HFNC) or non-invasive mechanical ventilation (NIMV), in obstetric patients was even poorer and based on case reports or series of no more than 4 patients.[12-16]

During the second wave of the pandemic, pregnant patients were particularly affected, presenting an increased risk of ICU admission and IMV compared to non-pregnant reproductive-age women.[17] To date, few case reports and retrospective case series -primarily from high-income countries-have described obstetric patients with COVID-19 requiring IMV.[1-4,8,9,11,18] Evidence-based decisions supporting terminating or continuing pregnancy in patients with pneumonia requiring any kind of ventilatory support is still up for debate. Given this scenario, we launched a prospective multicenter binational (Argentina/Colombia) study including pregnant/postpartum patients with COVID-19 requiring any type of advanced ventilatory support in ICU. Our primary objective was to describe maternal ventilatory parameters and the impact of delivery on them. Our secondary objective was to describe risk factors for invasive mechanical ventilation (IMV) and maternal/fetal/neonatal mortality.

Methods

We followed STROBE statement check-list for this study.[19]

Design: Multicenter, binational (Argentina/Colombia), prospective, cohort study.

Setting: 20 ICUs in 7 provinces in Argentina and 1 ICU in Colombia (16 medical-surgical and 5 obstetric ICUs).

Population: Pregnant/postpartum (<42 days) patients admitted to ICU between March 20 and December 31, 2021 due to COVID-19, confirmed by PCR testing of nasopharyngeal specimens requiring any type of advanced respiratory support: HFNC, NIMV or IMV.

Measurements: Demographic data, level of education (years), comorbidity (Charlson score[20], APACHE II[21] and $SOFA_{24}$ [22]), length of stay in ICU (ICU-LOS) and hospital (hospital-LOS), maternal mortality and fetal-neonatal mortality (spontaneous/induced abortion, fetal death, and 28-day mortality), hypertension and obesity[23]. Obstetric history: antepartum/postpartum admission, gestational age on admission to ICU and/or at delivery (weeks), preterm birth (<37 weeks) classified as late/early preterm (32-36.6 and <32, respectively)[24], minimal vs. standard prenatal care (minimum 1 vs. 5 visits for term pregnancies)[25], parity, frequency and type of fetal monitoring, route of delivery (vaginal/C-section) and reason for induced delivery, if occurred (maternal/fetal/both). Respiratory support on admission (nasal prongs (NP), non-rebreathing masks (NRM), HFNC, NIMV, IMV), type of maximum ventilatory support (HFNC, NIMV, IMV), tracheostomy and prone position. PaO_2/FiO_2 was registered on admission, before IMV (<2h), after intubation (days 0, 2, 7) and before (<2h), and after delivery (<2h and at 24h). For those requiring IMV: ventilatory support prior to IMV, peripheral oxygen saturation (SpO_2) before intubation and mechanical ventilation parameters (positive-end expiratory pressure [PEEP], plateau pressure [PP], driving pressure [DP], static compliance [SC]) after intubation (days 0, 2, 7) and before (<2h), and after delivery (<2h and at 24h). Neuromuscular blockers and vasopressors were recorded. Treatment received: steroid type/dose (per Recovery trial: for pregnant patients, prednisolone 40mg or hydrocortisone 80mg b.i.d and for postpartum patients, dexamethasone 6 mg/day for 10 days[26]), convalescent plasma, tocilizumab and anticoagulation. ICU complications were detailed: ARDS[27]. preeclampsia[28], septic shock[29], acute renal failure requiring dialysis, pulmonary embolism (PE)/deep vein thrombosis (DVT)[30] and acquired infections.

Statistical analysis: Categorical variables are presented as numbers(%) and continuous variables as mean±SD or median[IQR]. Variables were compared with Student *t*-test, Wilcoxon, chi-square or Fisher tests. Multiple comparisons of parametric and non-parametric variables were analysed with repeated-measures ANOVA and Friedman tests, respectively, while both post-hoc analyses were done with Bonferroni. A p-value ≤ 0.05 was considered significant. A binary logistic regression was built to find independent predictors of IMV and maternal/fetal/neonatal mortality. Variables with p-value of ≤ 0.20 were included in univariate analysis. The multivariable model included variables with p-value of ≤ 0.05 on Wald test and/or confounding effects (variation coefficient ≥20%). The model was calibrated with Hosmer-Lemeshow goodness-of-fit test to evaluate discrepancy between observed and expected ICU mortality and IMV. SPSS-15 was used for analysis.

Ethical Considerations: This study was approved by IRB of Argentinian Society of Critical Care Medicine (PRIISABA-5012). It was performed in accordance with ethical standards laid down in 1964 Declaration of Helsinki and later amendments and with provincial laws regarding research on human beings. Patient information was de-identified prior to analysis.

Informed written consent was waived; instead, written information regarding the study was given to patients/relatives.

Results

I. Population characteristics and outcomes

Forty-three ICUs were enrolled, but 22 were excluded for not recruiting patients. Twenty-one ICUs recruited 91 pregnant/postpartum patients, 73(80%) from the public and 18(20%) from the private health sector. General and obstetric characteristics and differences between survivors/non-survivors are presented in Table-1. Organ dysfunction was frequent and associated with differential mortality (Figure-1).

There were 16 maternal deaths (17.5%) and 14 fetal/neonatal losses (15.4%); however, only 5 of these deaths were both maternal *and* fetal. BMI and presence of at least one comorbidity (Charlson score ≥1) were the only risk factors for maternal mortality (OR95%CI 1.10[1.006-1.204];p0.037 and OR95%CI 4.15[1.212- 14.20];p0.023, respectively). Of the 14 fetal/neonatal losses, there were 2 spontaneous abortions, 4 fetal and 8 neonatal deaths. Of the 4 fetal deaths, 3 occurred in nonviable fetuses (two at 23 weeks and one at 26.1), and one at 35 weeks in a severely-ill patient (APACHEII=22, PaO_2/FiO_2=87, $SOFA_{24}$=5). The threshold for fetal viability in Argentina is considered to be approximately 26 weeks.[31] Risk factors for fetal/neonatal mortality were gestational age at delivery and $SOFA_{24}$ (Table-2).

II. Respiratory support, ventilatory parameters and impact of delivery

Respiratory support on admission and differences between survivors/non-survivors is illustrated in Figure-2. Of the 36 patients admitted with HFNC, 24(66.6%) required IMV and of the 28 admitted with NRM, 21(75 %) ended-up on IMV (p0.48). Respiratory support on admission did not affect days on IMV or ICU-LOS (Table-3). Among patients receiving non-invasive oxygen support on admission (49), the only independent risk factor for IMV was $SOFA_{24}$ (OR1.97[1.29-2.99]p0.001), even after adjusting for APACHEII and BMI.

Sixty-nine patients required IMV as maximal ventilatory support, 16 of whom died (23.2%). Forty-seven of these patients were pregnant at IMV onset (day-0); mechanical ventilation characteristics and differences between survivors/non-survivors over the first week are presented in Table-4 and Fig.-3. Delivery did not improve ventilatory parameters other than oxygenation (Table-5 and Figure-4).

Twenty patients required HFNC as maximal respiratory support, 12 of whom were admitted and remained on it until discharge, while 3 and 5 required HFNC after trials of NP and NRM, respectively. Patients remaining on HFNC vs. those requiring IMV differed respectively in: BMI (27.2±3.5 vs. 30.2±6, p0.010), APACHEII (7[5.5-12.5] vs. 14[9-19]p0.001) and $SOFA_{24}$ (2.5[2-4] vs. 5[4-7]p0.000). No maternal/fetal/neonatal deaths occurred among the HFNC group.

Four patients required NIMV during ICU-LOS: 2 were on NIMV on admission and both failed, requiring IMV; 2 patients were admitted with NRM but required NIMV as maximal respiratory support. The latter two patients received NIMV for 5 and 9 days, respectively, were admitted antepartum (at 28 and 35.3 weeks) and successfully continued their pregnancies after ICU discharge. Both presented obesity class II (BMI 38.7 and 39.1) but no other comorbidities-as per Charlson score. PaO_2/FiO_2 on admission was 150 and 250, and $SOFA_{24}$ was 3.

III. Obstetric and delivery characteristics

Twenty-eight patients (31%) delivered at 34±2.7 weeks and were admitted to ICU postpartum, while 63(69%) were admitted to ICU antepartum (at 29.2±4.9) and delivered there at 31±4.4 weeks (gestational age at delivery for patients admitted postpartum vs. antepartum- p0.002). Fetal monitoring in ICU consisted mainly of intermittent fetal heart rate monitoring (18/21 ICUs=86%) every 8-12h and doppler ultrasound (15/21=71.4%) every 2-3 days; only 1 ICU performed continuous cardiotocography. Reasons for induced delivery were: maternal (43/71;60.5%), maternal and fetal (21/71;29.5%) and fetal (7/71;9.9%). Among the 63 patients admitted antepartum, 43(68.3%) required delivery during ICU-LOS, 14(22.2%) were discharged pregnant, 2(3.2%) aborted spontaneously and 4(6.3%) resulted in fetal death. Most patients admitted antepartum requiring delivery gave birth during the first 24-48h of ICU admission; population median was 3[1-6.75] days. For the 14 patients who continued pregnancy after ICU discharge, maximal respiratory support in ICU was HFNC(8;57%), IMV(4;29%) and NIMV(2;14%) and $PaO2/FiO_2$ on admission was 157.5[120-240] vs. 180[100-240] for those requiring ICU delivery (p0.9).

IV. ICU management and complications

Of 69 patients requiring IMV, 64(92.7%) received neuromuscular blockers, 25 (36.2%) required tracheostomy, and 49(71%) required prone position-33(67%) of whom were admitted antepartum-with a median of 3[1-3] proning sessions for a duration of 30[21-48] hours each. Twenty-six (53%) of the 49 patients requiring prone position received pressure-point protection. Fifteen (30.6%) of the 49 patients placed in prone position developed skin lesions.

In the whole population, 46(50.5%) presented some hospital acquired infection, 35(38.5%) septic shock, 13(14.3%) acute renal failure requiring dialysis and 15(16.4%) preeclampsia. DVT/PE was documented in 2 patients (2.2%).

All patients (91) received steroids: 61(67%) per RECOVERY trial;[25] however, 30 (33%) received non-standardized steroid and/or dose. No patient received convalescent plasma or tocilizumab. Sixty-two patients (68%) received vasopressors and 35(38.5%) were treated with anticoagulants.

Discussion

To our knowledge, this is the first *prospective* study evaluating pregnant/postpartum patients admitted to ICU with respiratory failure requiring advanced ventilatory support that sequentially analyzes the impact of delivery on lung mechanics and oxygenation. The use of HFNC did not prevent intubation. The only risk factor for IMV was $SOFA_{24}$. Ventilatory parameters in pregnant patients were similar to those in general COVID-19 ICU populations. Delivery was mainly induced for maternal reasons but did not change ventilatory parameters other than PaO_2/FiO_2. Twenty-two percent of patients were discharged pregnant with good outcomes. Risk factors for maternal mortality were BMI and presence of comorbidities. Risk factors for fetal/neonatal mortality were $SOFA_{24}$ and gestational age at delivery.

I. Population characteristics and outcomes

Ninety-one pregnant/postpartum patients with COVID-19 requiring advanced ventilatory support in ICU were included in this multicenter, binational, prospective cohort study. Most belonged to the public health sector and none was fully vaccinated; this correlates with the time frame of the study, which was performed when vaccination was not recommended for pregnant patients.[18] Although in Argentina and Colombia the healthcare system is composed of public and private sectors, the quality of care is comparable in both sectors.[32,33] While most patients had no comorbidities, the presence of at least one was independently associated with maternal mortality, as was described for the general COVID-19 population [34,35]. Forty percent of patients presented obesity, also independently associated with increased maternal mortality. As noted in previous studies, pregnant patients with COVID-19 present higher maternal/fetal/neonatal mortality compared to pregnant patients without COVID-19.[36] They also have higher ICU and IMV requirements compared to non-pregnant COVID-19 patients, even those with no comorbidities or obesity.[37]

In this study, mortality in patients requiring IMV (23.2%) was considerably lower than in the general ICU COVID-19 population (37%-57%),[34,35] which might be explained by younger age and recovery capacity of these patients. However in this cohort, maternal mortality numbers were between those described for obstetric patients in high-income countries (0-8.4%)[1,4,8,9,11,18,37,38]and upper/lower middle-income countries (78-100%),[2,3] which may be related to health budgets, patient characteristics-such us underlying diseases, and healthcare variables-such as quality of care, accessibility or system overload, among others.

Patients were severely ill on admission according to their $SOFA_{24}$, similar to critically ill obstetric patients with other community acquired pneumonias.[39] Respiratory and cardiovascular were the most frequent dysfunctions and their associated mortality coincides with previous reports (18% and 16%, respectively).[39] However, renal dysfunction, although less frequent, was associated with the highest mortality in this group (23%) and exhibited higher mortality compared to general, non-COVID critically ill obstetric population (15%).[39] The proportion of obstetric patients with COVID-19 requiring dialysis was 14.3%, compared to 3.3% among critically ill obstetric patients in general,[33] which might explain why this particular group presented worse outcomes associated with renal dysfunction.

II. Respiratory support, ventilatory parameters and impact of delivery

The most frequently-used type of ventilatory support on admission were HFNC and NRM, followed by IMV; however, neither type of respiratory support nor oxygenation parameters on admission had impact on maternal mortality. Furthermore, use of HFNC did not prevent IMV requirement compared to use of NRM, contrary to what was reported in the last meta-analysis.[40] Discrepancy between our results and those from the meta-analysis may be related to sample size issues or different populations evaluated. In our study, 20 (22%) patients were able to remain on HFNC as maximal respiratory support, with excellent maternal/fetal/neonatal outcomes. These patients were less severely ill on admission and presented lower BMI than those requiring IMV. $SOFA_{24}$ was the only risk factor for IMV among patients admitted with non-invasive respiratory support. This may provide additional information to consider before intubating these patients.

Most patients required IMV as maximum respiratory support and the majority were pregnant when intubated. This is the first *prospective* study describing obstetric patients with community acquired pneumonia requiring IMV and the impact of delivery on ventilatory parameters. Current evidence available is from retrospective case series of patients with respiratory failure due to myriad obstetric and non-obstetric causes,[5-7,10] and limited retrospective case series of COVID-19 patients.[1-4,8,9,11,18,38] Pregnancy is characterized by decreased chest wall compliance due to gravid uterus, commonly believed to impact PP or DP as well as PEEP settings, leading some to suggest permitting, for example, higher PP (35 cmH_2O).[41] However, one relevant finding of our study was that pregnant patient lung mechanics was similar to those from general COVID-19 ICU population.[34,35] Therefore, as potential differences were not evident, we need to dig deeper for the explanation. In patients with acute lung injury, impact of chest wall on respiratory mechanics was insufficiently described; and excluding those with intra-abdominal hypertension[42], it might have been overestimated.[43] Changes in respiratory mechanics seem to be determined by abnormalities in lung versus chest wall mechanics.[44] Finally, although in pregnant patients intra-abdominal pressure can be higher than in non-pregnant critically ill patients, presence of intra-abdominal *hypertension* is rare.[45] These findings have clear clinical implications because they may guide healthcare professionals to adjust ventilator settings for pregnant patients with non-obstetric causes of respiratory failure to those proven to reduce mortality in general ICU population, such as PP $<30 cmH_2O$.[46]

One of the most controversial issues regarding pregnant patients with respiratory failure is the impact of delivery on maternal lung mechanics and oxygenation. To date, the evidence available comes from four retrospective case series, which indicate some improvement in oxygenation after delivery with only one describing improvement in DP.[5,7,10,18] Tomlinson et al. found decreased oxygen requirements after delivery in 10 patients on IMV (9 presenting pneumonia).[10] Lapinsky et al. described improvement in oxygenation index after delivery in 3 out of 10 patients and static compliance in 5 out of 10 patients, most of whom were ventilated due to non-obstetric causes.[7] Hung et al. recorded improvement in oxygenation and peak pressure after delivery, but only in the subgroup of patients with obstetric causes of respiratory failure.[5] Finally, Péju et al. described improvement in oxygenation and inconsistent improvement in DP after delivery.[18] This is the first *prospective* study evaluating impact of delivery on maternal lung mechanics and oxygenation. In COVID-19 pregnant patients, delivery did not change PP or DP, which are respiratory parameters strongly associated with mortality in ARDS patients;[34,47] instead, it only improved PaO_2/FiO_2, which is not independently associated with mortality. Our results for DP are not consistent with the COVIDPREG study[18]; however, their own limitations noted large interindividual variability. Furthermore, its retrospective nature could have increased missing data and reporting bias.

In most of these patients, delivery was chosen for maternal reasons, as described by Eman et al.,[2] highlighting another key finding of this study where unsupported beliefs lead to the removal of the fetus under the assumption that this will automatically improve maternal parameters.[5,6]

III. Obstetric and delivery characteristics

After maternal stabilization, interrupting pregnancy for fetal reasons when fetal alterations persist is completely warranted because continuing pregnancy would not benefit the fetus. Notably, in this population, fetal deaths occurred in non-viable fetuses, with only one occurring at 35 weeks, but this was due to an extremely adverse maternal condition. Fetal-neonatal mortality was independently associated with gestational age and $SOFA_{24}$.

Risking the fetus without significantly improving maternal conditions could be eliminated with these results. In this study, most deliveries were performed within 48h after admission, meaning $SOFA_{24}$ was readily available and might have potentially saved fetuses. Physicians should strive for equipoise to obtain maximum benefit for both mother and child.

IV. ICU interventions and complications

Evidence about prone position during pregnancy is scarce.[11,18,48] In this study, 33 patients required prone position for a median of 30 hours during pregnancy. Proning was deemed feasible, presenting only skin complications, which might have been related to inadequate use of pressure point protection. This information may encourage physicians to use prone position, so beneficial in treating ARDS, in this particular group of patients as well.[49]

In terms of treatment, although all patients received steroids, a third did not get evidenced-based formula or dose, per RECOVERY.[26] None received tocilizumab. In most patients receiving anticoagulants, thrombosis was not documented, underscoring common, unsatisfactory medical treatment for pregnant patients.[2,18]

V. Strengths and limitations

Strengths of this study are in the number of obstetric patients included and prospective design with consecutive enrollment. Community acquired pneumonia requiring advanced respiratory support during pregnancy is uncommon, but the pandemic affected obstetric patients in particular, increasing the number of cases to evaluate. The prospective design allowed us to minimize missing data, improve quality of data, and measure variables before outcomes occur, contributing to causal pathways. It also afforded us the opportunity to gather sequential data related to impact of delivery on maternal respiratory parameters, the first study ever to do so.

Limitations of this study are its observational nature, which could have introduced some bias and confounding; although the latter was controlled by regression analysis. Selection bias might also have occurred due to overrepresentation of patients from the public health sector. Response bias is possible due to inclusion of qualified ICUs more prone to participate in studies. Generalizability could be uncertain. Although evaluating the impact of maternal hypercapnia on fetal outcomes would have provided relevant information, we opted not to request daily pCO_2 given pandemic workload considerations. Finally, neonatal morbidity was not measured; instead, we focused entirely on fetal/neonatal mortality, as it is a non-biased outcome.

Interpretation

Maternal mortality in patients with COVID-19 requiring advanced ventilatory support was independently associated with BMI and presence of comorbidities, which are outside the control of critical care practitioners. Pregnant patient lung mechanics and ventilator settings were similar to those in general ICU COVID-19 populations; supporting utilization of evidenced-based ventilator settings proven to reduce mortality in non-obstetric ARDS patients. Ventilatory parameters associated with mortality in ARDS patients were not improved by inducing delivery. Fetal/neonatal mortality was independently associated with gestational age at delivery and $SOFA_{24}$. Given what we know now, the clinical practice of inducing delivery in pregnant patients with pneumonia to improve maternal conditions should be abandoned. Gestational age and $SOFA_{24}$ should be considered in the decision-making process, thereby improving both maternal and fetal outcomes, as well as considering the psychological impact of losing a child.

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Take-Home Points:

Study Question: What are ventilatory parameters for COVID-19 obstetric patients and how does delivery impact them?

Results: Pregnant patient lung mechanics were similar to the general COVID-19 ICU population and induced delivery did not improve ventilatory parameters associated with mortality in ARDS patients.

Interpretation: Recommended **v**entilatory settings for general ARDS patients should also be used for pregnant ARDS patients and delivery should not be indicated to improve maternal lung mechanics.

Figure Legends

- Figure 1: Organ dysfunction during the first 24h in ICU and its corresponding ICU mortality among 91 pregnant/postpartum patients with COVID-19

- Figure 2: Type of respiratory support on admission for 91 pregnant/postpartum patients with COVID-19 and differences between survivors and non survivors

- Figure 3: Mechanical ventilation and oxygenation parameters over the first week after intubation for 47 patients admitted ***antepartum*** due to COVID-19 and differences between survivors and non-survivors

- Figure 4: Mechanical ventilation and oxygenation parameters before (<2h) and after delivery (<2h and 24h) among 47 patients with COVID-19 admitted antepartum

Footnotes

- Figure 2 footnote: SV: survivors, NonSV: Non-Survivors, HFNC: high flow nasal cannula, NRM: non-rebreathing masks, IMV: invasive mechanical ventilation, NP: nasal prongs; NIMV: non-invasive mechanical ventilation. * *p* 0.71 for comparison of type of respiratory support on admission between SV and NonSV

- Figure 3 footnote: [a] difference between survivors and non-survivors ($p<0.05$); [b] differences in PaO_2/FiO_2 *over* the first week for the whole group (p0.000): post-hoc Bonferroni significant differences between day 0 vs. day 2 and day 0 vs. day 7 (p.000).

- Figure 4 footnote: Comparisons of variables before (<2h) and after delivery (<2h and 24h): *D-PaO2/FiO2= p0.022 for the whole group (p0.025 between “Before (<2h),” and at “24h of delivery” in the post-hoc Bonferroni analysis)

Tables

Table 1: Characteristics and outcomes of 91 pregnant/postpartum patients with COVID-19 requiring advanced respiratory support in 21 ICUs in Argentina and Colombia during 2021.

*	All	ICU status: Survivors	ICU status: Non-survivors	*p*
Number of patients	91	75 (82.4)	16 (17.6%)	
Age (years)	31±6	31.5 ±6	31.7 ± 7	0.90
Level of education (years)	11 ±3.5	11 ±3.5	10 ±3.6	0.43
Public health sector	73 (80.2)	57 (76)	16 (100)	0.04
No comorbidity (Charlson= 0)	74 (81.3)	65 (86.6)	9 (56.25)	0.005
BMI	30 ±6	28.9 ± 5.7	33.2 ± 7.6	0.013
Obesity	36 (39.5)	26 (34.6%)	10 (62.5%)	0.05
Obesity class				0.021[†]
Obesity class I (30-34.9 kg/m^2)	17 (18.7)	16 (21.3) [b]	1 (6.25)	
Obesity class II (35-39.9 kg/m^2)	15 (16.5)	8 (10.6)	7 (43.75)	
Obesity class III (≥40 kg/m^2)	4 (4.4)	2 (2.7)	2 (12.5)	
Vaccination (one dose) [&]	8/75 (10.6)	5/62 (8)	3/13 (23)	0.28
APACHE II score	13 [7-16]	12 [6-18]	14 [9.5-14.5]	0.31
APACHE II risk (%)	14 [5.2-21]	12.6 [5.1-23]	15 [7.9-19.3]	0.41
$SOFA_{24}$ [‡]	4 [3-6]	4 [3-6]	5 [4-7]	0.077

ICU-LOS (days)	15 [8- 28]	16 [8-31]	11 [9-15]	0.12
Hospital-LOS (days)	22 [11-36]	23 [13-37]	12 [10-17]	0.01
Obstetrical characteristics				
Antepartum admission	63/91 (69.2)	54/75 (72)	9/16 (56.25)	0.21
Parity	2 [1- 3]	2 [1- 3]	2 [1- 3]	0.65
Minimal prenatal care [§]	84 (92)	70 (93)	14 (87.5)	0.43
Standard prenatal care [ǀ]	43 (47)	38 (55)	5 (31)	0.36
Gestational age on admission (weeks)	31 ± 5	31 ± 4	29.5 ± 7	0.28
Gestational age at delivery (weeks)	32.5 ± 3	32.3 ± 3	30.9 ± 6.5	0.24
Births	74	61	13	0.79
Term (≥ 37 weeks)	7 (9.5)	6 (9.8)	1 (7.7)	
Late preterm (32-36.6 weeks)	40 (54)	33 (54.1)	7 (53.8)	
Early preterm (< 32 weeks)	27 (36.5)	22 (36.1)	5 (38.5)	
Route of delivery				0.68
Cesarean section	70 (96)	56	13	
Vaginal	3 (4)	3	0	

[*] Data are presented as: n (%), mean ± SD or median [IQR]; [†] p0.01 obesity class I vs. class II; [&] No patient received a full vaccination schedule- only 8 patients in total received 1 dose; [‡] SOFA within the first 24 h of ICU admission; [§] minimal prenatal care: at least 1 visit for term pregnancies; [ǀ] standard prenatal care: at least 5 visits for term pregnancies.

Table 2: Multivariable analysis of variables associated with fetal/neonatal mortality among 91 pregnant/postpartum patients admitted to ICU due to COVID-19 in 21 ICUs in Argentina and Colombia

Variable	Odds Ratio [95% Confidence Interval] *	*p*
Sequential Organ Failure Assessment$_{24h}$	1.53 [1.13-2.08]	0.006
Gestational age at delivery	0.67 [0.52-0.86]	0.002

* Hosmer and Lemeshow test significance 0.82.

Table 3: Days on invasive mechanical ventilation and ICU-LOS according to ventilatory support on admission among COVID-19 obstetric patients requiring IMV as maximum ventilatory support in 21 ICUs in Argentina and Colombia during 2021

	Type of respiratory support on admission					
	HFNC	**NRM**	**Nasal prong**	**Non-invasive mechanical ventilation**	**IMV**	***p***
N° (patients)	24	21	2	2	20	
Days on IMV	10[10-20]	14 [5-23]	18 [11-32]	18 [7-28]	21 [11-35]	0.22
ICU-LOS	14 [11-27]	18 [11-32]	21 [18-24]	26 [15-36]	30 [18-43]	0.07

HFNC: high flow nasal cannula, NRM: non-rebreathing masks, NP: nasal prongs; NIMV: non-invasive mechanical ventilation; IMV: invasive mechanical ventilation.

Table 4: Ventilatory and oxygenation parameters among 47 pregnant patients requiring invasive mechanical ventilation due to COVID-19 and differences between survivors/non-survivors in 21 ICUs in Argentina and Colombia during 2021

*	***All= 47***	***SV= 38***	***NonSV= 9***	***p***
PaO_2/FiO_2 before IMV (<2h)	121 [86.5-162.2]	123.5 [87.7-174]	102.5 [90-129]	0.20
SpO2 (%) before IMV	90 [88-94]	91 [90-95]	89 [88-90]	0.055
PaO_2/FiO_2 –IMV day 0 (<2h)	142 [110-176]	147.5 [120-176]	120 [100-142]	0.17
PaO_2/FiO_2 -day 2	200 [139-232.2]	203 [157-230]	144 [105-237]	0.31
PaO_2/FiO_2-day 7	183 [141.75-235.5]	186 [168- 236]	100 [80-188]	0.08
PEEP (cm H_2O)-day 0	11.1 ± 2.7	11 ± 2.4	11.8 ± 3.8	0.45
PEEP (cm H_2O)-day 2	11 ± 3	10.7 ± 2.6	11.8 ± 4	0.31
PEEP (cm H_2O)-day 7	10.2 ± 2.7	9.9 ± 2.4	11.8 ± 3.5	0.10
PP (cm H_2O)-day 0	24.3 ± 4.5	23.7 ± 4.5	26.8 ±3.9	0.062
PP (cm H_2O)-day 2	23.8 ± 6.4	22.7 ± 5.7	29.2 ± 7.1	0.011
PP-(cm H_2O)-day 7	25.1 ± 5.9	23.7 ± 4.7	31.8 ± 7.2	0.001
SC (ml/cm H_2O)-day 0	31 [26-40]	32.5 [26-41]	27 [23-38]	0.48
SC (ml/cm H_2O)-day 2	33 [23.2-42]	33 [24-42]	27 [21-40]	0.75
SC (ml/cm H_2O)-day 7	29 [23.7-38]	30 [24-38]	29 [21-34.5]	0.83
DP (cm H_2O)-day 0	12.5±3.3	12.1 ± 3.5	14.1 ±2.1	0.10

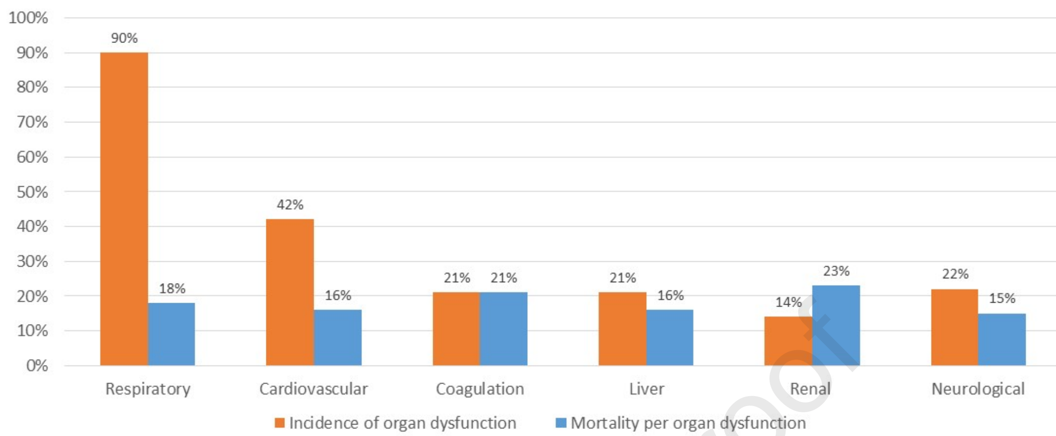
DP (cm H_2O)-day 2	12.6 ± 4.3	12.1 ± 4	15.3 ± 4.8	0.069
DP (cm H_2O)- day 7	13.8 ± 4.8	12.7 ± 3.7	19.3 ± 4.1	0.000

* Data are presented as: n (%), mean ± SD or median [IQR]; SV: survivors, NonSV: non-survivors; IMV: invasive mechanical ventilation; SpO_2: peripheral oxygen saturation; PP: plateau pressure; SC: static compliance; DP: driving pressure

Table 5: Ventilatory and oxygenation parameters before (< 2h) and after delivery (<2h and 24h) among 47 pregnant patients with COVID-19 requiring invasive mechanical ventilation in 21 ICUs in Argentina and Colombia during 2021

*	***Before Delivery (< 2h)***	***After Delivery (< 2h)***	***After Delivery (24h)***	***p***
PP (cm H_2O)	25.6±6.6	24±6.7	24.6±5.2	0.59
DP (cm H_2O)	13.6±4.2	12.9±3.9	13±4.4	0.69
SC (ml/cm H_2O)	28[22.5-39]	30[24.5-44]	30[24.5-44]	0.058
PaO_2/FiO_2	134[100-230]	168[136-185]	192[132-232.5]	0.022[#]
PEEP (cm H_2O)	11±3	12±4	11±2	0.8

** Data are presented as: n (%), mean ± SD or median [IQR]; PP: plateau pressure; SC: static compliance; DP: driving pressure; # In the post-hoc Bonferroni analysis, differences were observed between the subgroup before delivery and the subgroup at 24h after delivery (p0.025).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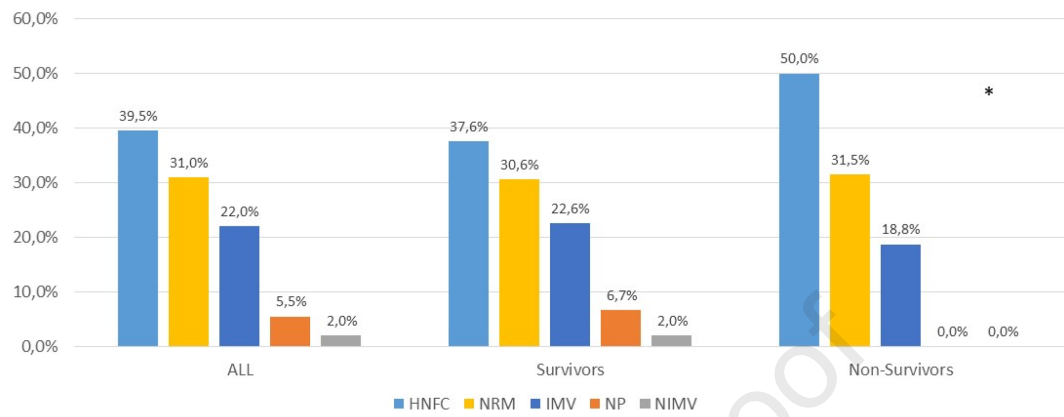
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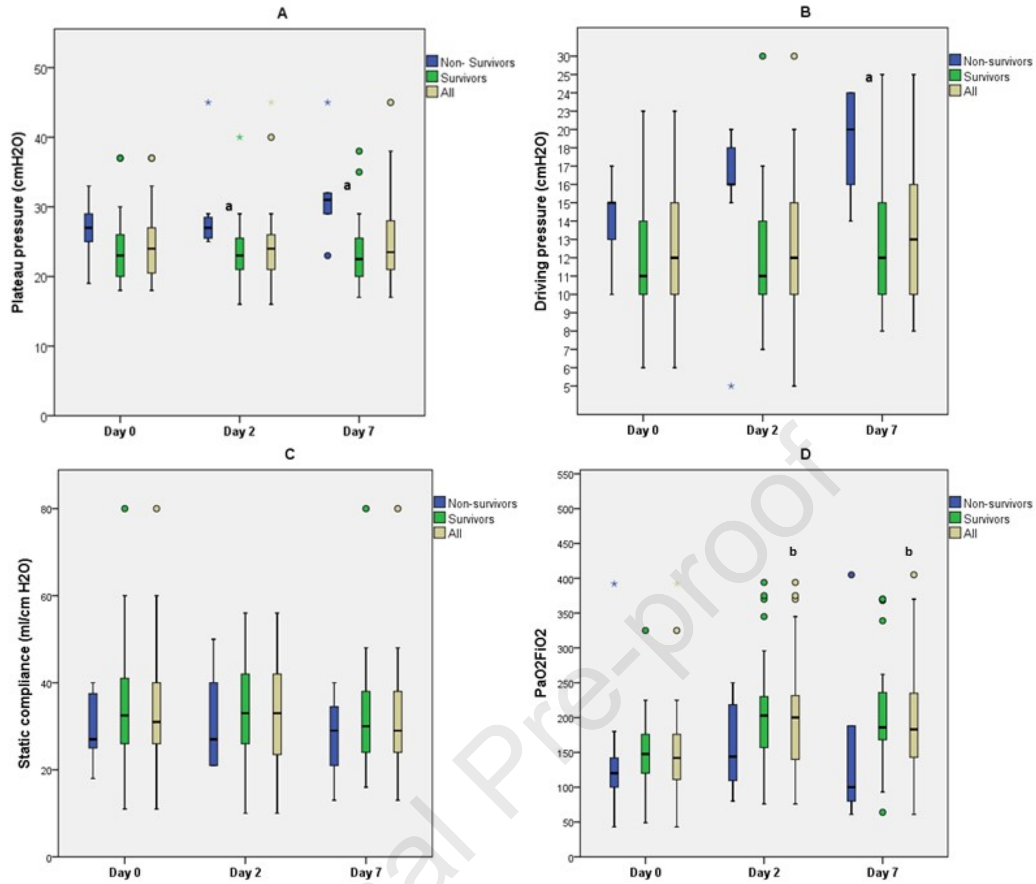
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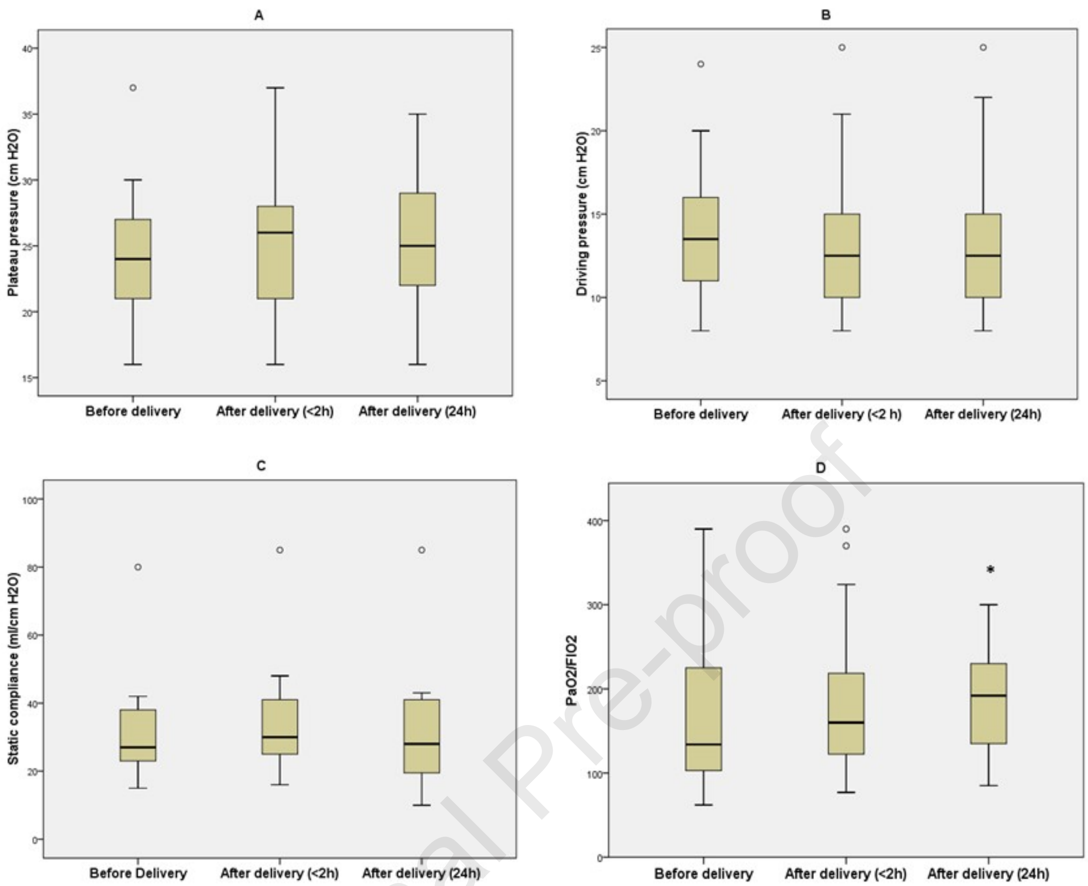
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