Özgün Araştırma / **Original Article**

Is SARS-CoV-2 a risk factor for hypotension during spinal anesthesia for obstetric patients?

Obstetrik hastalarda, SARS-CoV-2 spinal sonrası hipotansiyon için risk faktörü müdür?

AYGUN GULER [1]
NAMİK NEBİ OZCAN [1]

Orcid ID:0000-0003-0642-857X
Orcid ID:0000-0001-9310-712X

[1] Department of Anesthesiology and Reanimation, Ankara City Hospital, Ankara, Turkey

ÖZ

Amaç: COVID-19 pandemisinin başından itibaren, sezaryen operasyonlarında genel anestezide entübasyon ve ekstübasyon sırasında olası virüs yayılımını önlemek için Nöroaksiyel anestezi uygulanması önerilmektedir. Ancak yapılan bazı çalışmalarda aktif COVID-19 varlığında spinal anestezi güvenliğinin, hipotansiyon nedeniyle tartışmalı olduğu belirtilmektedir. Bu çalışmamızda amacımız COVID-19'lu gebe hastalardaki spinal sonrası hipotansiyon oranını literatürde ki COVID 19 olmayan hastalarla karşılaştırarak, Nöroaksiyel anestezinin güvenirliliğini tespit etmektir.

Gereç ve Yöntem: Pandeminin başından, Aralık 2020 yılına kadar olan COVID-19'lu gebelerin medikal kayıtları retrospektif olarak çalışmaya dahil edilmiştir. Demografik- vital, özellikle sistolik ve diastolik kan basınçları, kullanılan efedrin-atropin dozları, infüzyon volümleri ve bulantı- kusma sıklığı analiz edilmiştir.

Bulgular: Spinal anestezinin neden olduğu hipotansiyon hastaların 54'ünde görülmüştür. (%21,69). Vazopressor (efedrin) tüm hipotansif hastalarda kullanılmıştır. Demografik veriler, kullanılan bupivakain ve spinal anestezi öncesi kullanılan kristaloid volüm miktarı hipotansif olan ve olmayan hastalar arasında farklılık göstermemiştir.

Sonuç: Literatürde ilk defa çalışmamızda tek merkezli 249 COVID 19 (+) hastanın spinal anestezi sonrası hipotansiyon oranları ile literatürde ki spinal anestezi sonrası hipotansiyon oranları arasında istatiksel olarak fark olmadığı gösterilmiştir. COVID-19 hastalarında rejyonel anestezinin güvenle uygulanabileceğini önermekteyiz.

Anahtar kelimeler: Hipotansiyon, obstetrik anestezi, rejyonel anestezi, spinal anestezi, SARS-CoV-2

ABSTRACT

Background: Since the onset of COVID-19, recommendations suggest the use of neuraxial anesthesia, over general anesthesia for cesarian section to avoid the risks of aerosolization associated with intubation and extubation. But the safety of performing spinal anesthesia is unclear especially for post spinal hypotension, during the presence of active COVID-19. According to a few studies there was a controversial discussion about the safety of regional anesthesia. In this study we aimed to compare the incidence of hypotension in COVID-19 pregnant patients between non-COVID 19 pregnant patients in the literature to see if the spinal anesthesia is safe or if it poses an additional risk.

Materials and Methods: Medical records of COVID-19 pregnant women for cesarean section from the beginning of the pandemic up to December 2020 were retrospectively retrieved. All the demographic-vital data, including systolic and diastolic blood pressure (SBP-DBP), ephedrine-atropine doses, infusion volumes, and nausea and vomiting were retrospectively analyzed.

Results: Spinal anesthesia induced hypotension was seen 54 of the patients (21,69%). And vasopressors (Ephedrine) were used to all hypotensive patients. Demographic data's, the amount of bupivacaine and crystalloid volume which used before the spinal anesthesia showed no differences between hypotensive and non-hypotensive patients.

Conclusion: This is the first retrospective study which shows 249 COVID 19 patients' data in one center that no significant difference was seen in the incidence of hypotension associated with spinal anesthesia for COVID-19 cesarean section compared to non-COVID group in literature. We recommend using of regional anesthesia safely for patients and anesthesiologists during active COVID-19 patients.

Keywords: hypotension, obstetrical anesthesia, regional anesthesia, SARS-CoV-2, spinal anesthesia

INTRODUCTION

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has been defined as coronavirus disease 2019 (COVID-19), has prompted innumerable alterations in the practice of anesthesiology. The nature of the association between COVID-19 and pregnancy outcomes remains unclear, and meta-analyses involving patients with COVID-19 who are pregnant are limited. A 2020 systematic review suggested that people who are pregnant did not have an increased risk of SARS-CoV-2 infection or symptomatic COVID19, but they were at risk of severe COVID-19 when they are infected compared with those who were not. (1) And unlike previous viral pandemics, COVID-19 incidence, prognosis, and maternal and neonatal outcomes do not appear to be worse in pregnant women compared to the general population. (2)

In addition to the suggestion of regional anesthesia for the obstetric population, the higher rate of aerosol transmission to healthcare personnel, The American Society of Regional Anesthesia (ASRA), the European Society of Regional Anesthesia and Pain Medicine (ESRA) and the European Society of Anesthesiology (ESA) published guidance on employing regional anesthesia in patients with COVID-19. (3,4)

With regional anesthesia, the risk of person-to-person transmission, which is 6,6 times higher during the respiratory procedures performed in general anesthesia, is minimalized. (5)

The question is, "is regional anesthesia safe for pregnant COVID-19 patients undergoing cesarean section?". In a retrospective analysis at the beginning of the pandemic, Chen et al. reported a higher rate of hypotension after neuraxial blocks. (7) After this study, some questions about the safety of regional anesthesia appeared in minds. (7, 8). However, the effects of SARS-CoV-2 infection on the hemodynamics of pregnant women who underwent neuraxial anesthesia for cesarean delivery are still unclear.

Is there a higher risk of hypotension in COVID-19 pregnant women during regional anesthesia? The goal of this study was to compare the incidence of hypotension in COVID-19 pregnant patients to the incidence of hypotension in non-COVID 19 pregnant patients in the literature to see if spinal anesthesia is safe for this group of patients or if it poses an additional risk.

MATERIALS AND METHODS

After the approval of the local ethical committee, we retrospectively analyzed the files of COVID 19 patients who underwent cesarean section under spinal anesthesia to determine the incidence of hypotension and management strategies for hypotension. The study was carried out with the principles of the Helsinki Declaration. Medical records of COVID-19 pregnant women who were admitted to our hospital for cesarean section were retrospectively retrieved from the beginning of the pandemic up to December 2020. The diagnosis criteria followed the guidelines of the National Health Commission of Turkey, and the SARS-CoV-2 nucleic acid test positivity.

We accepted neuraxial anesthesia-related hypotension as hypotension from the time of local anesthetic injection until 15 min after delivery of the newborn. Hypotension was defined as a systolic blood pressure below 100 mm Hg or a mean arterial pressure below 70 mmHg. All the demographic-vital data, including systolic and diastolic blood pressure (SBP-DBP), ephedrine-atropine doses, crystalloids and colloid infusion volumes, newborn birth weight, and nausea and vomiting were recorded too.

SPSS 17.0 was used to conduct the statistical analysis (SPSS Inc, Chicago, IL, USA). Continuous variables were represented as mean, standard deviation, and median (min-max), while categorical variables were represented as numbers (percentage). The Kolmogorov-Smirnov test was used to assess conformity to normal distribution. When comparing normally distributed data, the student's t-test was used, when data is normally distributed data, the Mann Whitney U test was used. Pearson's chi-square or Fisher's test was used for comparison of categorical variables. For all tests, $p < 0.05$ was considered statistically significant.

RESULTS

249 confirmed COVID-19 patients were included for this study. 54 of 249 cases were hypotensive (21.69 %) and 195 (78.31 %) were normotensive. Demographic data and baseline hemodynamic values were similar between hypotensive and normotensive patients, and no statistical difference was found. 46 of the hypotensive patients and 126 of the non-hypotensive patients were asymptomatic for COVID-19. 8 of the hypotensive and 39 of the non-hypotensive COVID-19 group patients showed only one of the cough, fever, dyspnea, and tachypnea symptoms, and no statistically significant differences were found. The mean bupivacaine usage was 12,58 ± 0,89 mg (11-15 mg) for the hypotensive group and 12,61 ± 1,08 mg (10-15 mg) for the non-hypotensive group. The difference was insignificant

(p=0,74) (Table 1). There were no statistically significant differences between the groups (p =0,62) when 1154,72 ± 426,78 (500-2500) ml crystalloid was infused in the hypotensive group and 1169,70 ± 338,11 (500-2500) ml crystalloid was infused in the non-hypotensive group (Table 1). Colloid infusion was used for 19 of the non-hypotensive and 15 of the hypotensive patients and no statistically differences were found. (p=0.49).

Ephedrine was used for all the hypotensive patients. Atropine was used 3 of the hypotensive and 1 of the non-hypotensive group patients. Atropine usage was significant between groups (X2=5,53 p=0,019) (Table 1).

Table 1: Demographic properties and total amount of drugs of the groups.

	Mean arterial pressure> 70 mm Hg (n=195)	Mean arterial pressure<70 mm Hg (n=54)	p
Age	29,14 ± 5,21 (16-42)	29,74 ± 5,01 (22-45)	0,66
Weight	83,25 ± 17,83 (52-161)	82,21 ± 12,71 (61-110)	0,91
Hight	163,87 ± 7,47 (150-180)	161,00 ± 8,23 (150-175)	0,34
Bupivacaine dosage (mg)	12,61 ± 1,08 (10-15)	12,58 ± 0,89 (11-15)	0,74
Ephedrine dosage (mg)		14,72 ± 6,89 (5-35)	
Crystalloid amount (ml)	1169,70 ± 338,11 (500-2500)	1154,72 ± 426,78 (500-2500)	0,62

Data are expressed as mean ± SD

Newborn weight was 3030,39 ± 575,10 gr for the hypotensive COVID-19 group and 3064,10 ± 604,84 gr for the non-hypotensive COVID-19 group, and there was no statistical difference between the groups (p=0,59).

Nausea and vomiting were observed in 4 (7.41 %) of the hypotensive patients and 12 (6.15 %) of the non-hypotensive group (X2: 0.001, p=0,97).

DISCUSSION

This is the first retrospective study which shows 249 COVID 19 patients' data in one center that no significant difference was seen in the incidence of hypotension associated with spinal anesthesia for COVID-19 cesarean section compared to non-COVID group in literature.

COVID-19 has presented challenges to healthcare systems around the world and will continue to do so for months and perhaps years. The threats that the disease poses to both patients and healthcare workers have changed medical practice, but these changes can offer opportunity to those with subspecialty interests in areas such as regional anaesthesia.

At the beginning of the COVID-19 pandemic there wasn't enough data about which anesthesia technique must be use or which one is better for mother, newborn, and all health care workers (6-8).

All we know is that virus was transmitted by aerosol and the risk of transmission of acute respiratory infection to health professionals during tracheal intubation is 6,6 times higher in the group exposed (5). However, some of these potential benefits of regional anesthesia for healthcare workers and the institution rather than the patients themselves, and we must not forget that patients are at the center of the shared decision-making process when selecting the safest and most effective anesthetic technique for a surgical procedure.

According to a recent editorial, "it is reasonable to consider administering regional anesthesia to patients at higher risk of complications simply to avoid general anesthesia during the pandemic." But the question is, what complications are we dealing with, and what can we do about them?

At the beginning of the pandemic Chen et all state that they used continuous epidural anesthesia or combined spinal-epidural anesthesia (CSE) technique for COVID 19 cesarian section procedures and hypotension was significantly seen 12 of the 14 women —indeed, a high incidence of hypotension. (6). They didn't explain which technique or drug they used (epidural or combined spinoepidural anesthesia) for the anesthesia. In the correspondence of the article, they state that they didn't prefer spinal anesthesia because of possible virus location in the cerebrospinal fluid and the risk of viral spread and they chose epidural anesthesia (10). Epidural anesthesia, which is nowadays a less common choice for scheduled cases, then the high incidence of hypotension is more concerning. They explained the perioperative hypotension with SARS-CoV-2 binds to the angiotensin converting enzyme-II (ACE2) receptor and the ACE2 receptor is a cardio-cerebrovascular protective factor, which plays an important role in regulating blood pressure, in

addition to have an anti-atherosclerosis mechanism (11).

Zhang and Chen et al compared hypotension after regional anesthesia in COVID 19 and non-COVID 19 pregnant patients in another multicenter study (12). After propensity score matching, they included 286 subjects, 186 SARS-CoV-2-infected parturients, and 101 uninfected parturients. The incidence of neuraxial anesthesia-related hypotension in COVID-19 parturients was 57.4% versus 41.9 % in control parturients, indicating a significant difference between the groups. However, there were a few points that were contentious. The authors gathered all regional anesthesia data (spinal, epidural, and combined-spinal epidural (CSE) technique data), and hypotension was defined as a systolic blood pressure of less than 100 mmHg or a mean arterial blood pressure of less than 80% of the baseline value (the mean of repeated measurements before commencing anesthesia). They used vasopressors and fluids both prophylactically and after hypotension developed. The mean arterial pressure in the hypotensive group was 83,9 mmHg. Furthermore, the description of a mean arterial blood pressure below 80% of the baseline value is debatable (13). We only looked at data from spinal anesthesia patients, and hypotension was defined as a systolic blood pressure of less than 100 mm Hg or a mean arterial pressure of less than 70 mm Hg. Vasoconstrictors were only used to treat hypotension, not to prevent it.

In another study, Karasu et al. looked at the cesarian section practices of 61 COVID-19 patients. For 58 of the patients, spinal anesthesia was used, and the incidence of hypotension was 25,9%, which was similar to our findings. Hypotension was found to be prevalent in 21.69 percent of the participants in our study (14).

Before the COVID19 pandemic, a few studies looked at the effects of spinal anaesthesia on vital parameters in pregnant women. Mercier et al discovered that without pharmacologic prophylactic measures, hypotension can occur in up to 80% of women after spinal anaesthesia for caesarean section (15). Lato et al used Doppler sonography to evaluate 40 women before and after spinal anaesthesia. They discovered that after spinal anaesthesia, blood pressure dropped significantly in 90% of the women, and that 43% of the women experienced severe hypotension (16).

Many theories have been proposed to explain the high incidence and severity of hypotension during spinal anesthesia caesarean deliveries (17-18). Maternal age, BMI, weight gain, gravidity, history of hypotension, baseline heart rate, fluid pre-loading, and anesthetic adjuvant have all been shown to be predictors of spinal anesthesia-related hypotension in cesarean section (19). Other important factors include the height (T5-T4) and density of the sensory block, the increased sensitivity to local anesthetics combined with the effects of the sympathetic block during pregnancy, the amount of local anesthetic, the aggravating role of aortocaval compression by the gravid uterus-baby weight and experience of the anesthesiologist, ASA physical status, urgency of surgery, and surgical department to be predictive factors for spinal anesthesia related hypotension in cesarean delivery (19-22).

There were no differences between groups in terms of demographic data, baby weight and trimester, amount of local anesthetic, or volume of crystalloid infused in our study. Furthermore, all of the anesthesiologists had at least ten years of experience in obstetric anesthesia.

For many years, perioperative spinal hypotension was believed to arise primarily because of venous vasodilation. However, studies that have utilized cardiac output monitoring have demonstrated that arterial vasodilation is more likely to be responsible for the decrease in blood pressure following spinal anaesthesia, rather than decreased venous return and cardiac output, at least initially (23). Techniques such as fluid loading, vasopressor administration and lower limb compression have been shown to decrease the incidence of spinal-induced hypotension during cesarean section (17). However, no single regimen has eliminated clinically significant maternal hypotension, and combination of techniques may be beneficial, but vasopressors are now recognized as the most important option in the management of hypotension (23). After spinal anesthesia, there is a fall in the mean arterial pressure and a marked reduction in systemic vascular resistance despite increase in cardiac output, heart rate, and stroke volume in the first 15 min after induction of spinal anesthesia even after fluid therapy can be seen. In this situation best treatment is using vasoconstrictors for treatment (24, 25). In this study crystalloid infusion were coloaded during the spinal anesthesia performing for hypotension prophylaxis and treatment, and if the hypotension was persistent crystalloid- colloid volume replacement and intravenous ephedrine 10 mg were used.

We used ephedrine, which is one of the best choices due to its availability for vasopressor treatment in obstetric anesthesia, with a minimum dose of 5 mg and a maximum dose of 35 mg given to all hypotensive patients. In addition, parasympatholytic atropine was used in this study for three hypotensive and one

non-hypertensive group patients, which was statistically significant.

Several authors have reported that low-dose spinal anesthesia for cesarean delivery, using doses of 5-7 mg intrathecal bupivacaine, results in a lesser degree of sympathectomy, vasodilation, and hemodynamic changes, including hypotension. Although a lower intrathecal bupivacaine dose reduces the risk of hypotension and the associated nausea and vomiting, it increases the need for intraoperative analgesic supplementation. It also leads to a shorter duration of block and a slower onset speed (26). If a low-dose spinal anesthesia is planned, the combined-spinal epidural technique, which allows for the use of an epidural catheter to augment the block, if necessary, should be used. Low-dose CSE anesthesia, on the other hand, is superior to single-shot spinal anesthesia only in "complicated" patients (such as those with cardiovascular disease and compromised babies) and/or when a complicated or prolonged caesarean delivery is expected (27). Otherwise, for the majority of patients, single-shot spinal anesthesia is now an effective, quick, simple, and safe option. Furthermore, obstetric anesthesiologists must keep in mind that low-dose spinal anesthesia may necessitate additional analgesia or mask ventilation. During pandemics, mask ventilation or the need for general anesthesia increase the risk of exposure to patients' respiratory secretions as well as the risk of perioperative viral transmission to healthcare workers and other patients. Already we know that in pregnancy functional residual capacity, end-expiratory volumes and residual volumes decreases. Also decreased total lung capacity and inability to clear secretions can make pregnant women more susceptible to severe respiratory infections (28). We know that COVID-19 causes acute respiratory failure, with a major change in the ventilation- perfusion ratio and pulmonary shunt, leading to hemoglobin desaturation, and signs and symptoms of respiratory discomfort or failure (29). In a recent study showed that 82 (5.4%) of the COVID-19 patients with severe or critical illness during pregnancy, and 10 (0.7%) required mechanical ventilation (30). In light of all available information, general anesthesia poses a risk to both the patient and all medical personnel in the operating room.

There was no failure for regional anesthesia among the 249 patients in our retrospective analyses, and none of them were converted to mask ventilation or general anesthesia. When compared to non-COVID 19 pregnant women, we concluded that using spinal anesthesia in cesarean section is quick, effective, and safe for pregnant women with COVID-19 infection.

COVID 19 infection does not appear to be a risk factor for hypotension after spinal anesthesia in infected women.

REFERENCES

1-   Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. for PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020 Sep 1;370:m3320.

2-   Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. Am J Obstet Gynecol MFM. 2020 Aug;2(3):100134.

3-   Uppal V, Sondekoppam RV, Landau R, El-Boghdadly K, Narouze S, Kalagara HKP. Neuraxial anaesthesia and peripheral nerve blocks during the COVID-19 pandemic: a literature review and practice recommendations. Anaesthesia. 2020 Oct;75(10):1350-1363.

4-   COVID-19 Guidance for Regional Anesthesia Neuraxial Anesthesia and Peripheral Nerve Blocks. https://esraeurope.org/wp-content/uploads/2020/04/ESRAASRA-COVID-19-Guidelines-.pdf

5-   Wax RS, Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. Can J Anaesth. 2020 May;67(5):568-576.

6-   Chen R, Zhang Y, Huang L, Cheng BH, Xia ZY, Meng QT. Safety and efficacy of different anesthetic regimens for parturients with COVID-19 undergoing Cesarean delivery: a case series of 17 patients. Can J Anaesth. 2020 Jun;67(6):655-663.

7-   Benhamou D, Meyer HK, Morau E, Chassard D, Mercier FJ; French Obstetric Anesthesia Working Group (Club Anesthésie-Réanimation en Obstétrique [CARO]). Spinal anesthesia for Cesarean delivery in women with COVID-19 infection: questions regarding the cause of hypotension. Can J Anaesth. 2020;67(8):1097-1098.

8-   Hashemi M, Taheri M, Aminnejad R. Spinal anest-

hesia in COVID-19 patients, more research is needed. Braz J Anesthesiol. 2020;70(2):185-186.

9- Macfarlane AJR, Harrop-Griffiths W, Pawa A. Regional anaesthesia and COVID-19: first choice at last?. Br J Anaesth. 2020;125(3):243-247.

10- Chen R, Zhang YY, Zhou Q, Meng QT. In reply: Spinal anesthesia for Cesarean delivery in women with COVID-19 infection: questions regarding the cause of hypotension. Can J Anaesth. 2020 Aug;67(8):1099-1100.

11- Miller AJ, Arnold AC. The renin-angiotensin system in cardiovascular autonomic control: recent developments and clinical implications. Clin Auton Res 2019; 29: 231-43.

12- Zhang Y, Chen R, Cao C, et al. The Risk of Neuraxial Anesthesia-Related Hypotension in COVID-19 Parturients Undergoing Cesarean Delivery: A Multicenter, Retrospective, Propensity Score Matched Cohort Study. Front Med (Lausanne). 2021; 8:713733.

13- Madden N, Emeruwa UN, Polin M, Bejerano S, Gyamfi-Bannerman C, Booker WA. SARS-CoV-2 and hypertensive disease in pregnancy. Am J Obstet Gynecol MFM. 2021; 25;4(1):100496.

14- Karasu D, Kilicarslan N, Ozgunay SE, Gurbuz H. Our anesthesia experiences in COVID-19 positive patients delivering by cesarean section: A retrospective single-center cohort study. J Obstet Gynaecol Res. 2021 Aug;47(8):2659-2665.

15- Mercier FJ, Augè M, Hoffmann C, Fischer C, Le Gouez A. Maternal hypotension during spinal anesthesia for caesarean delivery. Minerva Anestesiol. 2013 Jan;79(1):62-73. Epub 2012 Nov 18.

16- Lato K, Bekes I, Widschwendter P, Friedl TWP, Janni W, Reister F, et al. Hypotension due to spinal anesthesia influences fetal circulation in primary caesarean sections. Arch Gynecol Obstet. 2018;297(3):667-674.

17- Dyer RA, Reed AR. Spinal hypotension during elective cesarean delivery: closer to a solution. Anesth Analg 2010; 111:1093-5.

18- Mercier FJ. Fluid Loading for Cesarean Delivery Under Spinal Anaesthesia: Have We Studied All the Options? Anesth Analg 2011; 113:677-80.

19- Fakherpour A, Ghaem H, Fattahi Z, Zaree S. Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: a multinomial logistic regression. Indian J Anaesth. (2018) 62:36-46.

20- Russell IF. Levels of anaesthesia and intraoperative pain at caesarean section under regional block. Int J Obstet Anesth 1995; 4:71-7.

21- Mercier FJ, Bonnet MP, De la Dorie A, Moufouki M, Banu F, Hanaf A et al. Spinal anaesthesia for caesarean section: fluid loading, vasopressors and hypotension. Ann Fr Anesth Reanim 2007; 26:688-93.

22- Kinsella SM, Whitwam JG, Spencer JA. Reducing aortocaval compression: how much tilt is enough? BMJ 1992; 305:539-40.

23- Langesaeter E, Rosseland LA, Stubhaug A. Continuous invasive blood pressure and cardiac output monitoring during cesarean delivery: a randomized, double-blind comparison of low-dose versus high-dose spinal anesthesia with intravenous phenylephrine or placebo infusion. Anesthesiology 2008; 109:856-863.

24- Sharwood-Smith G, Drummond GB. Hypotension in obstetric spinal anaesthesia: a lesson from pre-eclampsia. Br J Anaesth 2009; 102:291-4.

25- Dyer RA, Reed AR, van Dyk D, Arcache MJ, Hodges O, Lombard CJ, et al. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. Anesthesiology. 2009 Oct;111(4):753-65.

26- Roofthooft E, Van de Velde M. Low-dose spinal anaesthesia for Caesarean section to prevent spinal-induced hypotension. Curr Opin Anaesthesiol 2008;21(3):259-62

27- Benhamou D, Wong C. Neuraxial anesthesia for cesarean delivery: what criteria define the "optimal" technique? Anesth Analg. 2009 Nov;109(5):1370-3.

28- Goodnight WH, Soper DE. Pneumonia in pregnancy. Crit Care Med 33, Suppl: S390– S397, 2005.

29- Thomas-Rüddel D, Winning J, Dickmann P, Ouart D, Kortgen A, Janssens U, Bauer M. Coronavirus disease 2019 (COVID-19): update for anesthesiologists and intensivists March 2020. Anaesthesist. 2021 Dec;70(Suppl 1):1-10.

30- Adhikari EH, SoRelle JA, McIntire DD, Spong CY. Increasing severity of COVID-19 in pregnancy with Delta (B.1.617.2) variant surge. Am J Obstet Gynecol; 2021 Sep 14.