Nicardipine for treating severe antepartum hypertension during pregnancy: Nine years of experience in more than 800 women

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Abstract

Introduction: Women with severe hypertension during pregnancy require prompt stabilization with a combination of magnesium sulfate and rapidly acting intravenously administered antihypertensives. It remains unknown which antihypertensive is best suited for pregnancy. The present study evaluated the intravenous use of the calcium antagonist, nicardipine.

Material and Methods: This multicenter, retrospective case series included all pregnant women beyond 20 weeks of gestation with severe antepartum hypertension that were treated with intravenous nicardipine. Primary outcome measures: successful treatment, time to successful treatment, and maternal safety. Severe hypertension was defined as systolic blood pressure (SBP) of 160 mmHg or more and/or diastolic blood pressure (DBP) of 110 mmHg or more.

Results: This study included 830 women. After 1 h of treatment, two-thirds of the women had SBP below 160 mmHg and DBP below 100 mmHg. In three out of four women, the mean arterial pressure was below 120 mmHg. Within 2 h of treatment, 77.4% of women achieved successful treatment. In all cases, nicardipine was eventually effective. Within the first 2 h, 42.7% of women experienced temporary low DBP (ie below 70 mmHg) without clinical consequences for the mother or fetus. In all cases, the low DBP resolved after discontinuing or reducing the dosage of nicardipine. One case of fetal distress was attributable to maternal hypotension, and a cesarean section was performed at more than 2 h after initiating therapy. During treatment, headache, nausea, and vomiting decreased significantly.

Conclusions: To date, this was the largest case-series study on the use of nicardipine for treating severe antepartum hypertension in pregnancy. We found that nicardipine could effectively and safely treat this condition. Based on its high success rate and...
1 | INTRODUCTION

Pre-eclampsia and other hypertensive disorders are responsible for 14% of all maternal deaths worldwide, so these conditions comprise the second leading direct cause of maternal mortality. Women with pre-eclampsia and their (unborn) children are at increased risk of developing serious morbidity. Among women with antepartum severe hypertension, the incidence of maternal adverse events exceeds 25%. The general consensus recommends that persistent severe hypertension must be treated to reduce maternal mortality and morbidity. The administration of magnesium sulfate reduces the risk of eclampsia by more than half, and it probably reduces maternal mortality, but it has not shown a clear effect on serious maternal morbidity. A worldwide World Health Organization survey highlighted the fact that additional measures are needed.

In addition to magnesium sulfate, antihypertensive medication is mandatory to lower blood pressure and stabilize the patient. After stabilization, it must be determined whether to induce delivery or to postpone delivery for antenatal corticosteroid treatment, when indicated. The ideal antihypertensive drug would lower blood pressure within a short period, would have a short half-life (to facilitate titration), and would be safe for the fetus, the neonate, and the mother.

To date, the antihypertensive drugs that have been investigated most in clinical trials and systematic reviews are: (di)hydralazine, calcium antagonists (mostly nifedipine), labetalol, and ketanserin. The primary goal of the present observational study was to confirm our hypothesis that nicardipine would be effective and safe for treating severe antepartum hypertension in pregnancy.

2 | MATERIAL AND METHODS

2.1 | Trial design and participants

This multicenter, retrospective case series focused on routine clinical care. We identified eligible patients based on the nicardipine hospital pharmacy distribution list from two tertiary care hospitals in the Netherlands: the Isala Women’s and Children’s Hospital and the Erasmus Medical Center (MC). Data were collected from medical charts on patients treated from January 2006 to January 2015. The data were registered in an electronic database (SPSS 24.0). Eligible patients included all pregnant women beyond 20 weeks of gestation that had severe hypertension and were treated with intravenous nicardipine. Severe hypertension was defined as systolic blood pressure (SBP) of 160 mmHg or more and/or diastolic blood pressure (DBP) of 110 mmHg or more, measured at two separate times, 30 min apart, with a standard sphygmomanometer, based on phase V Korotkoff sounds. Patients were diagnosed with pregnancy-induced hypertension or pre-eclampsia (hypertension combined with de novo proteinuria of at least 300 mg/24 h). Patients were included, irrespective of previous or concomitant use of other oral antihypertensive medication.

2.2 | Intervention and outcome assessment

Nicardipine was administered by continuous infusion through a venous line. Nicardipine was continued as long as indicated, and for as long as the fetal and/or maternal condition did not warrant discontinuation, as judged by the attending obstetrician. During treatment, blood pressure was measured every 15 min, with a standard sphygmomanometer or an automated blood pressure device, or continuously, with an intra-arterial catheter in the radial artery. Mean arterial pressure (MAP) was calculated as: MAP = 1/3 (SBP–DBP) + DBP.

Key message

Nicardipine is safe for treating severe hypertension in pregnancy; it reduces blood pressure rapidly and effectively.

acceptable safety profile, nicardipine should be considered a first-line treatment in women with severe hypertension in pregnancy.

KEYWORDS

antihypertensive medication, maternal morbidity, neonatal morbidity, nicardipine, pre-eclampsia, severe hypertension
Patients were treated at the obstetric high dependency units of both participating hospitals.

At the Isala Women’s and Children’s Hospital, the starting dose of nicardipine was 1 mg/h. All patients received a loading dose of 500 mL colloids (a 6% hetastarch solution), at 1 h before starting nicardipine. The nicardipine dosage was increased every 15 min, by 0.5–1 mg/h, to a maximum of 10 mg/h infusion, or until the blood pressure reached the targeted level. In the Erasmus MC, nicardipine was started immediately, without a preload, at a starting dose of 1–3 mg/h. The dosage was increased every 15 min, by 0.5–1 mg/h, to a maximum of 10 mg/h, or until the blood pressure reached the targeted level. According to Dutch National Guidelines, all patients received a loading dose of 4 g magnesium sulfate over 20 min, followed by a maintenance dose of 1 g/h for seizure prophylaxis.

Fetal viability was set at 26 weeks of gestation and/or an estimated fetal weight of 500 g or greater. All women admitted between 25 and 34 weeks of gestation received antenatal corticosteroids to facilitate fetal lung maturation. Antenatal corticosteroids were administered in two intramuscular doses of 12 mg betamethasone each, 24 h apart.

### 2.3 | Outcomes

#### Primary outcomes:
- Successful treatment, defined as reaching the target SBP of less than 160 mm Hg and DBP of less than 100 mm Hg
- Treatment duration (minutes), which started at nicardipine administration and ended when successful treatment was achieved
- Maternal safety, defined as avoidance of low blood pressure (DBP < 70 mm Hg) and the absence of maternal adverse effects that required therapy discontinuation within the first 2 h of treatment

#### Secondary outcomes:
- Maternal hemodynamic parameters, measured 1 h after nicardipine initiation
- Maternal adverse effects during treatment, including headache, nausea, and vomiting, pulmonary edema, low calcium levels, reflex tachycardia (increases of more than 20 beats per minute [bpm]), bradycardia (below 40 bpm), or eclampsia
- Cesarean deliveries, based on fetal indications, as a result of maternal hypotension
- Apgar score, umbilical artery pH, and excess base in the maternal-fetal acid-base balance.

Pulmonary edema was defined as the presence of typical signs of pulmonary edema on a CT scan or chest X-ray and/or three or more clinical parameters of pulmonary edema (dyspnea, basal crepitations, oxygen saturation < 95%, arterial oxygen content < 10 kPa, need for supplemental oxygen and/or administration of diuretics).

### 2.4 | Statistical analyses

Categorical data are presented as the number (%) and groups were compared with the chi-squared test. Skewed data are presented as the median (minimum–maximum) and/or interquartile range, and groups were compared with the Mann–Whitney U test. Normally distributed data are presented as the mean (standard deviation) and groups were compared with the independent samples t test. Univariate logistic regression was performed to test associations between variables. Statistical analyses were performed with SPSS version 24 (IBM). Finally, all study results were compared between the two participating hospitals.

### 2.5 | Ethical approval

This study was reviewed and approved by the Medical Ethics Committees of the Erasmus MC (reference number MEC-2011-144 on May 10, 2011) and the Isala Women’s and Children’s Hospital.

### 3 | RESULTS

In total, 1042 pregnant women were treated with nicardipine during the study period, according to the hospital pharmacy distribution lists. We excluded 114 women from the study, because their blood pressure lowered without medication or they were mentioned twice on the list. Intravenous nicardipine administration was started in 928 patients. We excluded 98 women, because SBP and DBP were below 160 and 110 mm Hg, respectively, when the nicardipine infusion started, or they were transferred to another hospital, or nicardipine had been started in another hospital. One woman received nicardipine before 20 weeks of gestation. Finally, a total of 830 patients were included in this study. Table 1 shows the baseline demographics and clinical characteristics of all participants.

Data on primary outcomes are shown in Table 2. Data were missing on treatment success for 27 women. Nicardipine was effective in 100% of 803 women, and of these, 77.4% reached successful treatment within 2 h. Low DBP occurred temporarily within the first 2 h in 42.7% of women. In 21.5% of women, nicardipine was discontinued after successful treatment was achieved, because of maternal adverse effects.

The mean gestational age at delivery was 33 weeks (range 21–42 weeks). Vaginal deliveries were achieved in 338 women, and 485 women underwent cesarean sections.

At 1 h after nicardipine initiation, nicardipine resulted in significant reductions in SBP, DBP, and MAP (Table 3). The SBP was less than 160 mm Hg in nearly two out of three women. The MAP was below 120 mm Hg in three out of four women. In some women (11.5%), the maternal heart rate increased significantly, and reflex tachycardia occurred. Conversely, in other women (20.6%), the maternal heart rate decreased.
Nicardipine treatment reduced the occurrences of headache, nausea, and vomiting (Table 4). The incidence of pulmonary edema increased, and the median serum calcium decreased. One patient developed bradycardia, which immediately stopped after nicardipine was discontinued.

In one woman (0.1%), fetal distress due to maternal hypotension resulted in a cesarean section. In 46 women, fetal demise occurred because of pregnancy termination or a non-intervention policy (Table 5).

The success rate for nicardipine was 100% in both hospitals (Table 6), and the times to success were comparable. We noted no clinically relevant differences in hemodynamic parameters at 1 h after treatment initiation between the two hospitals. However, low DBP occurred significantly more frequently at Erasmus MC (47%) compared with Isala Women’s and Children’s Hospital (36%). Consequently, nicardipine was discontinued more frequently at Erasmus MC than at Isala Women’s and Children’s Hospital.

4 | DISCUSSION

This study showed that intravenous nicardipine successfully reduced blood pressure in all women. A previous study also showed successful treatment in all patients ($n = 27$), when they used nicardipine as an escape medication for other treatment options (ketanserin or dihydralazine). A previous review confirmed that nicardipine had a high success rate (91%) for treating severe hypertension in pregnancy. Both SBP and DBP were significantly reduced in all patients. Our definition of treatment success was based on previous evidence that the risk of stroke increased when
### Table 3: Hemodynamic parameters in pregnant women with hypertension, at 1 h after starting nicardipine

| Parameter                      | Before nicardipine, n = 826 | After 1 h, n = 800 | p value<sup>a</sup> |
|--------------------------------|-----------------------------|--------------------|---------------------|
| SBP (mm Hg)                    | 170 (140–270)               | 152 (86–288)       | <0.001              |
| DBP (mm Hg)                    | 105 (80–145)                | 91 (34–130)        | <0.001              |
| MAP (mm Hg)                    | 127 (107–177)               | 112 (51–161)       | <0.001              |
| Maternal heart rate (bpm)      | 81 (47–144)                 | 90 (40–149)        | <0.001              |
| Reflex tachycardia             | 92 (11.5%)                  |                    |                     |
| Decrease in heart rate         | 117 (20.6%)                 |                    |                     |
| SBP <160 mmHg                  | 507 (63.4%)                 |                    |                     |
| MAP <120 mmHg                  | 608 (75.8%)                 |                    |                     |

Note: Data are the mean (interquartile range) or the number (%).

Abbreviations: bpm, beats per minute; DBP, diastolic blood pressure; MAP, mean arterial blood pressure; SBP, systolic blood pressure.

<sup>a</sup>Evaluation of the mean differences between groups with 95% confidence intervals (two-sample t test).

### Table 4: Maternal adverse effects in pregnant women during nicardipine treatment for hypertension

| Adverse effects                  | Before nicardipine | During nicardipine | p value<sup>a</sup> |
|----------------------------------|--------------------|--------------------|---------------------|
| Headache                         | 354/827 (42.7%)    | 113/742 (15.2%)    | <0.001              |
| Nausea and vomiting              | 224/828 (27%)      | 39/742 (5.3%)      | <0.001              |
| Pulmonary edema<sup>b</sup>      | 4/830 (0.5%)       | 14/830 (1.7%)      | 0.027               |
| Calcium (mmol/L) corrected for serum albumin (g/L) | 2.26 (1.65–2.95) | 2.14 (1.34–2.48) | <0.001 |
| Tachycardia                      | 73/742 (9.8%)      |                    |                     |
| Bradycardia                      | 1/742 (0.1%)       |                    |                     |
| Eclampsia                        | 4/830 (0.5%)       | 1/830 (0.1%)       | 0.200               |

Note: Data are the number (%) or median (range).

<sup>a</sup>Evaluation of the mean differences between groups with 95% confidence intervals (two-sample t test).

<sup>b</sup>Pulmonary edema was defined as the presence of typical signs of pulmonary edema on CT or chest X-ray images and/or three or more of the following clinical signs: dyspnea, basal crepitations, oxygen saturation <95%, arterial oxygen content <10 kPa, need for supplemental oxygen and/or administration of diuretics.

### Table 5: Fetal and neonatal outcomes after pregnant mothers with hypertension were treated with nicardipine

| Fetal outcomes                                                                 | Number/total (%) |
|-------------------------------------------------------------------------------|------------------|
| Fetal demise                                                                  | 46/815 (5.6%)    |
| Fetal distress followed by emergency cesarean section                         | 297/830 (35.8%)  |
| Fetal distress followed by emergency cesarean section <4 h after starting nicardipine | 22/830 (2.7%)    |
| Fetal distress due to maternal hypotension, followed by emergency cesarean section <4 h after starting nicardipine | 1/830 (0.1%)    |
| Full course of antenatal corticosteroids                                      | 292/403 (72.5%)  |

| Neonatal outcomes                             | Number/total (%) |
|-----------------------------------------------|------------------|
| Umbilical artery pH                           | 7.25 (6.70–7.43) |
| Base excess                                   | -4.0 (-35 to 10) |
| Apgar score at 1 min                          | 7 (0–10)         |
| Apgar score at 5 min                          | 8 (1–10)         |
| Apgar score at 10 min                         | 9 (5–10)         |

Note: Data are the number (%) or median (range).
SBP was 160 mmHg or more and a consensus that DBP should be below 100 mmHg.

Previous studies showed that the desired blood pressure could be reached within a short time after initiating nicardipine. In one study, target blood pressures were reached within 23 min in 70% of patients, and within 130 min in 91% of patients. Hanff et al showed that target blood pressures were reached within a median of 23 min. Our data confirmed those findings. No data were available on the times to target blood pressures for other antihypertensives.

In our opinion, the intravenous route was preferable for achieving rapid blood pressure control. The California Maternal Quality Care Collaborative advised that, for severe hypertension, treatment should start within 1 h, to reduce blood pressure as soon as possible.

The high nicardipine success rate was comparable to the success rates of the more commonly prescribed calcium antagonist nifedipine (84%) and (di)hydralazine (88%), and higher than those achieved with labetalol (80%) and ketanserin (73%–79%). A previous systematic review and meta-analysis showed that the rates of achieving target blood pressures were not significantly different for diazoxide, nicardipine, nifedipine, hydralazine, and other agents. Another meta-analysis showed comparable success rates with nicardipine and labetalol, but nicardipine was more often associated with headache, tachycardia, and nausea, and labetalol was more often associated with hypotension. It is difficult to draw definitive conclusions about the effectiveness of different treatment options because of inconsistent results among studies and the different definitions for successful treatment. However, no previous study has shown 100% successful treatment and significant blood pressure reductions in all

### Table 6: Comparisons between the two participating hospitals (Isala Zwolle and Erasmus MC) for outcomes in pregnant mothers with hypertension treated with nicardipine

| Primary outcomes | Definition | Isala Zwolle | Erasmus MC | p valuea |
|------------------|------------|--------------|------------|----------|
| Successful treatment | SBP <160 and DBP <100 mmHg | 362 (100%) | 468 (100%) | — |
| Time to successful treatment (min) | 79 (5–1678) | 75 (5–3175) | 0.594 |
| Hypotension; N = 818 | DBP <70 mmHg | 130 (36.3%) | 219 (46.8%) | 0.001 |
| | DBP <60 mmHg | 35 (9.8%) | 74 (15.8%) | 0.008 |
| Maternal adverse effects that led to nicardipine discontinuation | Hypotension | 28 (7.7%) | 62 (13.2%) | 0.013 |
| | Low calcium | 18 (4.9%) | 0 (0%) | <0.001 |
| | Tachycardia | 1 (0.3%) | 3 (0.6%) | 0.465 |
| | Other | 21 (5.8%) | 37 (7.9%) | — |

### Secondary outcomes

- **Hemodynamics after 1 h**
  - SBP (mm Hg): 151 (92–205) vs. 153 (86–288), p = 0.043
  - DBP (mm Hg): 95 (54–125) vs. 90 (34–130), p < 0.001
  - MAP (mm Hg): 113 (70–147) vs. 111 (51–161), p = 0.013
  - Maternal heart rate (bpm), N = 569: 89 (40–143) vs. 91 (48–150), p = 0.067
  - Increase MHR >20 bpm: 44 (15.9%) vs. 48 (16.4%), p = 0.858
  - Decrease MHR <20 bpm: 56 (20.2%) vs. 61 (20.9%), p = 0.842
  - SBP <160 mmHg: 226 (64.4%) vs. 281 (62.6%), p = 0.599
  - MAP <120 mmHg: 263 (74.9%) vs. 345 (76.5%), p = 0.576

- **Maternal adverse effects**
  - Headache: 58 (16%) vs. 55 (11.8%), p = 0.075
  - Nausea and vomiting: 15 (4.1%) vs. 24 (5.1%), p = 0.506
  - Pulmonary edema: 4 (1.1%) vs. 10 (2.1%), p = 0.252
  - Calcium (corrected for serum albumin): 2.1 (1.34–2.41) vs. 2.17 (1.44–2.48), p < 0.001
  - Tachycardia: 44 (12.2%) vs. 29 (6.2%), p = 0.003
  - Bradycardia: 3 (0.8%) vs. 3 (0.6%), p = 0.752

- **Fetal outcome**
  - Full course of antenatal corticosteroids: 94 (73.4%) vs. 198 (72%), p = 0.764

Note: Data are the number (%) or median (range). Abbreviations: bpm, beats per minute; DBP, diastolic blood pressure; MAP, mean arterial blood pressure; MHR, median heart rate; SBP, systolic blood pressure.

aEvaluation of the mean differences between groups with 95% confidence intervals (two-sample t test).
patients. Nicardipine is licensed for treating acute severe hypertension and postoperative hypertension. For those indications, it has shown potent, rapid blood pressure reductions with intravenous administration.\textsuperscript{21} Here, we showed that, in pregnancy, nicardipine also potently and rapidly reduced blood pressure.

The high success rate and short time to success had some disadvantages. We found a high rate of maternal low blood pressure during nicardipine treatment. In 90 of 349 women, treatment had to be (temporarily) stopped because of low blood pressure. However, after stopping or reducing the dosage, the blood pressure resolved within minutes, in all cases, without compromising the maternal or fetal condition. Therefore, in this case series, only one case of clinically relevant hypotension occurred during nicardipine treatment. After an emergency cesarean section, a healthy neonate was born.

Pharmacokinetic data showed that nicardipine had a short half-life (2–5 min).\textsuperscript{21} The short half-life is a plausible explanation for why low blood pressure rapidly resolved after a dosage reduction. With longer intravenous infusions (24–48 h), the half-life increased (from 1 to 2 h). In our experience, this longer half-life did not result in an increase in low blood pressure occurrences because, in most women, blood pressure stabilized after 24–48 h or the infant was delivered. Other potential causes of maternal hypotension include epidural/spinal anesthesia during labor, a cesarean section, or co-medication. In addition, the concomitant use of calcium antagonists and magnesium sulfate may have a synergistic effect on blood pressure. Previous case reports found that neuromuscular blockade and hypotension occurred with nifedipine combined with magnesium sulfate, but they found no causal explanation.\textsuperscript{22,23} Two other studies found that magnesium sulfate combined with nicardipine had no adverse reactions.\textsuperscript{13,24} The concomitant use of magnesium sulfate and calcium antagonists should be monitored carefully.

The two hospitals we studied had distinct outcomes. A logistic regression analysis showed that a higher starting dosage ($>1$ mg/h) did not predict low blood pressure. However, the preload with colloid fluid might explain the lower incidence of low blood pressure in the Isala Women’s and Children’s Hospital. Currently, a preload is standard in both hospitals.

Pulmonary edema associated with pre-eclampsia has a multifactorial origin. The factors that appear to play a role include fluid overload, reduced plasma oncotic pressure, increased capillary permeability, and increased pulmonary capillary hydrostatic pressures, caused by elevated cardiac afterload.\textsuperscript{25} Studies have shown that nicardipine significantly decreased systemic vascular resistance (afterload) and increased cardiac output and ejection fraction.\textsuperscript{21,26} Accordingly, one might expect nicardipine to have a protective effect on pulmonary edema, consistent with the low incidence of pulmonary edema (1.7%) observed in our population, compared with previous studies (3%–10%).\textsuperscript{2} However, we found that the incidence of pulmonary edema increased during the nicardipine infusion. In considering potential causes, we ruled out several factors. In our population, none of the patients with pre-existing cardiac disease developed pulmonary edema. Volume overload was an unlikely factor, because most cases occurred in the Erasmus MC, and so, they did not receive a fluid preload. A logistic regression analysis showed that differences in demographic characteristics between the two cohorts were not associated with pulmonary edema, nor was the use of co-medication (labetalol, nifedipine, magnesium sulfate). The treatment-to-delivery interval was not significantly different between groups with and without pulmonary edema (3.5 days vs 3 days, respectively, $p = 0.427$). Therefore, the pre-delivery management did not increase the risk of developing pulmonary edema. However, another logistic regression analysis showed that gestational age at admission was a significant predictor of pulmonary edema. Women that developed pulmonary edema had an earlier gestational age (median 29 weeks) compared with women without pulmonary edema (median 32 weeks, $p < 0.001$). Therefore, a potential explanation could be that the pathophysiology was different between women with early-onset and late-onset pre-eclampsia, as mentioned previously.\textsuperscript{27} Early-onset pre-eclampsia may be initiated by compromised maternal cardiovascular adaptations, which can increase the risk of pulmonary edema.

During treatment, serum calcium declined and, in some women, the nicardipine infusion was stopped because of low serum calcium, although no maternal symptoms occurred. In our study population, low serum calcium was most likely caused by hypermagnesemia, which suppresses parathyroid hormone secretion.\textsuperscript{28} Hypocalcemia induced by nicardipine has not been described previously. Hence, when symptomatic hypocalcemia occurs (spasm, tetany, seizures, decreased cardiac function, prolonged QT interval) during the magnesium sulfate infusion, we advise to (temporarily) stop the magnesium sulfate infusion and correct calcium levels with intravenous calcium therapy. It might not be necessary to stop the nicardipine infusion, when hypocalcemia occurs.

Reflex tachycardia occurred frequently, and in a few cases (0.5%), it led to therapy discontinuation. However, nicardipine was associated with lower frequencies of other symptoms, like headache, nausea, and vomiting.

Severe bradycardia (10 bpm) occurred in one woman at 10 h after nicardipine was started. The bradycardia resolved after stopping the nicardipine infusion. Bradycardia during a nicardipine infusion has rarely been described in the literature.\textsuperscript{29} Direct sinus bradycardia due to nicardipine was described in a rat model.\textsuperscript{30} Arima et al concluded that the cause of bradycardia was unclear; potential contributing factors included sympathetic tone depression by epidural anesthesia, hypothermia, and paroxysmal atrial fibrillation.\textsuperscript{31} Hence, during a nicardipine infusion, obstetric care units should be equipped with tools for closely monitoring hemodynamic parameters (measurements every 15 min), particularly in the first 24 h after starting nicardipine. These features, combined with the fact that nicardipine must be administered intravenously, make it unsuitable for use in less-than-optimal circumstances and in low-income countries.

Our study had some limitations. It had a retrospective design, lacked a control group, and the treatment required the concomitant use of magnesium sulfate. Although magnesium sulfate may have a synergistic effect on lowering blood pressure, it cannot be withheld...
from pregnant women with severe hypertension, because it has pre-
ventive effects on eclampsia. Additionally, a control group was not
necessary to show treatment effectiveness, because the treatment
was 100% effective. The main strengths of our study were the large
cohort and the well-defined study population.

5 | CONCLUSION

To date, this study was the largest case series on the use of nicardi-
pine for treating severe antepartum hypertension in pregnancy. We
found that nicardipine was highly effective and safe for this indica-
tion. Based on its high success rate and acceptable safety profile,
nicardipine should be considered a first-line treatment for women
with severe hypertension in pregnancy.

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AUTHOR CONTRIBUTIONS

This study was conceived by SNB, MH, JC, SH, ME, and JD. SNB,
JD, and ME conducted the statistical analysis and wrote the first
draft of the manuscript. MH, JC, and SH contributed significantly
to data analysis, interpretation and writing of the manuscript. When
compiling the manuscript, EQUATOR reporting guidelines were fol-
lowed. All authors have read and approved the final version of this
manuscript.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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