

Non-Invasive Positive Pressure Ventilation (NIPPV) in the Pregnant Patient: A Case Series

Carlos Montufar-Rueda^{1*}, Agnès Ditisheim², Alfredo F. Gei³, Rolando Pinilla¹, Eddie Dinh³,
Jair Vélez³, Brenda Castillo³, Luis Farias³

¹Critical Care Obstetrics Unit, Complejo Hospitalario Metropolitano de la Caja de Seguro Social, Ciudad de Panamá, Panamá

²Center for Maternal-Fetal Medicine, La Tour Hospital, Geneva, Switzerland

³Research Division, Houston Center for Maternal Fetal Medicine, Houston, Texas, USA

Email: *monlat2002@yahoo.com

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Abstract

Rationale: Acute respiratory failure is an uncommon complication of pregnancy. However, it is the most frequent organ dysfunction associated with obstetric admissions to an intensive care unit. The obstetric population is a different group due to its physiology and the presence of the fetus that lacks evidence in the literature within the subject of ventilatory support. Noninvasive positive pressure ventilation (NIPPV) is often avoided due to the lack of knowledge on the safety and efficacy of this modality. Currently, there are no guidelines for the management of respiratory failure in pregnancy. **Objectives:** To provide evidence in support of the use of NIPPV as a safe and reasonable modality for pregnant patients with respiratory failure. **Methods:** We retrospectively reviewed medical records of 29 pregnant patients of the Obstetric Critical Care Unit of a tertiary hospital in Panamá City who received NIPPV from 2013 to 2015. Failure to respond was defined as the lack of increase in the $\text{paO}_2/\text{FiO}_2$ ratio or clinical deterioration 6 hours after initiating NIPPV. Demographics, indication for NIPPV, duration of treatment, as well as maternal and fetal outcomes were collected. **Measurements and Main Results:** Mean age was 28.4 ± 6 years, mean body mass index 27.4 ± 3.3 , and mean gestational age at admission was $30^{5/7} \pm 5$ weeks. Twenty-four patients (82.8%) met the criteria for acute lung injury (ALI) and an additional two (6.9%) for acute respiratory distress syndrome (ARDS). The mean duration of ventilation was 50.6 ± 17.27 hours. Statistically significant differences were noted between the $\text{paO}_2/\text{FiO}_2$ ratios in failure and successful patients within 2 hours of NIPPV therapy ($P = 0.007$) and $\text{paO}_2/\text{FiO}_2$ ratio within 6 hours of NIPPV therapy ($P = 0.03$). Success was defined when the patient was administered NIPPV, resulting in an improvement (increase in pa/FiO_2 ratio) of her ventilatory parameters. Three patients (10.3%) failed to respond to

NIPPV and needed to be converted to invasive mechanical ventilation. Patients who required intubation had a longer duration of ICU stay ($P = 0.006$) and overall hospital stay ($P = 0.03$). None of patients presented aspiration during NIPPV therapy. **Conclusion:** The current series is the largest report of pregnant patients requiring ventilatory support who received NIPPV as first line of therapy. This report shows the usefulness of this ventilation modality, avoiding intubation with its risks, of a significant number of patients, especially ventilator-associated pneumonia.

Keywords

Respiratory Support during Pregnancy, ARDS in Pregnancy, ALI in Pregnancy, Ventilatory Support, Non-Invasive Positive Pressure Ventilation

1. Introduction

Acute respiratory failure (ARF) is an uncommon but serious condition during pregnancy, complicating 0.1% to 0.2% of pregnancies, more commonly in the postpartum period [1]. It is one of the most frequent non-obstetric cause and the most common organ dysfunction associated with obstetric admissions to an intensive care unit (ICU) [2] [3] [4] [5].

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are two important causes of acute respiratory distress. Unfortunately, there is no evidence to guide the management of these conditions during pregnancy and current literature on the subject consists mainly of case reports and case series based on a small number.

Originally developed for chronic respiratory failure, the use of non-invasive positive pressure ventilation (NIPPV) for acute respiratory failure has increased considerably over the past decades and became a first line therapy for some indications [6] [7] [8].

The main concern for using NIPPV in pregnancy is a theoretical increased risk of pulmonary aspiration of gastric contents [9] [10]. Endotracheal intubation carries a risk of failed intubation up to 8 times greater in the pregnant cohort due to airway changes including edema and hyperemia [11] [12] [13]. Recent studies have recognized NIPPV as an ideal modality for the management of obstetric respiratory complications avoiding the risks of endotracheal intubation and ICU length of stay [1] [9] [14].

We decided to report a case series of acute respiratory failure during pregnancy managed with NIPPV as the first line of therapy.

2. Methods

We retrospectively reviewed the medical records of pregnant patient of the Obstetric Critical Care Unit of a tertiary hospital in Panamá City, (Complejo Hospitalario de la Caja de Seguro Social, Panamá), who received non-invasive posi-

tive pressure ventilation from 2013 to 2015. The research protocol and a standardized data extraction form were elaborated by members of the Multinational Consortium for Research in Critical Care Obstetrics (MCRCCOB) and available on a web-platform interface (www.mcrccob.org). Demographics, indication for NIPPV and duration of treatment, maternal and fetal outcomes were collected and reported on the web-platform.

Respiratory parameters were evaluated through arterial blood gases measurements performed before initiation of NIPPV. A $\text{paO}_2/\text{FiO}_2$ ratio was calculated before initiation of NIPPV, and after 2 and 6 hours of therapy to evaluate the response to NIPPV. Failure to response was defined as the lack of increase in the $\text{paO}_2/\text{FiO}_2$ ratio or clinical deterioration 6 hours after initiating NIPPV. The occurrence of aspiration and the need to convert to invasive ventilation were also documented, as well as the use of vasopressors. Neonatal outcome was evaluated by the Apgar score, NICU admission, duration of stay and neonatal death. This study was approved by the Ethic Committee of the institution and the need for the patient consent was waived for this retrospective study.

Data are expressed in mean (standard deviation) and in percentage (absolute number). Differences between groups of patients with failure and successful NIPPV therapy were evaluated with Chi square, Fisher exact test, Student's t test and Wilcoxon rank-sum as appropriate. A p value < 0.05 was considered statistically significant. All data analysis was performed with Stata software, version 12.1 (College Station; Texas).

3. Results

Data from 29 patients admitted to the Obstetric Critical Care Unit between 2013 and 2015 was collected. Characteristics of the cohort are shown in **Table 1** and **Table 2**. The maternal mean age was 28.4 ± 6.0 years with mean body mass index of 27.4 ± 3.3 kg/m^2 . The mean gestational age at admission was 30.7 ± 5.7 weeks. Eight women (27.5%) delivered while on ventilatory support; four (13.7%) of which were spontaneous labor and the other four (13.7%) were induced for preeclampsia with severe features. All other women delivered after being discharged from the ICU. Mean gestational age at delivery was 33.1 ± 4.9 weeks. There were no maternal deaths.

Respiratory and ventilatory characteristics of the cohort are summarized in **Table 3**. The two main conditions leading to acute respiratory failure were pneumonia and extrapulmonary sepsis. Twenty-four patients (82.8%) met the criteria for ALI and two additional patients (6.9%) met criteria for ARDS. All patients received ventilation in the bilevel positive airway pressure mode (Bi-PAP), with a full-face mask. Inspiratory positive airway pressure (IPAP) settings ranged from 14 - 16 cmH_2O , expiratory positive airway pressure (EPAP) ranges from 8 - 10 cmH_2O and the fraction of O_2 percentage from 40% - 100%, according to the clinical response to NIPPV. The mean duration of ventilation was 50.6 ± 17.2 hours at the term. Three patients (10.3%) failed to respond to NIPPV and needed to be converted to invasive mechanical ventilation (**Figure 1**).

Table 1. Non-invasive positive pressure ventilation in pregnancy. Characteristics of the cohort.

Demographics	
Age (years)	28.4 ± 6.0
Gestational age at admission (weeks)	30 ^{5/7} ± 5
Body mass index (kg/m ²)	27.4 ± 3.3
Condition leading to acute respiratory failure	
<i>Obstetric</i>	
Severe preeclampsia	4 (13.8%)
Post-partum hemorrhage	1 (3.4%)
<i>Non-obstetric</i>	
Septic shock	10 (34.5%)
Pneumonia	8 (27.6%)
Acute chest syndrome	3 (10.3%)
Cardiac failure	2 (6.9%)
Asthma	1 (3.4%)
Pregnancy outcome (*)	
Delivery during ICU stay	8 (27.6%)
Gestational age at delivery	33 ± 4
Cesarean section	5 (62.5%)
Spontaneous labor	4 (50%)

Data are expressed in mean ± standard deviation or absolute numbers (percentage); (*) Limited to patients who delivered during maternal ICU admission.

Table 2. Non-invasive positive pressure ventilation in pregnancy. Patient's characteristics at admission and after NIPPV therapy.

Patient number	Age	Gestational age	Condition	Vasopressor	sPO ₂	paO ₂	paCO ₂	paO ₂ /FiO ₂	paO ₂ /FiO ₂ (within 2 hrs)	Duration of NPPV (hrs)	Conversion to mechanical ventilation
1	25	33	Septic shock of urinary source	Yes	92	61	39	290	325	74	No
2	32	285	Community acquired pneumonia	Yes	91	58	41	276	346	28	No
3	28	32	Severe Preeclampsia w/pulmonary edema	No	92	68	38	226	240	47	No
4	35	213	Community acquired pneumonia	Yes	90	59	42	280	350	39	No
5	26	35	Sepsis on appendicitis w/peritonitis	No	90	60	38	285	320	36	No
6	27	32	Septic shock of urinary source	Yes	78	62	36	295	340	42	No
7	34	313	Community acquired pneumonia	Yes	88	63	39	300	425	40	No
8	22	324	Acute chest syndrome w/pneumonia	No	91	68	45	323	340	48	No

Continued

9	31	37	Severe Preeclampsia w/pulmonary edema	No	90	59	44	196	240	70	Yes
10	38	384	Severe Preeclampsia w/pulmonary edema	No	87	62	38	295	280	96	Yes
11	19	26	Severe sepsis of urinary source	No	92	64	40	304	320	70	No
12	24	283	Community acquired pneumonia	No	90	60	36	285	350	48	No
13	37	342	Acute chest syndrome w/pneumonia	Yes	89	61	42	290	350	52	No
14	27	36	Septic shock on acute cholecystitis	Yes	88	62	39	295	450	45	No
15	36	314	Septic shock on pyelonephritis	Yes	85	58	28	276	300	40	No
16	24	31	Septic shock of urinary origin	Yes	91	58	43	276	320	45	No
17	34	385	Pulmonary edema on rheumatic mitral valvular disease	No	88	60	39	285	336	40	No
18	36	34	Hypovolemic shock/PPH	No	91	58	42	276	340	48	No
19	28	152	H1N1 viral pneumonia	No	91	60	40	240	340	50	No
20	24	223	Community acquired pneumonia	No	90	59	39	280	360	45	No
21	35	25	Acute decompensated heart failure/dilated cardiomyopathy	No	89	59	45	280	346	48	No
22	25	31	Severe preeclampsia w/pulmonary edema	No	90	61	38	290	398	42	No
23	36	26	Septic shock of urinary origin	Yes	88	60	36	285	380	48	No
24	17	263	Acute Chest syndrome w/pneumonia	No	90	62	35	295	300	52	No
25	18	34	Severe sepsis on appendicitis	No	84	58	40	276	360	72	No
26	27	22	Severe asthma w/pneumonia	No	88	58	48	276	437	72	No
27	32	346	Septic shock on pyelonephritis	Yes	90	74	27	185	148	6	Yes
28	25	35	Community acquired pneumonia	No	90	59	32	280	450	50	No
29	23	362	Community acquired pneumonia	No	88	58	31	276	380	73	No

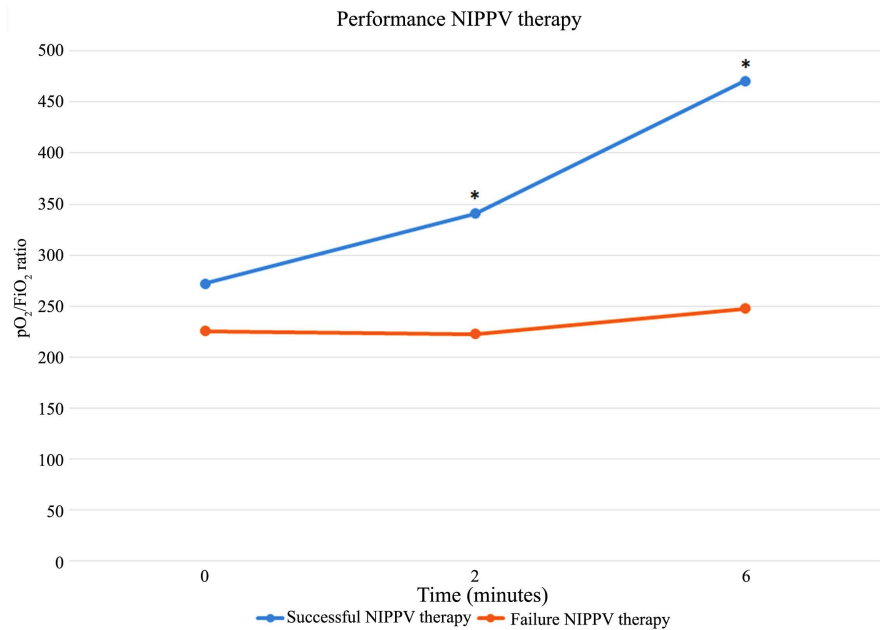


Figure 1. Non-invasive positive pressure ventilation in pregnancy. $\text{paO}_2/\text{FiO}_2$ ratio trends over time in successfully treated and failures. Legend: Statistically significant (*) differences were noted at 2 hours and 6 hours of therapy.

Table 3. Non-invasive positive pressure ventilation in pregnancy. Respiratory and ventilatory characteristics of the cohort.

Severity of acute respiratory failure	
Acute lung injury (ALI)	24 (82.8%)
Acute Respiratory Distress Syndrome (ARDS)	2 (6.9%)
$\text{paO}_2/\text{FiO}_2$ ratio at admission	276.4 ± 29.6
Need of vasopressor	11 (37.9%)
Ventilatory outcome	
Duration of ventilation (hours)	50.6 ± 17.2
Conversion to mechanical ventilation	3 (10.3%)

Data are expressed in mean \pm standard deviation or absolute number (percentage).

Statistically significant differences were noted between patients with successful and failed NIPPV therapy over time, in $\text{paO}_2/\text{FiO}_2$ ratio within 2 hours of NIPPV therapy ($P = 0.007$) and $\text{paO}_2/\text{FiO}_2$ ratio within 6 hours of NIPPV therapy ($P = 0.03$).

Correlation between $\text{paO}_2/\text{FiO}_2$ ratios in patients with successful and failed NIPPV therapy before initiation of NIPPV did not reach statistical significance.

Patients who required intubation had a longer duration of ICU stay ($P = 0.006$) and overall hospital stay ($P = 0.03$). None of the patients presented aspiration during NIPPV therapy.

Neonatal outcomes are shown in **Table 4**. The mean birthweight was 2002.5 ± 1016 grams.

Table 4. Non-invasive positive pressure ventilation in pregnancy. Neonatal outcomes (†).

Mean birthweight (grams)	2002.5 ± 932
Apgar score	
1 minute	6.5 (5 - 8)
5 minutes	8 (6 - 8)
NICU admission	4 (50%)
Neonatal morbidity	
Respiratory distress syndrome	4 (50%)
Jaundice	2 (25%)
Neonatal sepsis	1 (12.5%)
Neonatal death	1 (12.5%)

Data are expressed in mean ± standard deviation, median (range) or absolute number (percentage). (†) Limited to neonates who were born during maternal ICU admission.

4. Comment

The pregnant state is a predisposition for the development of ARDS, with reported incidence rates higher than those found in the general population [9] [15] [16] [17].

In non-pregnant adults, the use of NIPPV has shown to be associated with a reduced rate of endotracheal intubation, lower rates for associated complications and overall ICU length of stay [18] [19]. Pregnancy has so far been considered a relative contraindication due to theoretical risk of aspiration. Aspiration in pregnancy can be associated with an increased intraabdominal pressure, reduced gastroesophageal sphincter tone and decreased gastric emptying due to the mechanical effects of the uterus and increased levels of progesterone [9] [10]. On the other hand, endotracheal intubation during pregnancy is associated with higher failure rates due to changes in the airway including edema and congestion [11] [12] [13]. Pregnant women are also more susceptible to desaturation due to the increased metabolic rate and the oxygen demands of the fetus [20].

Several case reports and small series have pointed out favorable outcomes for pregnant women who were managed with NIPPV for respiratory failure, while emphasizing the importance of patient selection [21] [22] [23].

Pregnant women are typically young, able to cooperate and otherwise healthy or lacking chronic cardio-pulmonary conditions that would require prolonged mechanical ventilatory support. Most of them will have intact dentition, leading to fewer air leak, and will present with a lower acuity of illness (APACHE score), with moderate hypercarbia and acidemia [24] [25]. Most conditions leading to respiratory failure in women (pulmonary edema due to preeclampsia, sepsis and asthma) are transient and expected to respond to medical treatment within 48 to 72 hours [20] [26]. These characteristics make pregnant women an attractive subset of patient to avoid the most common predictors of failure for NIPPV, which we speculate is the reason behind the high rates of success of this modality

of ventilation in other reported series [27].

Of interest, in this study, the pregnant women (n = 3; 10.3%) who required invasive mechanical ventilation developed ventilator-associated pneumonia (VAP). The immunity of pregnancy is known to affect the response to infectious agents and avoiding an invasion of their airway may be a strategic goal of initial ventilator support.

Failure of NIPPV could be detected within 2 hours based on clinical response and $\text{paO}_2/\text{FiO}_2$ ratios. This finding can potentially assist clinicians to make preparations for invasive mechanical ventilation well in advance to respiratory claudication.

The strengths of this study include its number and the variety of pathologies treated. The favorable response rate cannot be attributed to a “healthy population bias” since over 90% of them met accepted criteria for ALI or ARDS [28]. One limitation of this study is the missing pregnancy and neonatal outcomes of patients who were treated with NIPPV and were able to continue their pregnancies. Most of these women deliver in their communities of origin. This fact limits the conclusions that can be made regarding the fetal/neonatal safety and complications of this modality of ventilation. Based on the oxygenation response we speculate that NIPPV attenuated the potentially hypoxemic effects of the background condition and allowed for pregnancy continuation that would otherwise be impossible.

5. Conclusions

In conclusion, this case series adds to the existing evidence in favor of the successful application of NIPPV for the management of respiratory failure in carefully selected and closely monitored pregnant patients. In this cases report, we show that in case of deciding to install ventilatory support, it is possible to do it with the non-invasive mechanical ventilation modality (CPAP or BiPAP) without the dreaded risk of bronchoaspiration; in addition, it is possible to avoid endotracheal intubation with its infectious consequences (ventilator-associated pneumonia), or a poor outcome due to airway management in some patients.

We believe that further trials will determine guidelines for the appropriate use of NIPPV in pregnant women, optimal patient selection and safety profile particularly regarding maternal and fetal/neonatal outcomes.

Conflicts of Interest

None of the authors are reporting any conflict of interest.

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