Original Article

Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: A multinomial logistic regression

Address for correspondence:
Dr. Haleh Ghaem, Department of Epidemiology, Shiraz University of Medical Sciences, School of Health, Alzahra Street, 16 Valley, Shiraz, Iran.
E-mail: ghaemhaleh@gmail.com

Atousa Fakherpour, Haleh Ghaem[1], Zeinabsadat Fattahi[2], Samaneh Zaree[3]

Department of Epidemiology, School of Health, Shiraz University of Medical Sciences, [1]Department of Epidemiology, Research Centre for Health Sciences, Institute of Health, School of Health, Shiraz University of Medical Sciences, [2]Department of Anaesthesia, Shiraz Anaesthesiology and Critical Care Research Centre, Shiraz University of Medical Sciences, [3]Shiraz Anaesthesiology and Critical Care Research Centre, Shiraz University of Medical Sciences, Shiraz, Iran

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.IJA_416_17

Quick response code

ABSTRACT

Background and Aims: Although spinal anaesthesia (SA) is nowadays the preferred anaesthesia technique for caesarean section (CS), it is associated with considerable haemodynamic effects, such as maternal hypotension. This study aimed to evaluate a wide range of variables (related to parturient and anaesthesia techniques) associated with the incidence of different degrees of SA-induced hypotension during elective CS. **Methods:** This prospective study was conducted on 511 mother–infant pairs, in which the mother underwent elective CS under SA. The data were collected through preset proforma containing three parts related to the parturient, anaesthetic techniques and a table for recording maternal blood pressure. It was hypothesized that some maternal (such as age) and anaesthesia-related risk factors (such as block height) were associated with occurance of SA-induced hypotension during elective CS. **Results:** The incidence of mild, moderate and severe hypotension was 20%, 35% and 40%, respectively. Eventually, ten risk factors were found to be associated with hypotension, including age >35 years, body mass index ≥25 kg/m^2, 11–20 kg weight gain, gravidity ≥4, history of hypotension, baseline systolic blood pressure (SBP) <120 mmHg and baseline heart rate >100 beats/min in maternal modelling, fluid preloading ≥1000 ml, adding sufentanil to bupivacaine and sensory block height >T_4 in anaesthesia-related modelling (P < 0.05). **Conclusion:** Age, body mass index, weight gain, gravidity, history of hypotension, baseline SBP and heart rate, fluid preloading, adding sufentanil to bupivacaine and sensory block hieght were the main risk factors identified in the study for SA-induced hypotension during CS.

Key words: Caesarean section, elective, hypotension, spinal anaesthesia

INTRODUCTION

Caesarean section (CS) is now one of the most commonly performed major operations in women throughout the world. While regional or general anaesthesia (GA) are both acceptable for caesarean delivery,[1] use of GA has decreased dramatically in the past few decades due to a higher risk of anaesthesia-related maternal mortality.[2] As a consequence, spinal anaesthesia (SA) is now the technique of choice for CS.[3] Although SA is generally well tolerated, it is still associated with considerable side effects, the most common of which is maternal hypotension, potentially endangering both mother and child. Since there is no autoregulation for the placental vascular bed, prolonged maternal hypotension can be

How to cite this article: 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.

detrimental to the foetus, induce lower foetal Apgar scores, foetal acidosis and hypoxia.[3,4] Therefore, in the present study, the researchers' attention was concentrated on pregnant women receiving SA, as a specialised subgroup of patients with the potential risk of uterine hypoperfusion and adverse neonatal outcomes.

Identification of the associated risk factors with SA-induced hypotension might help to prevent and recognise early patients most at risk, to avoid dramatic consequences in mother and neonate. This study aimed to investigate simultaneously a wide range of maternal and anaesthesia-related risk factors and the incidence of different severities of SA-induced hypotension during elective CS through multinomial logistic regression analysis.

METHODS

This prospective study was conducted on 511 full-term pregnant women (gestational age: 37–42 weeks) with American Society of Anaesthesiologists' (ASA) physical status grade I or II who were scheduled to undergo elective CS under SA, from December 2015 to February 2017. The study was approved by the Ethics Committee of Shiraz University of Medical Sciences.

The patients with known contraindications for SA including patient refusal, sepsis at the site of injection, indeterminate neurologic disease, coagulopathy, increased intracranial pressure, history of allergy to anaesthetics, discopathy, and diabetes were excluded from the study. The patients with duration of surgery >90 min, failed or partial SA, diagnosis of foetal distress, pre-eclampsia or eclampsia, intrauterine growth restriction, severe congenital abnormalities, stillbirth and multiple pregnancies were excluded from the study, as well.

The SA technique was as follows: at first, the patients were visited by anaesthetic residents on the evening before CS. After clinical examination, the patients received explanation about the study procedure, and then their written informed consents were obtained. In the next morning, the patients were placed at a supine position with 15° left lateral tilt on the operating table in the operating room. An 18-gauge intravenous cannula was inserted in to their forearm and preloading was done with 10 ml/kg/h Ringer's solution and IV 10 mg metoclopramide was given. Monitoring consisted of non-invasive blood pressure measurement, electrocardiogram and haemoglobin oxygen saturation. The mean value of the first two consecutive measurements (with a 10 min interval after connecting the monitoring unit to the patient) was defined as the baseline blood pressure.

Under strict aseptic precaution, SA was performed in sitting position by injection of a local anaesthetic (2 ml bupivacaine 0.5% with or without opioid) into the subarachnoid space ($L_3 - L_4$, $L_4 - L_5$ or $L_5 - S_1$) through a fine Quincke type spinal needle, in lateral bevel direction and at a rate of 0.2 ml per second. Immediately after the intrathecal injection, the patient was kept in supine left lateral tilt position, and 5 L/min supplemental oxygen was administered through a face mask. Sensory block height was measured by loss of cold sensation to alcohol swabs 10 min after induction of SA. After ensuring the appropriate level of blockade (T_4–T_6), surgery was started. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were monitored and recorded every 2 min until delivery and every 5 min following thereafter. Episodes of hypotension were considered only in the 30 min period after SA induction, to eliminate surgery-related causes for hypotension. Due to the fact that all the patients were not normotensive, considering an absolute value for SBP as a cut-off point for hypotension was not applicable to all patients. Therefore, according to the viewpoint of the study's clinical consultant, maternal hypotension was defined in such a way that, results could be compared with further studies. Three degrees of hypotension were determined according to reduction in initial SBP: mild, moderate and severe. Mild hypotension defined as a drop of ≥10% and ≤20% in baseline SBP, moderate hypotension defined as a drop of >20% and ≤30% in baseline SBP and severe hypotension defined as a drop of >30% in baseline SBP. A reduction of SBP to <10% of the baseline SBP was defined as 'no hypotension'. Any drop >20% in baseline SBP was treated with a bolus of 5 mg ephedrine, which was repeated every 2 min as required.

The data were collected prospectively and manually through preset questionnaires by trained anaesthetic staff. The percentage of the reduction in SBP was calculated by STATA software (StataCorp LLC, College Station, Texas, USA) version 13.0. The proforma contained three parts: maternal and anaesthesia-related variables and a table for recording maternal blood pressure and HR. Maternal data such as age, body

mass index (BMI), weight at delivery, height, weight gain during pregnancy, ASA physical status, gravidity, history of previous pregnancies, preoperative history of hypertension (HTN), hypotension, and hypothyroid, and baseline SBP, DBP, and HR gathered during preoperative phase. Variables related to the technique and conduct of SA were collected in parallel with the administration of SA.The present study aimed to evaluate these variables (related to parturient and anaesthesia techniques) associated with the incidence of different degrees of SA-induced hypotension during elective CS.

All parameters were coded, recorded and analysed using STATA software version 13.0. Descriptive statistics were presented as a mean ± standard deviation for continuous variables and number (%) for categorical ones. All parametric and non-parametric parameters were tested for normal distribution before further appropriated statistical analyses. Since the data failed to satisfy the proportional odds assumption, the ordinality of the outcome (degrees of hypotension) was ignored and multinomial logistic regression model was used. Univariate and multivariate multinomial logistic regression were employed and reported separately for each category of maternal and anaesthesia-related variables. In the models, 'no hypotension' was the base. On the other hand, due to problem in finding a specified definition for hypotension in the literature, in the present study, all the three above-mentioned hypotension degrees were included in multinomial logistic regression.

To estimate the sample size and increase the study reliability, a pilot study was conducted on 100 parturients, in our hospital. The least incidence was mild hypotension, which occurred in 19 patients. Then, the sample size was calculated for $\alpha = 0.05$ (level of statistical significance), minimum p = 20% (expected proportion), and d = 3.5% (margin of error in estimating p). The estimated sample size was 502.

RESULTS

Description of maternal and anaesthesia-related variables has been presented in Tables 1 and 2, respectively.

The incidence of hypotension varied according to its definition and cut-off point. The incidence of mild, moderate and severe hypotension were 20%, 35% and 40%, respectively.

Eventually, in multivariate analysis through multinomial logistic regression, seven maternal and three anaesthesia-related variables remained as the most important predictors of SA-induced hypotension [Table 3].

Amongst maternal variables, increasing age, body mass index (BMI) ≥25 kg/m^2, weight gain >10 kg during pregnancy, ASA II versus I, gravidity ≥3 versus 1, live births ≥ two versus no live births, history of one previous normal vaginal delivery (NVD) versus no prior history of NVD, history of ≥2 previous CS versus no prior history of CS, history of HTN, hypotension and hypothyroid, baseline SBP <120 mmHg, baseline DBP <80 mmHg and baseline HR >80 beats/min were associated with the development of hypotension in maternal univariate analysis [Appendix Table 1].

Age, BMI, weight gain during pregnancy, gravidity, history of hypotension, baseline SBP and baseline HR remained as the most important predictors of hypotension in the maternal multivariate model ($P < 0.05$) [Table 3 and Figure 1]. History of hypotension was significantly associated with the incidence of all hypotension degrees (relative risk ratio [RRR] = 4.49, 6.98 and 5.81 for mild, moderate and severe hypotension, respectively) [Table 3]. Age >35 years and gravidity ≥4 were also associated with the development of both moderate and severe hypotension. Moreover, BMI ≥30 kg/m^2 showed an association with RRR of 6.35 and 5.25, indicating a more than 6- and 5-fold increased risk of moderate and

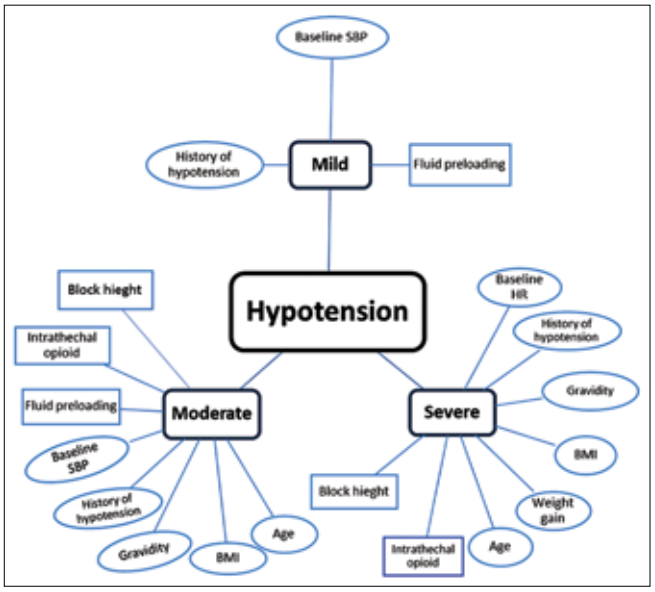

Figure1: The risk factors of different hypotension degrees based on final modelling

Table 1: Description of the maternal variables*

Variables	Total	Hypotension			
		No	Mild	Moderate	Severe
Age (year)					
15-25	78 (100.0)	7 (9.0)	20 (25.7)	25 (32.00)	26 (33.3)
26-35	306 (100.0)	15 (4.9)	62 (20.3)	104 (34.0)	125 (40.8)
>35	127 (100.0)	3 (2.4)	20 (15.7)	49 (38.6)	55 (43.3)
BMI (kg/m^2)					
18.5-<25	60 (100.0)	5 (8.4)	29 (48.3)	12 (20.0)	14 (23.3)
25-<30	188 (100.0)	10 (5.3)	32 (17.0)	67 (35.7)	79 (42.0)
≥30	263 (100.0)	10 (3.8)	41 (15.6)	99 (37.6)	113 (43.0)
Weight at delivery (kg)†	79.43±12.10	76.92±11.97	79.34±13.52	79.27±11.83	79.91±11.64
Height (cm)†	161.23±6.27	161.72±7.03	161.48±6.82	160.98±5.80	161.24±6.33
Weight gain during pregnancy (kg)					
≤10	154 (100.0)	11 (7.2)	39 (25.3)	63 (40.9)	41 (26.6)
11-20	264 (100.0)	9 (3.4)	50 (19.0)	83 (31.4)	122 (46.2)
>20	93 (100.0)	5 (5.4)	13 (14.0)	32 (34.4)	43 (46.2)
ASA classification					
I	333 (100.0)	22 (6.6)	69 (20.7)	120 (36.0)	122 (36.7)
II	178 (100.0)	3 (1.7)	33 (18.5)	58 (32.6)	84 (47.2)
Gravidity					
1	94 (100.0)	7 (7.5)	26 (27.6)	31 (33.0)	30 (31.9)
2	191 (100.0)	12 (6.3)	52 (27.2)	61 (31.9)	66 (34.6)
3	113 (100.0)	4 (3.5)	14 (12.4)	41 (36.3)	54 (47.8)
≥4	113 (100.0)	2 (1.8)	10 (8.8)	45 (39.8)	56 (49.6)
Frequency of live births					
0	124 (100.0)	6 (4.8)	29 (23.4)	51 (41.1)	38 (30.7)
1	265 (100.0)	16 (6.0)	56 (21.1)	86 (32.5)	107 (40.4)
≥2	122 (100.0)	3 (2.5)	17 (13.9)	41 (33.6)	61 (50.0)
History of stillbirth					
No	480 (100.0)	23 (4.8)	97 (20.2)	167 (34.8)	193 (40.2)
Yes	31 (100.0)	2 (6.5)	5 (16.1)	11 (35.5)	13 (41.9)
Number of previous NVD					
0	454 (100.0)	20 (4.4)	93 (20.5)	158 (34.8)	183 (40.3)
1	42 (100.0)	4 (9.5)	7 (16.7)	14 (33.3)	17 (40.5)
≥2	15 (100.0)	1 (6.7)	2 (13.3)	6 (40.0)	6 (40.0)
Number of previous CS					
0	153 (100.0)	9 (5.9)	31 (20.3)	57 (37.2)	56 (36.6)
1	247 (100.0)	12 (4.9)	54 (21.9)	88 (35.6)	93 (37.6)
≥2	111 (100.0)	4 (3.6)	17 (15.3)	33 (29.7)	57 (51.4)
Number of previous abortions					
0	383 (100.0)	19 (5.0)	79 (20.6)	131 (34.2)	154 (40.2)
1	90 (100.0)	5 (5.5)	16 (17.8)	33 (36.7)	36 (40.0)
≥2	38 (100.0)	1 (2.6)	7 (18.4)	14 (36.9)	16 (42.1)
History of HTN					
No	423 (100.0)	22 (5.2)	93 (22.0)	165 (39.0)	143 (33.8)
Yes	88 (100.0)	3 (3.4)	9 (10.2)	13 (14.8)	63 (71.6)
History of hypotension					
No	254 (100.0)	20 (7.9)	54 (21.2)	80 (31.5)	100 (39.4)
Yes	257 (100.0)	5 (2.0)	48 (18.7)	98 (38.1)	106 (41.2)
History of hypothyroid					
No	331 (100.0)	22 (6.7)	68 (20.5)	115 (34.7)	126 (38.1)
Yes	180 (100.0)	3 (1.7)	34 (18.9)	63 (35.0)	80 (44.4)
Baseline SBP (mmHg)					
≥120	150 (100.0)	15 (10.0)	31 (20.7)	58 (38.7)	46 (30.6)
<120	361 (100.0)	10 (2.8)	71 (19.7)	120 (33.2)	160 (44.3)
Baseline DBP (mmHg)					
≤80	255 (100.0)	16 (6.3)	52 (20.4)	97 (38.0)	90 (35.3)

Contd...

Table 1: Contd...

Variables	Total	Hypotension			
		No	Mild	Moderate	Severe
>80	256 (100.0)	9 (3.5)	50 (19.5)	81 (31.7)	116 (45.3)
Baseline HR (beats/min)					
60-80	90 (100.0)	7 (7.8)	20 (22.2)	42 (46.7)	21 (23.3)
81-100	267 (100.0)	14 (5.2)	64 (24.0)	85 (31.8)	104 (39.0)
>100	154 (100.0)	4 (2.6)	18 (11.7)	51 (33.1)	81 (52.6)

*Values are expressed as *n* (%) unless otherwise indicated, †Mean±SD. ASA – American Society of Anaesthesiologists; BMI – Body mass index; CS – Caesarean section; DBP – Diastolic blood pressure; HR – Heart rate; HTN – Hypertension; NVD – Normal vaginal delivery; SBP – Systolic blood pressure; SD – Standard deviation

severe hypotension, respectively. However, BMI of 25–30 kg/m^2 was just associated with the development of moderate hypotension (RRR = 4.9, P = 0.02). Besides, baseline SBP <120 mmHg with RRR of 6.5 (P = 0.01) and 4.8 (P = 0.001) was associated with the development of mild and moderate hypotension, respectively. Weight gain of 11–20 kg (RRR = 5, P = 0.003) and baseline HR >100 beats/min (RRR = 5.1, P = 0.02) were associated with the development of severe hypotension.

Amongst anaesthesia-related variables, fluid preloading >1000 ml, needle size 27-gauge versus 23-gauge, space L_5–S_1 versus L_4–L_5, bloody aspiration, having paraesthesia, adding intrathecal opioid to the injected local anaesthetic compared to pure bupivacaine, sensory block height higher than T_4, more than a 11 min interval between spinal puncture and delivery, administration of O_2 for mother and history of ≥2 previous SA and GA were associated with the development of hypotension degrees in anaesthesia-related univariate analysis [Appendix Table 1].

Amongst the factors in anaesthesia-related multivariate model, three were found to be statistically associated with hypotension. Fluid preloading ≥1000 ml (with RRR = 0.25 [P = 0.003] and RRR = 0.34 [P = 0.04] for mild and moderate hypotension, respectively) and adding 1 μg sufentanil to the injected local anaesthetic compared to pure bupivacaine (with RRR = 0.19 [P = 0.02] and RRR = 0.15 [P = 0.008] for moderate and severe hypotension, respectively) were associated with decreased risk of hypotension. However, sensory block height higher than T_4 was related to a higher incidence of hypotension (with RRR = 5.07 [P = 0.04] and RRR = 7.33 [P = 0.01] for moderate and severe hypotension, respectively) [Table 3 and Figure 1].

DISCUSSION

In this prospective study, the the incidence of mild, moderate and severe SA-induced hypotension was 20%, 35%, and 40%, respectively. Second, in maternal modelling, age, BMI, weight gain, gravidity, history of hypotension, baseline SBP and baseline HR were found to be statistically associated with the development of hypotension. Amongst them, baseline SBP <120 mmHg (RRR = 6.53), history of hypotension (RRR = 6.98) and gravidity ≥4 (RRR = 6.84) were the strongest predictors for mild, moderate and severe hypotension, respectively. Finally, in anaesthesia-related modelling, fluid preloading, adding 1 μg sufentanil to the injected local anaesthetic and sensory block height were identified to be related to the incidence of hypotension. Amongst anaesthesia-related predictors, sensory block height ≥T_4 was the strongest predictor (RRR = 7.33).

Our findings support those of the previous reports that demonstrated a high incidence of hypotension after SA during CS.[5-7] Although parturients' physiological changes might be a logical reason, the present study findings revealed ten independent variables associated with the incidence of SA-induced hypotension during elective CS.

Advanced age is a factor that has been repeatedly identified in the current literature as a predictor of SA-induced hypotension.[5-8] Different studies have demonstrated a tendency towards a greater decrease in SBP in older age groups. In accordance with previous studies, our study suggested that age >35 years was the cut-off point,[6,7] whereas the onset of tendency towards hypotension was later in non-parturient patients receiving SA.[8] It seems that reduction in cardiac reserve and changes in baroreceptor and sympathetic nervous system responses may play certain roles in increasing the risk of hypotension in older patients.[9-11]

In consistent with prior studies, the present research also confirmed raised BMI as a risk factor for SA-induced hypotension.[5,7,12-14] The cut-off

Table 2: Description of the anaesthesia-related variables*

Variables	Total	Hypotension			
		No	Mild	Moderate	Severe
Fluid preloading (ml)					
0-250	84 (100.0)	3 (3.6)	30 (35.7)	26 (30.9)	25 (29.8)
251-500	218 (100.0)	3 (1.4)	30 (13.8)	91 (41.7)	94 (43.1)
501-1000	102 (100.0)	7 (6.9)	25 (24.5)	31 (30.4)	39 (38.2)
≥1000	107 (100.0)	12 (11.2)	17 (15.9)	30 (28.0)	48 (44.9)
Needle size (gauge)					
23	53 (100.0)	2 (3.8)	11 (20.7)	18 (34.0)	22 (41.5)
24	129 (100.0)	3 (2.3)	19 (14.7)	47 (36.5)	60 (46.5)
25	271 (100.0)	9 (3.3)	63 (23.2)	95 (35.1)	104 (38.4)
27	58 (100.0)	11 (19.0)	9 (15.5)	18 (31.0)	20 (34.5)
Space of spinal puncture					
L_4-L_5	414 (100.0)	18 (4.3)	85 (20.5)	148 (35.8)	163 (39.4)
L_3-L_4	59 (100.0)	1 (1.7)	7 (11.9)	19 (32.2)	32 (54.2)
L_5-S_1	38 (100.0)	6 (15.7)	10 (26.3)	11 (29.0)	11 (29.0)
Type of SA					
Median	434 (100.0)	22 (5.1)	84 (19.3)	147 (33.9)	181 (41.7)
Paramedian	77 (100.0)	3 (3.9)	18 (23.4)	31 (40.2)	25 (32.5)
Frequency of attempts for spinal puncture					
1	347 (100.0)	19 (5.5)	57 (16.4)	132 (38.0)	139 (40.1)
2	112 (100.0)	5 (4.5)	36 (32.1)	26 (23.2)	45 (40.2)
≥3	52 (100.0)	1 (1.9)	9 (17.3)	20 (38.5)	22 (42.3)
Aspiration					
Clear	478 (100.0)	21 (4.4)	93 (19.5)	168 (35.1)	196 (41.0)
Bloody	33 (100.0)	4 (12.1)	9 (27.3)	10 (30.3)	10 (30.3)
Paraesthesia					
No	446 (100.0)	23 (5.1)	92 (20.6)	146 (32.7)	185 (41.5)
Yes	65 (100.0)	2 (3.1)	10 (15.4)	32 (49.2)	21 (32.3)
Added intrathecal opioid to the local anaesthetic					
None	61 (100.0)	2 (3.3)	10 (16.4)	20 (32.8)	29 (47.5)
Sufentanil (1 μg)	80 (100.0)	14 (17.5)	28 (35)	18 (22.5)	20 (25.0)
Fentanyl (10 μg)	105 (100.0)	8 (7.6)	27 (25.7)	36 (34.3)	34 (32.4)
Pethidine (10 mg)	265 (100.0)	1 (0.4)	37 (14.0)	104 (39.2)	123 (46.4)
Sensory block height					
≥T4	382 (100.0)	23 (6.0)	83 (21.7)	136 (35.6)	140 (36.7)
<T4	129 (100.0)	2 (1.5)	19 (14.7)	42 (32.6)	66 (51.2)
Time interval between spinal puncture and delivery (min)					
5-10	179 (100.0)	13 (7.3)	19 (10.6)	70 (39.1)	77 (43.0)
11-15	282 (100.0)	11 (3.9)	53 (18.8)	100 (35.5)	118 (41.8)
>15	50 (100.0)	1 (2.0)	30 (60.0)	8 (16.0)	11 (22.0)
Administration of O_2 for mother					
No	352 (100.0)	22 (6.3)	79 (22.4)	126 (35.8)	125 (35.5)
Yes	159 (100.0)	3 (1.9)	23 (14.5)	52 (32.7)	81 (50.9)
Number of previous GA					
0	259 (100.0)	15 (5.8)	50 (19.3)	95 (36.7)	99 (38.2)
1	187 (100.0)	8 (4.3)	42 (22.4)	68 (36.4)	69 (36.9)
≥2	65 (100.0)	2 (3.1)	10 (15.4)	15 (23.1)	38 (58.4)
Number of previous SA					
0	332 (100.0)	15 (4.5)	62 (18.7)	118 (35.5)	137 (41.3)
1	143 (100.0)	6 (4.2)	34 (23.8)	48 (33.5)	55 (38.5)
≥2	36 (100.0)	4 (11.1)	6 (16.7)	12 (33.3)	14 (38.9)

*Values are expressed as *n* (%). GA - General anaesthesia; L - Lumbar vertebrae; S - Sacral vertebrae; SA - Spinal anaesthesia; T - Thoracic vertebrae

point for BMI varied from 25 to 35 kg/m^2 in the current literature.[15] A previous study has suggested that the extent of sensory block was correlated to lumbosacral cerebrospinal fluid (CSF) volume.[16] Thus, it seems that decrease in CSF volume due to elevated abdominal pressure and compression of

Table 3: Multivariate multinomial logistic regression analysis for maternal and anaesthesia-related risk factors of spinal anaesthesia-induced hypotension

Variable	Hypotension								
	No	Mild			Moderate			Severe	
	Ref	RRR	95% CI	*P*	RRR	95% CI	*P*	RRR	95% CI	*P*
Maternal variables										
Age (year)										
15-25	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
26-35	-	1.58	0.51-4.82	0.42	2.25	0.75-6.77	0.15	2.38	0.79-7.18	0.12
>35	-	2.85	0.55-14.71	0.21	5.56	1.10-28.05	0.03*	5.43	1.07-27.45	0.04*
Weight gain during pregnancy (kg)										
≤10	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
11-20	-	2.47	0.83-7.38	0.10	2.07	0.71-6.08	0.18	5.07	1.72-14.94	0.003*
>20	-	0.60	0.15-2.41	0.47	0.71	0.19-2.65	0.61	1.62	0.43-6.02	0.47
BMI (kg/m^2)										
18.5-<25	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25-<30	-	0.75	0.20-2.84	0.67	4.90	1.21-19.77	0.02*	3.93	0.99-15.61	0.052
≥30	-	1.23	0.31-4.78	0.76	6.35	2.23-39.15	0.002*	5.25	1.76-29.90	0.006*
Gravidity										
1	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
2	-	1.19	0.36-3.86	0.77	1.16	0.36-3.74	0.81	1.58	0.48-5.11	0.44
3	-	1.06	0.23-4.93	0.94	2.54	0.58-11.13	0.22	3.98	0.91-17.40	0.06
≥4	-	1.51	0.23-9.70	0.66	5.98	1.01-35.25	0.048*	6.84	1.32-46.33	0.02*
History of hypotension										
No	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	-	4.49	1.36-14.72	0.01*	6.98	2.17-22.40	0.001*	5.81	1.81-18.69	0.003*
Baseline SBP (mmHg)										
≥120	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<120	-	6.53	1.63-26.21	0.008*	4.79	1.21-19.00	0.02*	2.68	0.67-10.71	0.16
Baseline HR (beats/min)										
60-80	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
81-100	-	1.28	0.40-4.03	0.68	0.75	0.24-2.30	0.62	1.99	0.63-6.32	0.24
>100	-	1.23	0.28-5.38	0.78	1.48	0.36-6.07	0.58	5.10	1.21-21.37	0.02*
Anaesthesia-related variables										
Fluid preloading (ml)										
0-250	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
251-500	-	0.78	0.14-4.32	0.78	2.46	0.44-13.63	0.30	2.67	0.48-14.94	0.26
501-1000	-	0.30	0.07-1.33	0.11	0.40	0.08-1.80	0.23	0.51	0.11-2.36	0.39
≥1000	-	0.25	0.02-0.47	0.003*	0.34	0.05-0.91	0.04*	0.34	0.08-1.48	0.15
Added intrathecal opioid to the local anaesthetic										
Non	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sufentanil (1 μg)	-	0.41	0.07-2.26	0.31	0.19	0.02-0.74	0.02*	0.15	0.02-0.55	0.008*
Fentanyl (10 μg)	-	0.87	0.15-5.03	0.87	0.61	0.11-3.32	0.57	0.42	0.08-2.24	0.31
Pethidine (10 mg)	-	8.28	0.66-102.97	0.10	11.33	0.96-134.28	0.054	9.55	0.82-111.42	0.07
Sensory block height										
<T_4	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
≥T_4	-	3.74	0.74-18.81	0.11	5.07	1.03-25.03	0.04*	7.33	1.50-35.07	0.01*

*P<0.05. BMI – Body mass index; CI – Confidence interval; HR – Heart rate; Ref – Reference category; RRR – Relative risk ratio; SBP – Systolic blood pressure

the subarachnoid cavity, as in obesity or pregnancy, is a possible mechanism for more extensive spinal blockade in such subjects. Nevertheless, a relatively poor correlation was found between lumbosacral CSF volume and BMI ($r = 0.4$), which might be insufficient to reliably predict CSF volume.[17] On the other hand, several recent publications have documented that higher risk for relevant hypotension in obese patients did not coincide with an expected increase in the level of anaesthesia.[7,14]

The findings in the present study pointed out that a 11–20 kg weight gain during pregnancy above the antenatal weight was a risk factor, with a 5-fold increase in the risk of developing severe hypotension. However, a previous study indicated

that inadequate (<11 kg) weight gain was a risk factor for SA-induced hypotension.[18]

Indeed, parturients with gravidity ≥4 versus 1 were associated with a more than 5-fold and 7-fold increase in the risk of developing moderate and severe hypotension, respectively. Previous studies have proposed a reduction in peripheral vascular tone during a healthy pregnancy.[19] The magnitude of the decrease in systemic vascular resistance secondary to pregnancy was greater in multiparous women compared to nulliparous ones.[20] Consequently, induction of sympathectomy by SA in multiparous pregnant women has been thought to be accompanied with further SA-induced hypotension.[19]

In addition to the previously identified risk factors, the results demonstrated that having a history of hypotension in pregnancy was associated with an increased risk of developing all three degrees of hypotension. The reason for this observation is not clear. Yet, it might be attributed to the fact that history of hypotension represents more changes in the regulation of autonomic nervous system during pregnancy. Thus, pregnant women would be more susceptible to sympathectomy due to SA.

Similar to earlier findings,[10,11,21] our study results revealed that baseline SBP <120 mmHg was associated with an increased risk of developing hypotension. Moreover, there was some evidence in the literature that prior history of HTN could predict hypotension.[6,9,14] However, it was not significantly confirmed in the current study.

In accordance with previous studies, the results of the present research showed a significantly increased incidence of hypotension in the group with a higher baseline HR.[22] To our mind, since preoperative anxiety may cause generalised sympathetic activation,[23] patients with increased HR secondary to preoperative fear or anxiety would experience more hypotension after induction of SA.[23] However, Toyama failed to address baseline HR as a good predictor of SA-induced hypotension.[19]

In spite of all controversies, fluid pre-loading with crystalloid or colloid has been widely been used in up to 87% of the cases undergoing SA for CS.[24,25] In contrast to the earlier findings,[24,25] our results showed that mild and moderate hypotension were significantly reduced in patients preloaded with larger volumes (≥1000 ml) of crystalloid. Nevertheless, this has been proved disappointing in preventing severe hypotension. On the other hand, some evidence has indicated that large volumes of crystalloid fluid could lead to acute haemodilution or increasing the risk of pulmonary oedema, especially in pregnant women.[24] Consequently, pre-hydration of crystalloid does not appear to confer additional benefit over small volumes (250 ml), and large volumes might be detrimental to parturients.[26]

The present study results provided clear statistical confirmation of one previously anaesthesia-related predictor for SA-induced hypotension, sensory block height.[5,7,11,12,14,21] Higher sensory block was believed to result in blockage of cardioaccelerator fibres, eventually changing cardiovascular parameters.[13,21] Similarly, in the present investigation, higher sensory levels were correlated to a greater decrease in SBP.

Nowadays, addition of various opioids to local anaesthetics has become a widely used strategy for SA in CS, which may improve intra- and post-operative analgesic effects and reduce side effects.[27] The current study findings suggested that SA with a combination of 1 μg sufentanil and low-dose bupivacaine (10 mg) versus pure bupivacaine were associated with a lower incidence of moderate and severe hypotension. However, most researchers failed to establish a significant relationship between the use of intrathecal sufentanil and hypotension.[27] Olofsson *et al*. showed that addition of sufentanil to bupivacaine prevented maternal hypotension in non-pregnant patients.[28] Hence, further research is required to reach a clear conclusion.

The strengths of this study included prospective data collection processes, relatively large sample size, evaluation of a wide range of variables and using different severities of hypotension in the modelling. Yet, the ultimate determination of the independent effect of any single factor awaits a prospective, clinical, randomised and blinded study. The research was also limited in several ways including the time-consuming process of data gathering and ignoring the impact of surgical-related factors during the 30 min period after SA induction on the development of hypotension. Clearly, further researches on the issue would be of interest. In our future research, we intend to concentrate on other side effects of SA during elective CS.

CONCLUSION

The risk factors for spinal anaesthesia induced hypotension during CS could be age, BMI, weight gain, gravidity, history of hypotension, baseline SBP and HR (maternal risk factors), and fluid preloading, addition of sufentanil to bupivacaine and sensory block height (anaesthesia-related risk factors).

Financial support and sponsorship

This study was financially supported by Shiraz University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

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Appendix Table 1: Univariate multinomial logistic regression analysis for maternal and anaesthesia-related risk factors of spinal anaesthesia-induced hypotension

Variable	Hypotension									
	No	Mild			Moderate			Severe		
	Ref	RRR	95% CI	*P*	RRR	95% CI	*P*	RRR	95% CI	*P*
Maternal variables										
Age (year)										
15-25	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
26-35	-	1.44	0.51-4.05	0.48	1.94	0.71-5.26	0.19*	2.24	0.83-6.05	0.11*
>35	-	2.33	0.53-10.33	0.26	4.57	1.09-19.22	0.03†	4.93	1.18-20.64	0.03†
BMI (kg/m^2)										
18.5-<25	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25-<30	-	0.55	0.17-1.80	0.32	2.79	0.81-9.61	0.10*	2.82	0.84-9.50	0.09*
≥30	-	0.70	0.22-2.29	0.56	4.12	1.20-14.10	0.02†	4.03	1.20-13.51	0.02†
Weight gain during pregnancy (kg)										
≤10	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
11-20	-	1.56	0.59-4.15	0.37	1.61	0.63-4.12	0.32	3.63	1.41-9.40	0.008†
>20	-	0.73	0.21-2.50	0.62	1.12	0.36-4.49	0.85	2.30	0.74-7.22	0.15*
ASA classification										
I	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
II	-	3.51	0.98-12.56	0.054*	3.54	1.02-12.33	0.047†	5.05	1.46-17.41	0.010†
Gravidity										
1	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
2	-	1.17	0.41-3.31	0.77	1.15	0.41-3.20	0.79	1.28	0.46-3.58	0.63
3	-	0.94	0.23-3.78	0.93	2.31	0.62-8.61	0.21	3.15	0.85-11.64	0.08*
≥4	-	1.34	0.24-7.61	0.74	5.08	0.99-26.10	0.052*	6.53	1.28-33.44	0.02†
Frequency of live births										
0	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-	0.72	0.25-2.05	0.54	0.63	0.23-1.72	0.37	1.05	0.38-2.89	0.92
≥2	-	1.17	0.26-5.30	0.84	1.60	0.38-6.82	0.52	3.21	0.76-13.06	0.11*
Number of previous NVD										
0	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-	0.38	0.10-1.40	0.15*	0.44	0.13-1.48	0.18*	0.46	0.14-1.52	0.20*
≥2	-	0.43	0.04-4.98	0.50	0.76	0.08-6.63	0.80	0.65	0.07-5.72	0.70
Number of previous CS										
0	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-	1.31	0.49-3.44	0.59	1.16	0.46-2.92	0.76	1.24	0.49-3.14	0.64
≥2	-	1.23	0.33-4.60	0.75	1.30	0.37-4.56	0.68	2.29	0.66-7.87	0.19*
History of HTN										
No	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	-	0.71	0.18-2.84	0.63	0.58	0.15-2.19	0.42	3.23	0.93-11.19	0.06*
History of hypotension										
No	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	-	3.55	1.24-10.20	0.02†	4.9	1.76-13.63	0.002†	4.24	1.53-11.73	0.005†
History of hypothyroid										
No	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	-	3.66	1.02-13.11	0.04†	4.02	1.16-13.95	0.03†	4.65	1.35-16.06	0.01†
Baseline SBP (mmHg)										
≥120	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<120	-	3.51	0.98-12.56	0.054*	2.63	0.75-9.19	0.13*	1.66	0.47-5.83	0.43
Baseline DBP (mmHg)										
≥80	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<80	-	1.71	0.69-4.22	0.24	1.48	0.62-3.54	0.37	2.29	0.97-5.42	0.059*
Baseline HR (beats/min)										
60-80	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
81-100	-	1.83	0.67-4.99	0.24	1.15	0.45-2.97	0.76	2.83	1.05-7.59	0.04†
>100	-	2.40	0.55-10.45	0.24	3.24	0.81-12.98	0.10*	10.28	2.51-42.17	0.001†

Contd...

Appendix Table 1: Contd...

Variable		Hypotension								
	No	Mild			Moderate			Severe		
	Ref	RRR	95% CI	*P*	RRR	95% CI	*P*	RRR	95% CI	*P*
Anaesthesia-related variables										
Fluid preloading (ml)										
0-250	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
251-500	-	0.99	0.18-5.36	1.00	3.50	0.66-18.38	0.14*	1.82	0.71-19.77	0.12*
501-1000	-	0.35	0.08-1.52	0.16*	0.51	0.12-2.18	0.36	0.09	0.16-2.83	0.58
≥1000	-	0.14	0.03-0.57	0.006†	0.29	0.07-1.13	0.07*	0.02	0.12-1.86	0.29
Needle size (gauge)										
23	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
24	-	1.15	0.16-7.99	0.88	1.74	0.27-11.29	0.56	1.82	0.28-11.62	0.53
25	-	1.27	0.24-6.70	0.77	1.17	0.23-5.88	0.85	1.05	0.21-5.20	0.95
27	-	0.15	0.02-0.85	0.032†	0.18	0.03-0.93	0.04†	0.16	0.03-0.84	0.03†
Space of spinal puncture										
L_4-L_5	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
L_3-L_4	-	1.48	0.17-12.80	0.72	2.31	0.29-18.30	0.43	3.53	0.45-27.42	0.23
L_5-S_1	-	0.35	0.11-1.09	0.07*	0.22	0.07-0.67	0.008†	0.20	0.06-0.61	0.005†
Aspiration										
Clear	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Bloody	-	0.51	0.14-1.80	0.30	0.31	0.09-1.08	0.067*	0.26	0.08-0.92	0.038†
Paraesthesia										
No	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	-	1.25	0.25-6.10	0.78	2.52	0.56-11.23	0.10*	1.30	0.29-5.93	0.73
Added intrathecal opioid to the local anaesthetic										
Non	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sufentanil (1 μg)	-	0.40	0.07-2.08	0.27	0.13	0.02-0.64	0.01†	0.10	0.02-0.48	0.004†
Fentanyl (10 μg)	-	0.67	0.12-3.73	0.65	0.45	0.09-2.32	0.34	0.29	0.06-1.50	0.14*
Pethidine (10 mg)	-	7.40	0.61-90.15	0.12*	10.40	0.90-120.24	0.06*	8.48	0.74-96.77	0.08*
Sensory block height										
≥T_4	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<T_4	-	2.63	0.57-12.14	0.21	3.55	0.80-15.70	0.09*	5.42	1.24-23.68	0.02†
Time interval between spinal puncture and delivery (min)										
5-10	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
11-15	-	3.30	1.26-8.60	0.015†	1.69	0.71-3.98	0.23	1.81	0.77-4.25	0.17*
>15	-	20.52	2.48-169.91	0.005†	1.48	0.17-12.90	0.72	1.85	0.22-15.62	0.57
Administration of O_2 for mother										
No	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	-	2.13	0.58-7.77	0.25	3.03	0.87-10.55	0.082*	4.75	1.40-16.39	0.01†
Number of the previous GA										
0	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-	1.57	0.61-4.07	0.35	1.34	0.54-3.34	0.53	1.30	0.52-3.25	0.56
≥2	-	1.50	0.29-7.61	0.62	1.20	0.24-5.70	0.83	2.88	0.63-13.19	0.17*
Number of previous SA										
0	-	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-	1.37	0.48-3.85	0.55	1.02	0.37-2.77	0.97	1.00	0.37-2.72	0.99
≥2	-	0.36	0.09-1.45	0.15*	0.38	0.10-1.33	0.13*	0.38	0.11-1.31	0.13*

*0.05 ≤ *P* ≤0.2, †*P*<0.05. ASA – American Society of Anaesthesiologists; BMI – Body mass index; CS – Caesarean section; CI – Confidence interval; DBP – Diastolic blood pressure; GA – General anaesthesia; HR – Heart rate; HTN – Hypertension; L – Lumbar vertebrae; NVD – Normal vaginal delivery; Ref – Reference category; RRR – Relative risk ratio; S – Sacral vertebrae; SA – Spinal anaesthesia; SBP – Systolic blood pressure; T – Thoracic vertebrae