Incidence and Associated Factors for Neuraxial Anaesthesia-Related Hypotension in COVID-19 Parturients Undergoing Caesarean Delivery: A Multicenter Case-Control Study

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Research

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Abstract

Background: COVID-19 continues to spread globally and results in additional challenges for perioperative management in parturients. The purpose of this study was to determine the incidence and identify associated factors for neuraxial anaesthesia-related hypotension in COVID-19 parturients during caesarean delivery.

Methods: We performed a multicenter case-control study at 3 medical institutions in Hubei province, China from 1th January to 30th May 2020. All ASA Physical Status II full term pregnant women who received caesarean delivery under neuraxial anaesthesia were eligible for inclusion. The univariate analysis and binary logistic regression analysis were used to identify the independent predictors of neuraxial anaesthesia-related hypotension.

Results: Present study included 102 COVID-19 parturients. The incidence of neuraxial anaesthesia-related hypotension was 58%. Maternal abnormal lymphocyte count (OR = 3.41, p = 0.03), full stomach (OR = 3.22, p = 0.04), baseline heart rate (OR = 1.04, p = 0.03), experience of anaesthetist (OR = 0.86, p = 0.02) and surgeon (OR = 0.76, p = 0.03), and combined spinal-epidural anaesthesia technique (OR = 3.27, p = 0.02) were associated with neuraxial anaesthesia-related hypotension. The area under the receiver operating characteristic curve achieved 0.83 which was significantly higher than 0.5 (p < 0.001). And the sensitivity, specificity and percentage correct were 75%, 79% and 75%, respectively. The Hosmer-Lemeshow test showed a good calibration of the model (H = 2.01, DF = 8, p = 0.98).

Conclusions: Maternal abnormal lymphocyte count, full stomach, baseline heart rate, experience of anaesthetist and surgeon, and combined spinal-epidural anaesthesia technique were identified as the independent predictors of neuraxial anaesthesia-related hypotension.

Background

With increased levels of testing and effective contact tracing and isolation, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is no longer uncontrollable. However, COVID-19 continues to spread globally. Furthermore, modelling studies have suggested a second COVID-19 epidemic wave would occur and peak in the end of 2020 or the beginning of 2021 due to gradual relaxing of test-trace-isolate strategy and reopening of public transport (Malki, Atlam et al., 2020; Panovska-Griffiths, Kerr et al., 2020).

Although the clinical characteristics of COVID-19 parturients is similar with non-pregnant COVID-19 patients(Allotey, Stallings et al., 2020), COVID-19 results in additional challenges for perioperative management in parturients (Zheng, Hebert et al., 2020) and the outcomes of maternal and fetal appeared barely satisfactory (Yu, Li et al., 2020). Based on clinical practices and expert opinions, neuraxial anaesthesia in preference to general anaesthesia for caesarean delivery in COVID-19 parturients(Bhatia, Columb et al., 2020). However, more attention should be focused on neuraxial anaesthesia-related hypotension in COVID-19 parturients.
According to previous studies, the incidence of neuraxial anaesthesia-related hypotension in healthy parturients was 12.6–93.3%, depending on the different definitions of hypotension and neuraxial anaesthesia regimen (Pereira, Grando et al., 2011; Sun, Liu et al., 2016; Chiang, Hasan et al., 2017; Riffard, Viet et al., 2018; Hasanin, Amin et al., 2019; Kaufner, Karekla et al., 2019; Salama and Elkashlan, 2019; Knigin, Avidan et al., 2020). And the associated factors for neuraxial anaesthesia-related hypotension in obstetric and non-obstetric patients have been examined well (Pereira, Grando et al., 2011; Rimsza, Perez et al., 2019; Knigin, Avidan et al., 2020). What's more, a scoring system, based on maternal age, preoperative mean arterial blood pressure (MAP) and heart rate, has been used to predict neuraxial anaesthesia-related hypotension in parturients (Bishop, Cairns et al., 2017). However, the effects of these factors on the incidence of neuraxial anaesthesia-related hypotension in COVID-19 parturients are yet to be explored. Therefore, the aim of this study was to investigate the incidence and associated factors for neuraxial anaesthesia-related hypotension in COVID-19 parturients.

Materials And Methods

Design and Setting

We conducted a multicenter case-control study at Renmin Hospital of Wuhan University, Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology, and Yichang Central People's Hospital from 1th January to 31th May, 2020. The methodology in this study was based on the international guidelines for observational studies according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) 2010 statement (von Elm, Altman et al., 2014). The three medical institutions were designated as the diagnosis and treatment center for COVID-19 patients (including pregnant women) in Hubei province, China. SARS-CoV-2 nucleic acid test was used to screen COVID-19 in all parturients. And the chest CT scan was performed on parturients after delivery.

We planned to collect all ASA Physical Status II full termed pregnant women who received caesarean delivery (ICD-10 codes O82.0–O82.9 and O84.2) under neuraxial anaesthesia. Parturients who had a cesarean delivery after failed vaginal delivery were also included. The exclusion criteria included inadequate blockade (requiring the addition of a general anaesthetic administration) or incomplete data.

Anaesthesia Protocol

Neuraxial anaesthesia techniques was according to the established protocol of institutions. All parturients had an intravenous line placed before anaesthesia puncture. And non-invasive blood pressure (BP), electrocardiograph, pulse oximetry was used from anaesthesia commence to surgery finish. Parturients received puncture procedure in the upright position under strict aseptic precaution and then kept in supine left lateral tilt position until the end of surgery. Sensory block height was assessed bilaterally using loss of cold sensitivity to alcohol every 3 to 5 minutes. All BP recordings in this study were performed with the patient in the supine position.
Data And Definition

The data were independently collected from the electronic medical records using a prefabricated table, and crossed-check by two investigators in each institution. The table mainly addressed maternal variables: age, BMI, gravidity, delivery times, preoperative laboratory parameters (the count of white blood cell and lymphocyte, the concentration of hemoglobin (Hb), C-reactive protein (CRP) and fasting glucose), the count of COVID-19 signs and symptoms, and neonatal weight. Anaesthetic and surgical variables were also included: urgency of surgery (emergency or elective), full stomach, baseline heart rate, systolic blood pressure (SBP) and MAP, antiemetic, vasoconstrictor oxytocin and calcium preparation utilization, infusion volume, experience of surgeon and anaesthetist. The other variables were neuraxial anaesthesia technique (epidural anaesthesia (EA), spinal anaesthesia (SA) or combined spinal-epidural anaesthesia (CSE)), site, approach frequency and local complications of anaesthesia puncture, local anaesthetic dose, block-surgery time and sensory block height.

Hypotension was defined as the SBP below 100 mmHg, the MAP below 80% of the baseline value (the mean of repeated measurements before commencing anaesthesia). Infusion volume over 1000 ml or vasoconstrictor utilization were also considered as the presence of hypotension. Neuraxial anaesthesia-related hypotension was based on a single episode of defined hypotension from the time of local anaesthetic injection until 15 minutes after delivery of the newborn. Block-surgery time was defined as the interval between local anaesthetic injection and skin incision. Experience of surgeon and anaesthetist were defined as the length of employment.

Statistics

The data was imported to IBM SPSS Statistics 25 for analysis. Outliers of continuous variables were replaced by the value of specific percentile (5% or 95%) value. Univariate analysis was conducted by the t test, Mann-Whitney U test, χ² test or Fisher’s exact test as appropriate. The variables at a two-tailed p-value ≤ 0.20 in univariate analysis were identified and entered into binary logistic regression model by backward elimination (likelihood ratio) method after collinearity test by linear regression with enter method. The model’s discriminative power was checked with a receiver operating characteristic (ROC) curve according to the probabilities obtained from binary logistic regression analysis. The goodness model was tested by Hosmer-Lemeshow test. The variables at a two-tailed p-value < 0.05 in the binary logistic regression analysis were considered as the independent associated factors for hypotension in this study.

Results

During the study period, 102 ASA Physical Status II full termed COVID-19 parturients without preoperative comorbidities (such as chronic hypertension and hypertensive disorders of pregnancy) were available (Fig. 1). Among of them, SBP lower than 100 mmHg was found in 27 parturients and MAP lower than
80% of the baseline value was found in 4 parturients. Twelve parturients received volume infusions more than 1000 ml and 38 parturients were treated with vasoconstrictor. The incidence of neuraxial anaesthesia-related hypotension was 59 (58%) in present study (Table 1).

| Definition                                      | Count |
|------------------------------------------------|-------|
| SBP ≤ 100 mmHg                                 | 27 (27%) |
| MAP < 80% of baseline value                    | 4 (4%) |
| Infusion volume > 1000 ml                      | 12 (12%) |
| Vasoconstrictor utilization                    | 38 (38%) |
| Count                                          | 43 (42%) |
| 7 (7%)                                         | 23 (23%) |
| 11 (11%)                                       | 2 (2%)  |
| 3 (3%)                                         | 9 (9%)  |
| 4 (4%)                                         |        |
| 59 (58%)                                       |        |

SBP, systolic blood pressure; MAP, mean arterial blood pressure; baseline value, the mean of repeated measurements before commencing anaesthesia.

All of COVID-19 parturients with neuraxial anaesthesia-related hypotension were employed as case group (n = 59). The others were employed as control group (n = 43). Parturients in case group had a relatively lower age (p = 0.10) than that in control group. Singleton pregnancy occurred in all parturients. Most of COVID-19 parturients had a history of cesarean delivery, followed by primigravida. There were relatively higher abnormal rate of lymphocyte count (p = 0.02) and more parturients present signs and symptoms of COVID-19 (p = 0.16) in case group. However, statistically significant differences were not observed between two groups regarding the others maternal variables and the neonatal weight (Table 2).
Table 2
The comparison of maternal variables in COVID-19 parturients with neuraxial anaesthesia-related hypotension (Case group) and without (Control group). Values are presented as median (IQR) or number (proportion).

| Variables                                      | Case group          | Control group        | p-value |
|------------------------------------------------|---------------------|----------------------|---------|
| Age; years                                     | 25 (22 to 33)       | 28 (24 to 33)        | 0.103*  |
| BMI; kg/m²                                     | 27.0 (21.9 to 29.6) | 25.5 (19.9 to 29.1)  | 0.228   |
| Delivery times                                 |                     |                      | 0.572   |
| 1                                              | 19 (32%)            | 18 (42%)             |         |
| 2                                              | 39 (66%)            | 24 (56%)             |         |
| 3                                              | 1 (2%)              | 1 (2%)               |         |
| Abnormal white blood cell count                | 8 (14%)             | 6 (14%)              | 0.954   |
| Abnormal lymphocyte count                      | 37 (63%)            | 17 (40%)             | 0.021*  |
| Hemoglobin; g.l⁻¹                              |                     |                      | 0.505   |
| < 100                                          | 23 (39%)            | 14 (33%)             |         |
| ≥ 100                                          | 36 (61%)            | 29 (67%)             |         |
| Abnormal C-reactive protein concentration      | 4 (7%)              | 3 (7%)               | 0.969   |
| Impaired fasting glucose                       | 3 (5%)              | 3 (7%)               | 0.688   |
| Count of COVID-19 signs and symptoms           |                     |                      | 0.161*  |
| 0                                              | 19 (44%)            | 13 (22%)             |         |
| 1                                              | 15 (35%)            | 24 (41%)             |         |
| 2                                              | 7 (16%)             | 15 (25%)             |         |
| 3                                              | 4 (10%)             | 1 (2%)               |         |
| 4                                              | 3 (5%)              | 1 (2%)               |         |
| Neonatal weight; kg                            | 3.51 (3.15 to 3.73) | 3.53 (3.11 to 3.85)  | 0.522   |

BMI, body mass index; Count of COVID-19 signs and symptoms, fever (body temperature more than 37.3°C), cough, fatigue, chest distress, dyspnoea and diarrhea. The chi-square test or Fisher’s exact test was used to compare the two groups for categorical variables, Mann-Whitney U test for continuous variables.

* Compare Case group with Control group, p-value < 0.20.
There were relatively higher rate of emergency surgery (54% vs 35%, $p = 0.05$), full stomach (41% vs 21%, $p = 0.04$) and second puncture (32% vs 19%, $p = 0.12$), higher baseline heart rate ($p = 0.04$), more experience of surgeon ($p = 0.02$) and anaesthetist ($p = 0.03$) in case group than those in control group. There were no significant differences in baseline SBP and MAP, the rate of oxytocin and calcium preparation utilization and the infusion volume in two groups. All COVID-19 parturients received dexamethasone. Over 70% parturients were treated with metoclopramide, however, fewer than half of parturients had 5-HT$_3$ receptor antagonist intervention. The commonly used vasoconstrictor was methoxamine followed by phenylephrine, metaraminol and noradrenaline (Table 3).
Table 3
The comparison of anaesthetic and surgical variables in COVID-19 parturients with neuraxial anaesthesia-related hypotension (Case group) and without (Control group). Values are presented as median (IQR) or number (proportion).

| Variables                        | Case group      | Control group    | p-value |
|----------------------------------|-----------------|------------------|---------|
| n = 59                           | n = 43          |                  |         |
| Urgency of surgery               |                 |                  | 0.053*  |
| Elective                         | 27 (46%)        | 28 (65%)         |         |
| Emergency                        | 32 (54%)        | 15 (35%)         |         |
| Full stomach                     | 24 (41%)        | 9 (21%)          | 0.035*  |
| Baseline heart rate; bpm          | 87 (82 to 107)  | 82 (80 to 98)    | 0.037*  |
| Baseline SBP; mmHg                | 115 (107 to 127)| 117 (109 to 127)| 0.692   |
| Baseline MAP; mmHg                | 83 (74 to 90)   | 82 (80 to 98)    | 0.456   |
| Antiemetic utilization           |                 |                  |         |
| Metoclopramide                   | 43 (73%)        | 32 (74%)         | 0.862   |
| 5-HT3 receptor antagonist        | 28 (48%)        | 16 (37%)         | 0.302   |
| Vasoconstrictor utilization      | -               |                  |         |
| Methoxamine                      | 17 (29%)        | -                |         |
| Metaraminol                      | 8 (14%)         | -                |         |
| Phenylephrine                    | 12 (20%)        | -                |         |
| Noradrenaline                    | 1 (2%)          | -                |         |
| Oxytocin utilization             | 15 (25%)        | 13 (30%)         | 0.591   |
| Calcium preparation utilization  | 8 (14%)         | 6 (14%)          | 0.954   |
| Infusion volume                  | 750 (550 to 850)| 700 (600 to 800)| 0.688   |
| anaesthesia puncture frequency   |                 |                  | 0.124*  |
| 1                                | 40 (68%)        | 35 (81%)         |         |

SBP, systolic blood pressure; MAP, mean arterial blood pressure; Baseline value, the mean of repeated measurements before commencing anaesthesia; Experience, the length of employment. The chi-square test was used to compare the two groups for categorical variables, Mann-Whitney U test for continuous variables.

* Compare Case group with Control group, p-value < 0.20.
| Variables                      | Case group | Control group | p-value |
|-------------------------------|------------|---------------|---------|
|                               | n = 59     | n = 43        |         |
| 2                             | 19 (32%)   | 8 (19%)       |         |
| Experience of surgeon; years  | 4 (4 to 5) | 5 (4 to 7)    | 0.016*  |
| Experience of anaesthetist; years | 3 (2 to 7) | 8 (3 to 10)  | 0.028*  |

SBP, systolic blood pressure; MAP, mean arterial blood pressure; Baseline value, the mean of repeated measurements before commencing anaesthesia; Experience, the length of employment. The chi-square test was used to compare the two groups for categorical variables, Mann-Whitney U test for continuous variables.

* Compare Case group with Control group, p-value < 0.20.

Contrast with control group, the majority of anaesthetic technique was CES (40% vs 63%) but not EA (61% vs 37%) in case group (p = 0.02). The case group had a relative higher dose of lidocaine (p = 0.11) and ropivacaine (p = 0.05) than those in control group. And, there were significant differences in the site (p = 0.14), but not in approach and local complications of anaesthesia puncture, block-surgery time and sensory block height in two groups. All CES were performed through the median approach and no additional local anaesthetic were applied epidurally until the end of the surgical procedure (Table 4).
Table 4
The comparison of neuraxial anaesthesia technique in COVID-19 parturients with neuraxial anaesthesia-related hypotension (Case group) and without (Control group). Values are presented as median (IQR) or number (proportion).

| Variables                                   | Case group           | Control group          | p-value |
|---------------------------------------------|----------------------|------------------------|---------|
| Neuraxial anaesthesia technique             |                      |                        | 0.021*  |
| EA                                          | 22 (37 %)            | 26 (60%)               |         |
| CSE                                         | 37 (63%)             | 17 (40%)               |         |
| Frequency of anaesthesia puncture           |                      |                        | 0.137*  |
| L2-3                                        | 19 (32%)             | 22 (51%)               |         |
| L3-4                                        | 31 (53%)             | 15 (35%)               |         |
| L4-5                                        | 9 (15%)              | 6 (14%)                |         |
| Approach of anaesthesia puncture            |                      |                        | 0.383   |
| Median                                      | 58 (98%)             | 41 (95%)               |         |
| Lateral                                     | 1 (2%)               | 2 (5%)                 |         |
| Local complications                         |                      |                        |         |
| Bleeding                                    | 3 (5%)               | 2 (5%)                 | 0.920   |
| Paresthesia                                 | 2 (3%)               | 1 (2%)                 | 0.753   |
| Lidocaine dose; mg                          |                      |                        | 0.110*  |
| EA                                          | 340 (320 to 360)     | 300 (270 to 370)       |         |
| Ropivacaine dose **; mg                     |                      |                        | 0.049*  |
| EA                                          | 60 (51 to 62)        | 45 (38 to 75)          |         |
| CES                                         | 12 (11 to 13.5)      | 14 (10.5 to 14)        |         |
| Block-surgery time **; min                  |                      |                        | 0.369   |

EA, epidural anaesthesia; CES, combined spinal-epidural anaesthesia; Block-surgery time, the interval between local anaesthetic injection and skin incision. The chi-square test or Fisher’s exact test was used to compare the two groups for categorical variables, Mann-Whitney U test for continuous variables.

* Compare Case group with Control group, p-value < 0.20.

** Variables were transformed by square root method.
| Variables                  | Case group          | Control group        | p-value |
|----------------------------|---------------------|----------------------|---------|
|                            | n = 59              | n = 43               |         |
| EA                         | 20 (15 to 25)       | 18 (15 to 25)       |         |
| CES                        | 7 (5 to 9)          | 5 (2 to 8)          |         |
| Sensory block height       |                     |                      | 0.204   |
| T2                         | 2 (3%)              | 0                    |         |
| T4                         | 16 (27%)            | 7 (16%)              |         |
| T6                         | 41 (70%)            | 35 (81%)             |         |
| T8                         | 0                   | 1 (2%)               |         |

EA, epidural anaesthesia; CES, combined spinal-epidural anaesthesia; Block-surgery time, the interval between local anaesthetic injection and skin incision. The chi-square test or Fisher’s exact test was used to compare the two groups for categorical variables, Mann-Whitney U test for continuous variables.

* Compare Case group with Control group, p-value < 0.20.

** Variables were transformed by square root method.

Based on these results and clinical practice, maternal age, count of COVID-19 signs and symptoms, lymphocyte count, urgency of surgery, full stomach, baseline heart rate, frequency of anaesthesia puncture, experience of surgeon and anaesthetist and neuraxial anaesthesia technique were identified as candidate variables. After collinearity test, no significant collinearity was found among those candidate variables (Table 5). Binary logistic regression analysis revealed that abnormal lymphocyte count (OR (95% CI) = 3.41 (1.17 to 9.94), p = 0.03), full stomach (OR (95% CI) = 3.22 (1.06 to 9.84), p = 0.04), baseline heart rate (OR (95% CI) = 1.04 (1.01 to 1.08), p = 0.03), experience of anaesthetist (OR (95% CI) = 0.85 (0.75 to 0.97), p = 0.02) and surgeon (OR (95% CI) = 0.76 (0.60 to 0.97), p = 0.03), and combined spinal-epidural anaesthesia technique (OR (95% CI) = 3.27 (1.17 to 9.13), p = 0.02) were significantly associated with neuraxial anaesthesia-related hypotension (Table 6). The area under the ROC curve was 0.83 and the asymptotic 95% CI was 0.79 to 0.91 (p < 0.001). And the threshold of 59% showed the best relationship between sensitivity (75%) and specificity (79%) for predicted probability (Table 7). The Hosmer-Lemeshow test demonstrated good calibration of the model (H = 2.01, DF = 8, p = 0.98). The percentage of correctly categorized patients on the basis of this threshold was 75%.
Table 5
The collinearity test for candidate variables of neuraxial anaesthesia-related hypotension in COVID-19 parturients undergoing caesarean delivery.

| Variables                                      | Tolerance | Variance inflation factor |
|------------------------------------------------|-----------|---------------------------|
| Age                                            | 0.989     | 1.089                     |
| Count of COVID-19 signs and symptoms           | 0.868     | 1.152                     |
| Abnormal lymphocyte count                      | 0.836     | 1.195                     |
| Urgency of surgery                             | 0.878     | 1.139                     |
| Full stomach                                   | 0.950     | 1.053                     |
| Baseline heart rate                            | 0.968     | 1.034                     |
| Frequency of anaesthesia puncture              | 0.873     | 1.145                     |
| Experience of anaesthetist                     | 0.924     | 1.083                     |
| Experience of surgeon                          | 0.889     | 1.125                     |
| Neuraxial anaesthetic technique                | 0.936     | 1.068                     |

Count of COVID-19 signs and symptoms, fever (body temperature more than 37.3°C), cough, fatigue, chest distress, dyspnoea and diarrhea. Baseline value, the mean of repeated measurements before commencing anaesthesia; Experience, the length of employment. The variables at tolerance < 0.1 and variance inflation factor ≥ 10 were identified the presence of collinearity.
Table 6
The binary logistic regression analysis for candidate variables of neuraxial anaesthesia-related hypotension in COVID-19 parturients undergoing caesarean delivery. Values are presented as odds ratio (95% CI).

| Variables                                      | OR (95% CI)          | p-value |
|------------------------------------------------|----------------------|---------|
| Age                                            | 0.947 (0.868 to 1.003) | 0.220   |
| Count of COVID-19 signs and symptoms           | 1.719 (0.997 to 2.966) | 0.051   |
| Abnormal lymphocyte count                       | 3.406 (1.168 to 9.938) | 0.025*  |
| Full stomach                                    | 3.222 (1.056 to 9.835) | 0.040*  |
| Baseline heart rate                             | 1.043 (1.005 to 1.083) | 0.026*  |
| Experience of anaesthetist                      | 0.854 (0.751 to 0.971) | 0.016*  |
| Experience of surgeon                           | 0.764 (0.604 to 0.968) | 0.026*  |
| CSE technique                                   | 3.267 (1.169 to 9.134) | 0.024*  |

Count of COVID-19 signs and symptoms, fever (body temperature more than 37.3°C), cough, fatigue, chest distress, dyspnoea and diarrhea. Baseline value, the mean of repeated measurements before commencing anaesthesia; Experience, the length of employment; CES, combined spinal-epidural anaesthesia.

*p-value < 0.05.
Table 7
The receiver operating characteristic curve analysis for continuous candidate variables of neuraxial anaesthesia-related hypotension in COVID-19 parturients undergoing caesarean delivery. Values are presented as odds ratio (95% CI).

| Variables                              | Area (95% CI)                | p-value | Sensitivity | Specificity | Cut off value |
|----------------------------------------|------------------------------|---------|-------------|-------------|---------------|
| Predicted probability                  | 0.827 (0.794 to 0.905)       | < 0.001*| 75%         | 79%         | 59%           |
| Count of COVID-19 signs and symptoms   | 0.637 (0.582 to 0.746)       | 0.019*  | 78%         | 44%         | 0.5           |
| Baseline heart rate                    | 0.621 (0.510 to 0.733)       | 0.037*  | 75%         | 54%         | 82.5          |
| Experience of anaesthetist             | 0.374 (0.261 to 0.487)       | 0.030*  | 19%         | 52%         | 8.5           |
| Experience of surgeon                  | 0.365 (0.255 to 0.475)       | 0.020*  | 14%         | 63%         | 5.5           |

Count of COVID-19 signs and symptoms, fever (body temperature more than 37.3°C), cough, fatigue, chest distress, dyspnoea and diarrhea. Baseline value, the mean of repeated measurements before commencing anaesthesia; Experience, the length of employment.

*p-value < 0.05.

Discussion

Hypotension is the most commonly complication of neuraxial anaesthesia in parturients undergoing caesarean delivery. Investigating factors associated with neuraxial anaesthesia-related hypotension is a valuable strategy to reduce the incidence of it. Current study reported that the incidence of neuraxial anaesthesia-related hypotension in COVID-19 parturients undergoing caesarean delivery was 58% and abnormal lymphocyte count, full stomach, baseline heart rate, experience of anaesthetist and surgeon, CSE technique were the independent predictors of it.

Latest meta-analysis showed that vasoconstrictor (such as metaraminol, norepinephrine and phenylephrine) intervention was effective and safe in preventing and treating neuraxial anaesthesia-related hypotension in healthy parturients. Leg compression and fluid load might be also helpful (Pereira, Grando et al., 2011; Chooi, Cox et al., 2020; Singh, Singh et al., 2020). Present study also reported similar intervention of vasoconstrictor and fluids in COVID-19 parturients. Thus, vasoconstrictor utilization and extra infusion volume were considered as the presence of hypotension in COVID-19 parturients.

Prior studies found that maternal age (Bishop, Cairns et al., 2017; Fakherpour, Ghaem et al., 2018), emergency surgery (Hartmann, Junger et al., 2002), baseline heart rate (Bishop, Cairns et al., 2017; Fakherpour, Ghaem et al., 2018) and experience of anaesthetist (Shitemaw, Jemal et al., 2020), but not
BMI (Bishop, Cairns et al., 2017; Bishop, Cairns et al., 2017) and preoperative haemoglobin concentration (Bishop, Cairns et al., 2017), were linked with neuraxial anaesthesia-related hypotension in parturients receiving caesarean delivery. Consistent results were observed in COVID-19 parturients. In emergency parturients, SA or CES seems to be the more common anaesthetic regimens due to the simplicity of implementation and the speed of onset. Yet, those advantages of SA or CES allow a higher incidence of hypotension, when compared with EA. Additionally, in emergency medical scenarios, inadequate preoperative preparation, full stomach, sympathetic hyperactivity would increase the risk of hemodynamic instability. Although significant collinearity was not been found between anaesthetic technique and urgency of surgery in present study, the effects of COVID-19 epidemic on urgency of surgery and the choice of anaesthetic technique should be taken into account.

A higher baseline heart rate always means a higher activation of sympathicus that will result in a relatively greater reduction in sympathetic resistance induced by neuraxial anaesthesia. However, baseline heart rate remain controversial in predicting neuraxial anaesthesia-related hypotension. Low-frequency/high-frequency ratio of heart rate might be another applicable method (Bishop, Cairns et al., 2017).

As reported, maternal BMI was a risk factor of neuraxial anaesthesia-related hypotension (Hartmann, Junger et al., 2002; Fakherpour, Ghaem et al., 2018; Shitemaw, Jemal et al., 2020). Moreover, a higher incidence of hypotension occurred in obese parturients during neuraxial anaesthesia, which partly contributed to vascular compression by hypertrophic uterus (Nani and Torres, 2011). Yet, a recent study declared that the hemodynamic parameters derived from a noninvasive cardiac output monitoring system were not statistically different between the left-tilt and supine position (Tsai, Yeh et al., 2019). More researches should be focused on the effects of position and BMI on hemodynamic stability in parturients.

Previous studies had reported that baseline SBP (Fakherpour, Ghaem et al., 2018; Shitemaw, Jemal et al., 2020) and MAP (Bishop, Cairns et al., 2017), block-surgery time (Shitemaw, Jemal et al., 2020), sensory block height (Hartmann, Junger et al., 2002; Fakherpour, Ghaem et al., 2018; Shitemaw, Jemal et al., 2020) and oxytocin utilization (Rumboll, Dyer et al., 2015; Miyoshi, Kaneko et al., 2020) were linked with neuraxial anaesthesia-related hypotension. Nevertheless, present data failed to find the statistically significant differences in COVID-19 parturients regarding these factors. Notably, the count of COVID-19 sign and symptoms, abnormal lymphocyte count and experience of surgeon were found to be associated factors for neuraxial anaesthesia-related hypotension.

The second wave of COVID-19 has been widely concerned. We have to pay more attention to the experience of clinical practice during COVID-19 pandemic to cope with unexpected medical scenarios. Present study provided available information on neuraxial anaesthesia-related hypotension in COVID-19 parturients undergoing caesarean delivery, although historical study design and small sample size were the limitation. More evidences derived from a larger sample size and randomized controlled trials are also needed to validate these associated factors.
Abbreviations

SBP: systolic blood pressure; MAP: mean arterial blood pressure; EA: epidural anaesthesia; CES: combined spinal-epidural anaesthesia; BMI: body mass index.

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board at Renmin Hospital of Wuhan University (approval number WDRY2020-K077), Wuhan, China and the need for written informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yuan Zhang, Rong Chen, Chen Cao and Yuan Gong contributed to the data analysis and writing of the article. Qin Zhou and Hui-hui Cheng performed the data collection and interpretation. Qing-tao Meng and Xiang-dong Chen contributed to the study conception and study design. Min Wei and Zhong-yuan Xia conceived the study and participated in its design and coordination. All authors read and approved the final manuscript.

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References
Allotey, J., E. Stallings, et al. (2020). Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* **370**, m3320.

Bhatia, K., M. Columb, et al. (2020). The effect of COVID-19 on general anaesthesia rates for caesarean section. A cross-sectional analysis of six hospitals in the north-west of England. *Anaesthesia*.

Bishop, D.G., C. Cairns, et al. (2017a). Heart rate variability as a predictor of hypotension following spinal for elective caesarean section: a prospective observational study. *Anaesthesia* **72**, 603-608.

Bishop, D.G., C. Cairns, et al. (2017b). Obstetric spinal hypotension: Preoperative risk factors and the development of a preliminary risk score - the PRAM score. *S Afr Med J* **107**, 1127-1131.

Chiang, C.F., M.S. Hasan, et al. (2017). Injection speed of spinal anaesthesia for Caesarean delivery in Asian women and the incidence of hypotension: A randomised controlled trial. *J Clin Anesth* **39**, 82-86.

Chooi, C., J.J. Cox, et al. (2020). Techniques for preventing hypotension during spinal anaesthesia for caesarean section. *Cochrane Database Syst Rev* **7**, CD002251.

Fakherpour, A., H. Ghaem, et al. (2018). Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: A multinomial logistic regression. *Indian J Anaesth* **62**, 36-46.

Hartmann, B., A. Junger, et al. (2002). The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. *Anesth Analg* **94**, 1521-1529, table of contents.

Hasanin, A., S. Amin, et al. (2019). Norepinephrine versus phenylephrine infusion for prophylaxis against post-spinal anaesthesia hypotension during elective caesarean delivery: A randomised controlled trial. *Anaesth Crit Care Pain Med* **38**, 601-607.

Kaufner, L., A. Karekla, et al. (2019). Crystalloid coloading vs. colloid coloading in elective Caesarean section: postspinal hypotension and vasopressor consumption, a prospective, observational clinical trial. *J Anesth* **33**, 40-49.

Knigin, D., A. Avidan, et al. (2020). The effect of spinal hypotension and anesthesia-to-delivery time interval on neonatal outcomes in planned cesarean delivery. *Am J Obstet Gynecol* **223**, 747 e741-747 e713.

Malki, Z., E.S. Atlam, et al. (2020). ARIMA models for predicting the end of COVID-19 pandemic and the risk of second rebound. *Neural Comput Appl*, 1-20.

Miyoshi, Y., S. Kaneko, et al. (2020). Comparison of the benefits and hemodynamic side effects of oxytocin between intravenous infusion with and without bolus injection during caesarean section. *J*
Nani, F.S. and M.L. Torres (2011). Correlation between the body mass index (BMI) of pregnant women and the development of hypotension after spinal anesthesia for cesarean section. *Rev Bras Anestesiol* **61**, 21-30.

Panovska-Griths, J., C.C. Kerr, et al. (2020). Determining the optimal strategy for reopening schools, the impact of test and trace interventions, and the risk of occurrence of a second COVID-19 epidemic wave in the UK: a modelling study. *Lancet Child Adolesc Health* **4**, 817-827.

Pereira, I.D., M.M. Grando, et al. (2011). Retrospective analysis of risk factors and predictors of intraoperative complications in neuraxial blocks at Faculdade de Medicina de Botucatu-UNESP. *Rev Bras Anestesiol* **61**, 568-581, 311-568.

Riffard, C., T.Q. Viet, et al. (2018). The pupillary light reflex for predicting the risk of hypotension after spinal anaesthesia for elective caesarean section. *Anaesth Crit Care Pain Med* **37**, 233-238.

Rimsza, R.R., W.M. Perez, et al. (2019). Time from neuraxial anesthesia placement to delivery is inversely proportional to umbilical arterial cord pH at scheduled cesarean delivery. *Am J Obstet Gynecol* **220**, 389 e381-389 e389.

Rumboll, C.K., R.A. Dyer, et al. (2015). The use of phenylephrine to obtund oxytocin-induced hypotension and tachycardia during caesarean section. *Int J Obstet Anesth* **24**, 297-302.

Salama, E.R. and M. Elkashlan (2019). Pre-operative ultrasonographic evaluation of inferior vena cava collapsibility index and caval aorta index as new predictors for hypotension after induction of spinal anaesthesia: A prospective observational study. *Eur J Anaesthesiol* **36**, 297-302.

Shitemaw, T., B. Jemal, et al. (2020). Incidence and associated factors for hypotension after spinal anesthesia during cesarean section at Gandhi Memorial Hospital Addis Ababa, Ethiopia. *PLoS One* **15**, e0236755.

Singh, P.M., N.P. Singh, et al. (2020). Vasopressor drugs for the prevention and treatment of hypotension during neuraxial anaesthesia for Caesarean delivery: a Bayesian network meta-analysis of fetal and maternal outcomes. *Br J Anaesth* **124**, e95-e107.

Sun, S., N.H. Liu, et al. (2016). Role of cerebral oxygenation for prediction of hypotension after spinal anesthesia for caesarean section. *J Clin Monit Comput* **30**, 417-421.

Tsai, S.E., P.H. Yeh, et al. (2019). Continuous haemodynamic effects of left tilting and supine positions during Caesarean section under spinal anaesthesia with a noninvasive cardiac output monitor system. *Eur J Anaesthesiol* **36**, 72-75.
von Elm, E., D.G. Altman, et al. (2014). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* **12**, 1495-1499.

Yu, N., W. Li, et al. (2020). Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis* **20**, 559-564.

Zheng, H., H.L. Hebert, et al. (2020). Perioperative management of patients with suspected or confirmed COVID-19: review and recommendations for perioperative management from a retrospective cohort study. *Br J Anaesth* **125**, 895-911.

**Figures**

![Study Flowchart](image_url)

**Figure 1**

The study flowchart.