Original Article

Factors Associated with Respiratory Support after Cesarean Hysterectomy

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Background: Cesarean hysterectomy is a major operation that causes massive hemorrhage and larger fluid resuscitation. Thus, postoperative mechanical ventilation support is required in some patients, involving longer hospital stay and high cost of hospital care.

Objective: To find the predictive factors for postoperative respiratory support in pregnant women underwent cesarean hysterectomy.

Materials and Methods: A retrospective review of patients underwent cesarean hysterectomy between January 2014 and June 2019 was conducted. Patient characteristics, anesthetic records and hospital length of stay were reviewed. The relationship between factors and postoperative mechanical ventilator (PMV) was also analyzed.

Results: A total of 180 patients were included in the present study, wherein, 64 patients (35%) required PMV and 30 patients (16%) needed postoperative oxygen support. Multivariable logistic regression was used to identify the relationship between PMV and the associated factors. The authors found the American Society of Anesthesiologists (ASA) classification and the volume of intraoperative blood components replacement (packed red blood cells [PRC] and fresh frozen plasma [FFP]) were significantly related to PMV: ASA3 16.51 (95% CI 1.89 to 144.33), ASA4 183.25 (95% CI 2.92 to 11,500.65), p=0.003; PRC 1.0028 (95% CI 1.0008 to 1.0047), p=0.001; FFP 1.0022 (95% CI 1.0000 to 1.0043), p=0.029, respectively.

Conclusion: Postoperative mechanical ventilation was found in one-third of the cesarean hysterectomy patients and associated with ICU admission along with increased in post-operative length of hospital stay. The ASA classification and intraoperative volume of blood components replacement were significantly associated with PMV. Factors associated significantly with respiratory support were ASA classification and duration surgery.

Keywords: Factors associated; Respiratory support; Cesarean hysterectomy

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Cesarean hysterectomy is a major operation for treatment of morbidly adherent placenta and postpartum hemorrhage(1). The incidence of both increased placenta previa and adherent placenta is associated with caesarean sections(2). A Cesarean hysterectomy usually causes massive obstetric hemorrhages and requires large volume resuscitation. Moreover, some pregnant women may receive large intravenous fluid therapy that can develop pulmonary edema. Massive blood transfusions and inappropriate intravenous fluid therapy are related to respiratory events such as bronchospasm, atelectasis, acute respiratory distress syndrome (ARDS), transfusion-related acute lung injury (TRALI), postoperative oxygen requirement or mechanical ventilation(3-5).

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Pregnant women may have a higher risk of postoperative respiratory problems than general population, as physiological changes during pregnancy include a reduced functional residual capacity and increased oxygen consumption, which may lead to rapid desaturation(6,7). Pregnant women, because of anatomical changes, have a high risk of aspiration, due to delayed gastric emptying time and difficult intubation(6,7). Uteroplacental blood flow increases to 1,000 mL/minute at term which causes massive bleeding during a cesarean hysterectomy(7). Pregnant women are at risk for acute pulmonary edema, due to low colloid osmotic pressure to the left ventricular end-diastolic pressure gradient and mild impairment of systolic and diastolic function(8).

In non-cardiothoracic surgery, the incidence of postoperative respiratory complications ranges from 2% to 40%(9-11). Regarding to the previous literature(10,11), abdominal surgery, surgical duration or anesthesia and emergency surgery had increased risk of pulmonary complication more than other factors. Moreover, there are other studies in a non-obstetric population, such as, Weinger et al[12] studied general postoperative complication in placenta acceta pregnant women, reported the postoperative respiratory complications as aspiration and pulmonary embolism, while other postoperative respiratory complications were not studied.

There have been lack of data on postoperative respiratory support among pregnant women, who are a population at risk. The present study aimed to find the predictive factors for postoperative respiratory support in the pregnant women underwent cesarean hysterectomy.

Materials and Methods

The approval was obtained from the Institutional Review Board and the Ethics Committee of Faculty of Medicine, Prince of Songkla university (REC number 62-332-8-1). The retrospective descriptive study was conducted at a tertiary hospital, in the south of Thailand. The present study was carried out between January 2014 and June 2019. Cesarean sections were performed on approximately 7,200 patients over a period of 6 years. The search term "cesarean hysterectomy", "postpartum hemorrhage", "placenta previa", "placenta accreta", "placenta increta", "placenta percreta", and "uterine atony" were identified in the anesthetic records, so as to include the patients in the present study. Inclusion criteria were pregnant women who underwent cesarean hysterectomy. The electrical medical and anesthetic records were manually reviewed to verify patients. To search for the risk factors associated with the postoperative respiratory support, patient characteristics (including gestational age, preeclampsia or severe preeclampsia, gestational diabetes mellitus [GDM]), indication for hysterectomy, and anesthetic management (anesthetic technique, fluid resuscitation, estimated blood loss, urine output) were reviewed. In addition, postoperative mechanical ventilator (PMV) and postoperative oxygen supplementation (POS) were also assessed, including duration of POS and duration of PMV. The intensive care unit (ICU) admission, length of ICU admission and hospital length of stay after operation were also reviewed.

Outcomes of the study

The primary outcome was factors associated with respiratory support (oxygen support and postoperative mechanical ventilation support). The secondary objectives were ICU admission rate, postoperative length of stay, and mechanical ventilation duration.

Statistical analysis

From the postoperative pulmonary complications of the Canet et al study, the sample size was calculated from odd ratio of surgical duration[10] and respiratory support data in a tertiary hospital in the south of Thailand. A case-control formula with a 95% confidence interval (CI) and type II error of 0.2 was used. The estimated sample size was 180 patients; this included a 10% drop out to compensate for excluded cases. In analysis, the data were performed using RStudio, version 1.2.5001. Continuous variables were presented with mean ± standard deviation (SD), and median (interquartile range [IQR]). Categorical variables were presented with frequency and percentage. The normally, or non-normally distributed variables used ANOVA F-test, and Kruskal-Wallis test. The categorical variables used chi-square or Fisher's exact test. After bivariate analysis for variables that were p-value less than 0.2, multivariable logistic regression was used to model the relationship between PMV and factors. A p-value of less than 0.05 was considered significant.

Results

During the study period, there were 180 pregnant women who underwent cesarean hysterectomy, and met the inclusion criteria; thus, they were enrolled in the present study (Figure1). Mean age (±SD) was 34.82±4.98. The three most common indications of hysterectomy were placenta previa, adherent placenta and postpartum hemorrhage. One hundred and sixteen (64%) of the cesarean hysterectomy were performed under emergency settings. Twenty-five percent of the patients had the American Society of Anesthesiologists (ASA) classification 3 or 4. There were 108 patients (60%) with intraoperative massive blood loss (blood loss ≥2,500 mL). About half of the patients received postoperative respiratory support, as oxygen supplements [either via nasal cannula or face mask (16%)] and mechanical ventilation (36%). Post-operatively, one-third of the patients (n=60) were admitted ICU.

Table 1 compared pre-operative characteristics of patients, by types of respiratory support. Mechanical ventilation was commonly need by patients with pre-eclampsia and ASA class 3 and 4. Age, weight and height were not different among the 3 groups of postoperative respiratory support. Table 2 compared the intraoperative anesthetic data among the 3 groups of respiratory support. Patients who received only

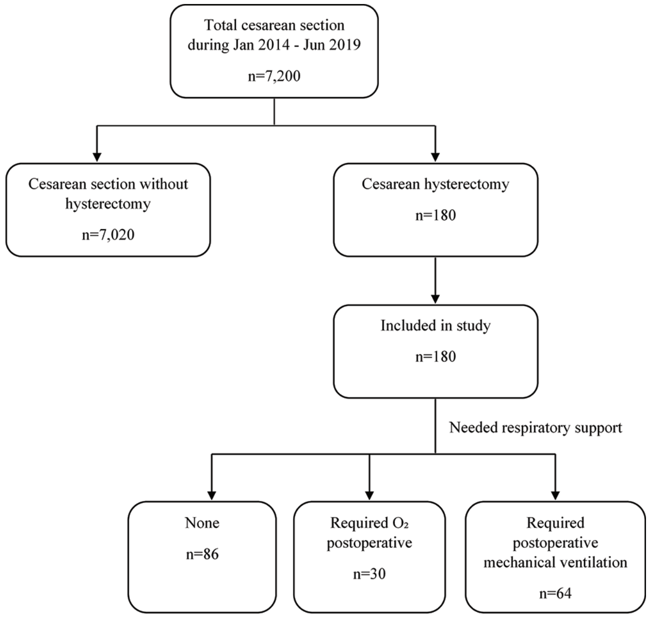

Figure 1. Flow chart of pregnant women undergoing cesarean hysterectomy and respiratory supporting included in the study.

Table 1. Pre-operative patients' characteristics and types of respiratory support (n=180)

	None (n=86); n (%)	Oxygen therapy (n=30); n (%)	Ventilator support(n=64); n (%)	p-value
Age (year); median (IQR)	35 (32.0, 38.0)	35 (32.2, 39.0)	36 (31.0, 39.0)	0.98
Weight (kg); mean±SD	66.4±8.7	69.3±11.6	65.8±10.3	0.27
Height (cm); mean±SD	157.1±5.5	155.4±4.5	156.5±6.1	0.35
Emergency hysterectomy	49 (57)	21 (70)	46 (71.9)	0.13
ASA classification				0.002
2	74 (86.0)	19 (63.3)	41 (64.1)	
3	11 (12.8)	11 (36.7)	18 (28.1)	
4	1 (1.2)	0 (0.0)	5 (7.8)	
Comorbidity				
Anemia	36 (41.9)	14 (46.7)	38 (59.4)	0.10
Preterm labor	43 (50.0)	13 (43.3)	38 (59.4)	0.30
Pre-eclampsia	2 (2.3)	3 (10.0)	9 (14.1)	0.015
GDM	9 (10.5)	3 (10.0)	9 (14.1)	0.76
Hysterectomy indication				
Placenta previa	58 (67.4)	16 (53.3)	42 (65.6)	0.37
Adherent placenta	50 (58.1)	15 (50.0)	37 (57.8)	0.72
PPH	30 (34.9)	14 (46.7)	22 (34.4)	0.46
Uterine atony	28 (32.6)	12 (40.0)	17 (26.6)	0.41
Abruptio placenta	0 (0.0)	0 (0.0)	5 (7.8)	0.008

ASA=American Society of Anesthesiologists; GDM=gestational diabetes mellitus; PPH=postpartum hemorrhage; IQR=interquartile range; SD=standard deviation

general anesthesia showed a higher proportion of postoperative mechanical ventilation requirement than combined with regional anesthesia or regional anesthesia followed by general anesthesia. Also, volume of blood loss, volume of received blood components, and the duration of operation were more

Table 2. Intra-operative data by types of respiratory support (n=180)

	None (n=86); median (IQR)	Oxygen (n=30); median (IQR)	Ventilator (n=64); median (IQR)	p-value
Anesthetic technique; n (%)				<0.001
GA	42 (48.8)	16 (53.3)	52 (81.2)	
GA with TAP block	25 (29.1)	5 (16.7)	3 (4.7)	
RA followed by GA	19 (22.1)	9 (30.0)	9 (14.1)	
Intra-operation intake (mL)				
Crystalloid	3,100 (2,356.2, 3,600.0)	3,125 (2,062.5, 3,812.5)	3,350 (2,187.5, 4,425.0)	0.53
Colloid	500 (0, 1000)	500 (350, 1,000)	1,000 (500, 1,500)	<0.001
Blood component	1,021 (478.5, 1,499.8)	1,530.5 (352.8, 2,182.5)	3,736 (2,945.2, 4,715.8)	<0.001
Intra-operation output				
Massive blood loss; n (%)	33 (38.4)	15 (50.0)	60 (93.8)	<0.001
Urine (mL/kg/hour)	1.3 (1.0, 1.9)	1.6 (0.9, 2.4)	1.6 (1.0, 2.3)	0.41
Surgery duration (minute)	167.5 (140.0, 200.0)	160 (140.0, 202.5)	210 (173.8, 256.2)	<0.001

GA=general anesthesia; RA=regional anesthesia; TAP=transversus abdominis plane; IQR=interquartile range

Table 3. ICU admission and hospital length of stay

	None (n=86)	Oxygen (n=30)	Ventilator (n=64)	p-value
ICU admission; n (%)	0 (0.0)	6 (20.0)	54 (84.4)	<0.001
Post-operative length of stay (days); median (IQR)	4 (4, 6)	5 (4, 7)	6.5 (5, 8)	<0.001

ICU=intensive care unit; IQR=interquartile range

common in patients with postoperative respiratory support.

From 60 patients admitted immediately after surgery to the ICU (Table 3), 54 patients were received mechanical ventilation. These were significant in 6 patients received oxygen supplement (p<0.001). Median duration of ICU stay was 1 day (IQR 0, 1). Patients who received mechanical ventilation stayed about 1 to 2 days longer than those who did not. Although, intensive care was needed in 60 patients, postoperative chest film was performed in only three-quarters of the patients. None of these revealed radiological signs of volume overload, with the exception of one patient who developed TRALI. Post-operative length of stay increased for those who had a mechanical ventilator requirement. The duration of postoperative hospital stay with mechanical ventilator, oxygen supplement and no oxygen required was 6.5 days (median IQR 5, 8), 5 days (median IQR 4, 7) and 4 days (median IQR 4, 6), respectively; p<0.001.

The authors analyzed the patients needed mechanical ventilator (n=64) compared with no mechanical ventilator required (n=116). Factors associated with the postoperative mechanical ventilation requirement were ASA classification and volume of intraoperative blood components replacement. Patients with pre-operative ASA classification 3 and 4 had significantly higher chances of requiring mechanical ventilation than patients with ASA classification 2 (Table 4).

After analyzed with multivariate, the authors compared respiratory support (oxygen support or mechanical ventilator, n=94) and no respiratory support (n=86). Factors associated with the postoperative respiratory support were ASA classification and surgery duration. The patient required postoperative respiratory support was found significantly in ASA classification 3 and 4. Patients with longer operative duration had significantly higher chances of requiring respiratory support (Table 5).

Discussion

Cesarean hysterectomy is a high risk surgery, due to massive bleeding that may be related with respiratory complications such as postoperative respiratory support, ARDS and TRALI[13]. From the present retrospective study, the authors found that half of the patients required postoperative respiratory support were associated with massive bleeding and large volume resuscitation. The pregnant women kept intubated postoperatively because they had ASA classification 3 or 4 and received large

Table 4. Factors associated with mechanical ventilation support after cesarean hysterectomy

	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Age (year)	0.98 (0.92 to 1.04)	0.97 (0.83 to 1.13)	0.684
ASA classification (ASA2=ref.)			0.003
ASA3	1.86 (0.90 to 3.83)	16.51 (1.89 to 144.33)	
ASA4	11.34 (1.28 to 100.15)	183.25 (2.92 to 11,500.65)	
Anemia	1.93 (1.04 to 3.58)	0.28 (0.06 to 1.41)	0.107
Preterm labor	0.64 (0.34 to 1.18)	0.38 (0.10 to 1.45)	0.147
Crystalloid (mL)	1.0002 (1.0000 to 1.0004)	0.9996 (0.9990 to 1.0002)	0.135
Packed red blood cell (mL)	1.0042(1.0032 to 1.0063)	1.0028 (1.0008 to 1.0047)	0.001
Fresh frozen plasma (mL)	1.0047 (1.0032 to 1.0063)	1.0022 (1.0000 to 1.0043)	0.029
Platelet (mL)	1.0085 (1.0062 to 1.0108)	1.0027 (0.9988 to 1.0066)	0.168
Massive blood loss (≥2,500 mL)	21.25 (7.23 to 62.41)	8.46 (0.77 to 93.09)	0.055
Urine output (mL/kg/hour)	1.21 (0.91 to 1.62)	0.54 (0.22 to 1.30)	0.153
Surgery duration (minute)	1.0164 (1.0096 to 1.0233)	1.0099 (0.9944 to 1.0257)	0.195

ASA=American Society of Anesthesiologists; OR=odds ratio; CI=confidence interval

Table 5. Factors associated with oxygen or mechanical ventilation support after cesarean hysterectomy

	Crude OR (95%CI)	Adjusted OR (95%CI)	p-value
ASA classification (ASA2=ref.)			0.024
ASA 3	3.25 (1.50 to 7.04)	5.83 (1.47 to 23.05)	
ASA 4	6.17 (0.70 to 54.22)	5.58 (0.38 to 82.46)	
Anemia	1.72 (0.95 to 3.10)	0.46 (0.17 to 1.25)	0.115
Pre-eclampsia	6.15 (1.33 to 28.30)	4.00 (0.38 to 42.19)	0.233
Packed red blood cell (mL)	1.0024 (1.0016 to 1.0032)	1.0010 (0.9995 to 1.0025)	0.178
Fresh frozen plasma (mL)	1.0026 (1.0018 to 1.0034)	1.0009 (0.9994 to 1.0024)	0.236
Platelet (mL)	1.0077 (1.0053 to 1.0102)	1.0034 (0.9998 to 1.0070)	0.057
Massive blood loss (≥2,500 mL)	6.34 (3.26 to 12.33)	1.92 (0.60 to 6.18)	0.272
Urine output (mL/kg/hour)	1.24 (0.93 to 1.67)	1.37 (0.80 to 2.33)	0.257
Surgery duration (minute)	1.01 (1.01 to 1.02)	1.01 (1.00 to 1.02)	0.037

ASA=American Society of Anesthesiologists; OR=odds ratio; CI=confidence interval

volume resuscitation or vasopressor. In addition, anesthesiologist and obstetrician had an opinion that patients should require postoperative mechanical ventilation. One-third required postoperative mechanical ventilation. ICU admission was necessary for some patients as they had unstable hemodynamic and required vasopressor, intensive monitoring such as intra-arterial line. Hence, they had prolonged postoperative length of hospital stay.

The main indications in the present study for cesarean hysterectomy were placenta previa, adherent placenta, and postpartum hemorrhage. Uteroplacental blood flow >1,500 mL/minute at term[7] causes bleeding during a cesarean hysterectomy. Most placenta previa was positioned at the uterine incision site; hence, surgery through inevitably placental incision[14]. After fetus delivery, hysterectomy from adherent placenta was performed, without placenta removal. Therefore, placental incision and hysterectomy without placenta removal caused bleeding during the operation. Large volume resuscitation (crystalloid, colloid, blood component) was received. Thus, the patients who had massive blood loss (93.8%) also received PMV. The ASA classification 3 or 4, packed red blood cells and fresh frozen plasma replacement were associated with PMV.

Age was reported as a factor for postoperative pulmonary complications[10,15], but in the present study, the median age in the three groups were similar. Preoperative anemia (Hb <10 g/dL) was almost 3 times more likely to increased risk of postoperative pulmonary complications[10]. Preoperative anemia in massive bleeding surgery increased the rate of receiving blood transfusions. However, pregnant women can tolerate more blood loss than non-pregnant women due to hematologic change. For this reason, anemia was not significant in the present study. Gestational age is related to uteroplacental blood flow, which is a higher blood flow at term rather than preterm[7]. Thus, term pregnant women may increase risk of intraoperative massive bleed more than preterm pregnant women. The result of present study found that the gestational age was not related to PMV and POS.

The previous studies in non-cardiothoracic surgery and ASA classification 3 concerning postoperative pulmonary complications include respiratory failure[11], illustrated as a factor of postoperative pulmonary complications in surgeries with a duration of more than 2 hours, and emergency surgeries. The present study reported the median duration of surgery in all three groups was more than 2 hours. The PMV group had the highest surgery duration. However, the respiratory support was significant in surgery duration. Populations and operations in the previous studies were different from the present study. Most pregnant women in the present study were healthy, so, the results were different. Preoperative respiratory infection, underlying respiratory disease, and smoking are risk factors of postoperative pulmonary complications[10]. The authors also collected data showing that most patients had no history of preoperative respiratory infection, underlying respiratory diseases, or smoking. Hence, the authors did not analyze these factors in obstetric patients for PMV.

The choice of anesthetic for cesarean hysterectomy in the present study was general anesthesia, because it provided appropriate hemodynamic stability for prolonged surgical duration. Most patients in the PMV group received general anesthesia. Regional anesthesia (spinal anesthesia), followed by general anesthesia was performed in postpartum hemorrhage from uterine atony.

Preeclampsia altered endothelial permeability and reduced plasma colloid osmotic pressure, so there was the risk of pulmonary edema[8]. Cesarean hysterectomy in preeclampsia patients carries a risk of massive intraoperative hemorrhages; hence, intravenous fluid therapy was of concern. The PMV may be related with preeclampsia, even though the results were insignificant.

Severe abruptio placenta is a high risk for maternal complications, including respiratory complications, such as respiratory failure and pulmonary edema[16]. In the present study, five abruptio placenta patients were severe; due to fetal death, hysterectomy and required postoperative mechanical ventilation. The number of cases is few so the multivariate could not be analyzed. But, the result is significant in abruptio placenta in univariate.

The PMV group received the highest amount of crystalloid, colloid, and blood components, when compared with the other groups, due to high intraoperative hemorrhages.

Strength and limitation

The strength of the present study was its obstetric population. The multivariate model was performed to reduce potential confounding variables.

The limitation was that the present study was a retrospective study. The weight gain had missing data for 57 patients (31.7%). Data concerning volume of preoperative fluid resuscitation were also limited. The duration of ICU admission in the electrical medical records had data as day. Most of the population did not have chest X-rays and arterial blood gas performed after their operation, thus, the authors did not review other respiratory complications, such as atelectasis, and pulmonary edema.

Conclusion

Postoperative mechanical ventilation was found in one-third of cesarean hysterectomy patients and was associated with ICU admission and increased post-operative length of hospital stay. The ASA classification and intraoperative volume of blood components replacement were significantly associated with PMV. Factors associated significantly with respiratory support were ASA classification and duration of surgery.

What is already known on this topic?

Massive blood loss and blood component resuscitation are the factors associated with mechanical ventilation support after non-cardiothoracic surgery.

What this study adds?

This study revealed the factors associated with postoperative mechanical ventilation in the pregnant women underwent cesarean hysterectomy are no differences form the non-pregnant factors.

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Conflict of interest

There are no potential conflicts of interests to declare.

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