



EFFECT OF WAIST HIP RATIO AND BODY MASS INDEX ON SENSORY BLOCK LEVEL OF SPINAL ANAESTHESIA AND HAEMODYNAMIC CHANGES DURING CAESAREAN SECTION

Dr Vindu Yadav^{1*}, Dr Priyanka Singh², Dr Jharna Mili³

^{1*}Department of Anaesthesia, King George's Medical University, Lucknow, India

²Department of anaesthesia, King George's Medical University, Lucknow, India

³Department of anaesthesia, King George's Medical University, Lucknow, India

***Corresponding Author:** Dr.Vindu Yadav

*MD anaesthesia, King George's Medical University, Lucknow, India

Abstract:

we aimed to determine the effect of some anthropometric values on sensorial block characteristics of spinal anesthesia and hemodynamics in patients undergoing elective cesarean sections performed under spinal anesthesia. Weight, length, and body mass index, waist and hip circumferences ratio of 200 patients were measured. Spinal anesthesia was applied while the patient was sitting erect. The time of sensorial block to reach the T4 level and the maximum sensorial block level were recorded in each case. Cases who developed hypotension and bradycardia during the spinal anesthesia were recorded. In this study hypotension was observed in 54% of patients and it was determined that the prevalence of hypotension increased in patients with a higher body mass index, a higher waist/hip ratio. It was found that the prevalence of bradycardia increased in patients with a higher body mass index and a higher waist/hip ratio. This study also determined a positive correlation between the values of height, weight and the time of sensorial block to reach the T4 dermatome; and a positive correlation between the body mass index and the dermatome area of the maximum sensorial block. In line with the values provided by simple and non-time consuming anthropometric measurements the patients who are planned to receive a spinal anesthesia may be priorly prepared against adverse effects of bradycardia and hypotension that may develop, and to estimate the sensorial block characteristics of the spinal anesthesia.

Key words: waist-hip ratio, anthropometric measurement, spinal anesthesia, body mass index

Introduction

When selecting the anaesthesia method in caesarean operations, attention must be paid to the urgency of the operation, pre-existing maternal systemic problems, general status of the fetus, and the surgeon's and patient's preference. Although general or regional anaesthesia can be used in caesarean operations, regional anaesthesia is the most widely preferred anaesthesia method for caesarean sections in developed countries. Regional anaesthesia offers many advantages to the mother as follows: mother is awake during the labour, very little or no requirement for airway intervention, protection of airway reflexes, reduced blood loss, reduced probability of drug-related fetal depression, and the continuation of analgesia in the postoperative period^{1,2}.

One of the most frequently used regional anaesthesia techniques is spinal anaesthesia, in which nerve transmission is temporarily halted with the injection of local anesthetic into the cerebral spinal fluid³.

As there is a greater amount of epidural fat tissue in obese patients, the epidural veins are widened and the epidural space is narrowed. Therefore, there is a need for 20-25% less local anesthetic in spinal and epidural anaesthesia. In circumstances that lead to an increase in intra-abdominal pressure or widening of the epidural veins, unwontedly higher levels of block are induced. A high level of block easily causes respiratory depression. Pregnant patients display higher sensitivity to local anesthetics during regional anaesthesia and the dosage requirement can be reduced down to 30%. Neural blockage forms at low concentrations of local anesthetics.

With increasing rates of maternal obesity and the accompanying comorbidities throughout the world, maternal obesity has been reported to be a significant public health problem⁵. Maternal obesity is accepted as a factor which increases the risk of complications during pregnancy and the labor, including stillbirth, childhood obesity and diabetes⁶. It is recommended that anthropometric measurements should be performed for all pregnant women because of the negative effects of obesity on the health of both mother and her child⁷. In the last 20 years, as in developed countries, there has been an increase in socio-economic conditions and alteration of the nutritional habits in Turkey which resulted in an increase in the rates of obesity. The main reason that obesity is seen more often in females is excessive weight gain before and during pregnancy⁸.

Taking these changes into consideration, the aim of this study was to determine the effects of calculated values or measurements such as body mass index (BMI), and waist:hip ratio on the hemodynamic and sensorial block characteristics of spinal anaesthesia applied to patients undergoing elective caesarean section operations.

Material and methods

A prospective, observational study, was conducted in Department of Obstetrics and Gynaecology at King George Medical University and Queen Mary Hospital Lucknow. Before commencing the study, approval was obtained from the institutional ethical committee. Participants in this study were explained about the anesthetic procedure and informed, written consent was taken.

Preoperatively, all patients were weighed, and their height was measured and BMI (body weight/height²) of the patients was calculated. Demographic information and gestational weeks of each patient was recorded. With the patient standing upright, Abdominal circumference was measured from the mid-point between the upper part of the iliac bone and the 12th costal and hip circumference was measured the most prominent part of the gluteal muscles and these measurements were recorded. (waist- hip ratio calculated by this method).

In the premedication room, an IV line was secured on the back of the left hand with a 20G IV cannula and 20 minutes before the operation an infusion of Ringer's Lactate was started at the rate of 10 ml/kg/hour.

For all the parturient women, an automated noninvasive blood pressure device was installed on the right arm and a pulse oximetry and electrocardiograph were installed on the left arm prior to spinal anaesthesia, in order to record blood pressure and heart rate. The initially measured blood pressure and heart rate were defined as the resting blood pressure and resting heart rate. During the intravenous injection of Hartmann crystalloid solution (15 ml/kg), the SFH was measured by a single person who palpated the edge of the uterine fundus from the . Following 20 minutes of intravenous injection of the Hartmann crystalloid solution, the parturient women were converted to the right lateral recumbent position. Dural puncture was performed with a 25G Quincke needle in a midline approach after disinfecting the puncture area between the L3-L4 lumbar vertebrae. After checking the cerebrospinal fluid outflow, the drug was injected at the rate of 0.1 ml/sec without changing the direction of the bevel. Regarding the dose. of 18 the drug, fentanyl 20 µg was mixed with the hyperbaric 0.5% bupivacaine , and the mixture was injected. Immediately after injecting the drug, the patients took the supine position and the uterus was transposed to the left by tilting the

table by 15 degree to the left, in order to prevent supine hypotensive syndrome. For the sensory nerve block, a cold feeling examination was performed with an alcohol swab and pin prick test every 1,3,5,8,12,15 minute from the umbilicus and epigastric region to the center of the neck along the midline of the parturient women, until the height did not change any more; this was done to determine the maximum sensory blockade level when heart rate decrease to 40 bpm considered as bradycardia.

When the systolic blood pressure dropped below 90 mmHg, or decreased by more than 30% of the resting blood pressure, considered as hypotension.

The measurements of heart rate (bpm), mean arterial pressure (MAP), systolic arterial pressure (SAP), and diastolic arterial pressure (DAP) was performed and recorded at 1-min intervals until a sufficient block level for surgery was reached, then at 3-min intervals after an adequate block level will be achieved. These measurements was repeated at 8, 12 and 15 mins after the surgical incision preoperatively; and at 5, 15, 30 and 60 min postoperatively.

The collected data was subjected to statistical analysis to find out the result.

RESULT

A prospective observational study was conducted in KGMU, Lucknow from December 2019 to July 2022. 200 patients who undergone elective caesarean section in KGMU were included in the study. The relationship of waist-hip ratio, uterine size and body mass index to sensori-motor block and incidence of hypotension was examined.

Table 1:-Distribution of waist hip ratio of study subjects.

Waist hip ratio	Frequency	Percentage
<1	87	43.50%
>=1	113	56.50%
Mean ± SD	1.15 ± 0.2	
Median(25th-75th percentile)	1.2(0.92-1.4)	
Range	0.86-1.8	

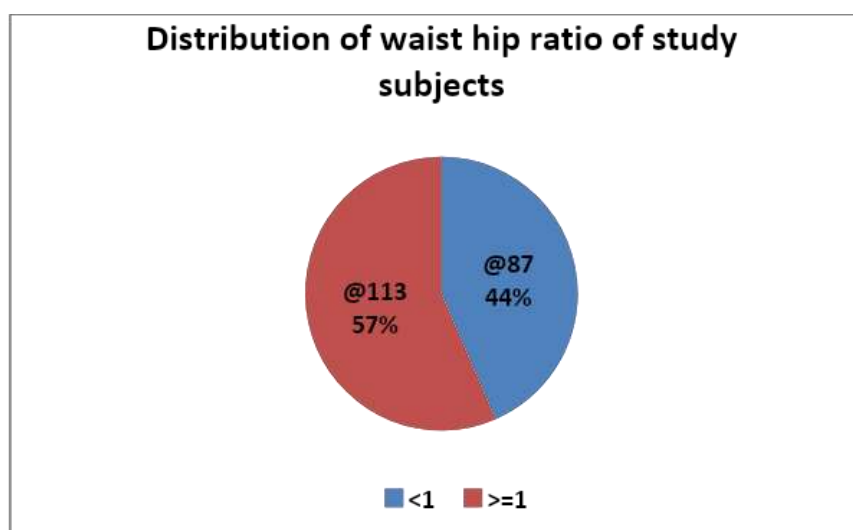


Figure 1:-Distribution of waist hip ratio of study subjects.

In present study (43.50%) of patients, waist hip ratio was <1 and Waist hip ratio was >=1 in 113patients (56.50%).

Table 3:-Distribution of body mass index(kg/m²) of study subjects.

Body index(kg/m ²)	mass	Frequency	Percentage
<30		85	42.50%
>=30		115	57.50%
Mean ± SD		31.46 ± 3.21	
Median(25th-75th percentile)		33.5(28-34)	
Range		25-36	

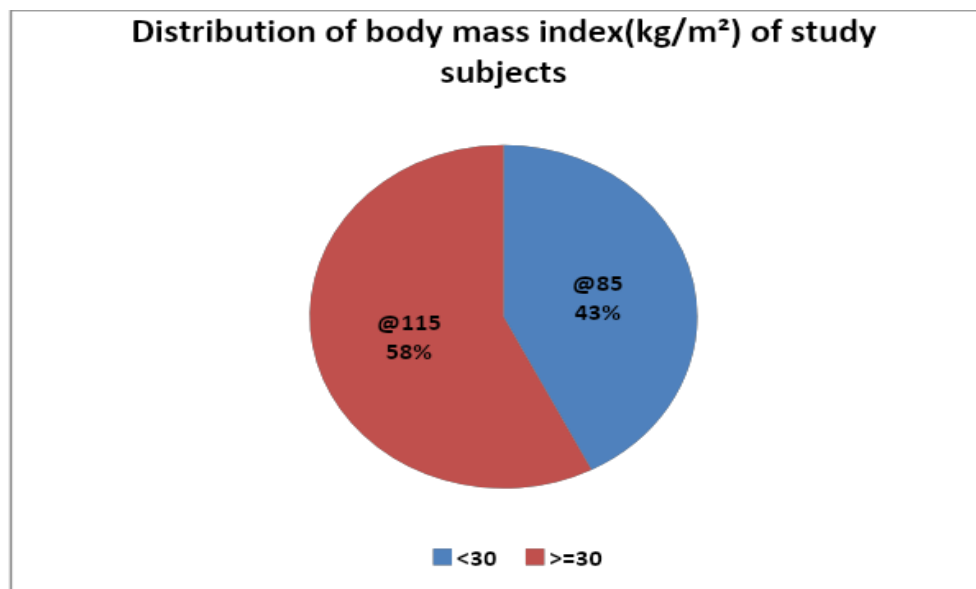


Figure 3:-Distribution of body mass index(kg/m²) of study subjects.

In present study, in majority (57.50%) of patients, body mass index(kg/m²) was >=30{obese}. Body mass index(kg/m²) was 25-29.99of only 85 out of 200 patients (42.50%).

Table 5:- Occurrence of bradycardia with waist hip ratio after spinal anaesthesia.

Time of occurrence of bradycardia	<1	>=1	P value
At 3 minute	2 (2.29%)	7 (6.19%)	0.374 [†]
At 8 minutes	5 (5.74%)	6 (5.30%)	

† Fisher's exact test

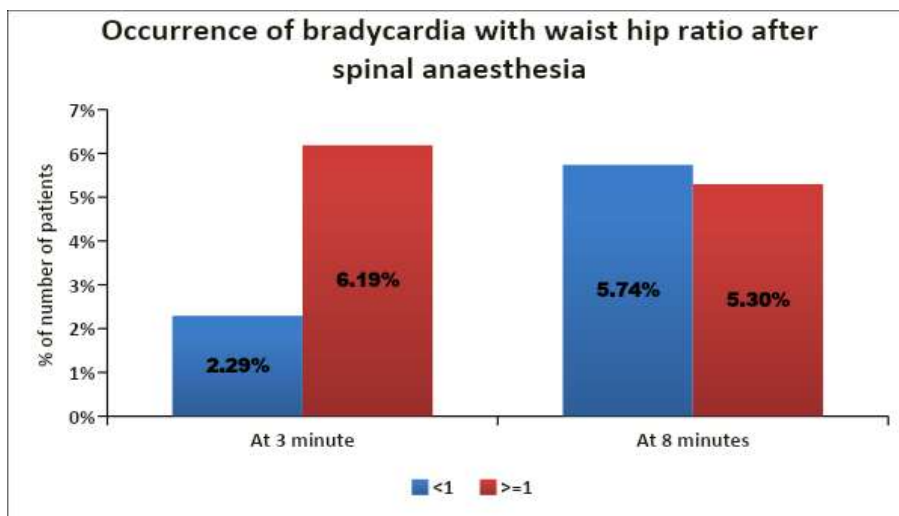


Figure 5:- Occurrence of bradycardia with waist hip ratio after spinal anaesthesia.

Occurrence of bradycardia was seen in 2 out of 87 patient and 5 out of 87 patient with waist hip ratio <1, 7 out of 113 patient and 6 out of 113 patient at 3 minute and 8 minute after spinal anaesthesia. It is shown in table 5 and figure 5.

Table 7:- Occurrence of hypotension with waist hip ratio after spinal anaesthesia at 3 and 8 minute.

Time of occurrence of hypotension	<1	>=1	P value
At 3 minute	12 (13.79%)	107 (94.69%)	0.483†
At 8 minutes	12 (13.79%)	100 (88.49%)	

† Fisher's exact test

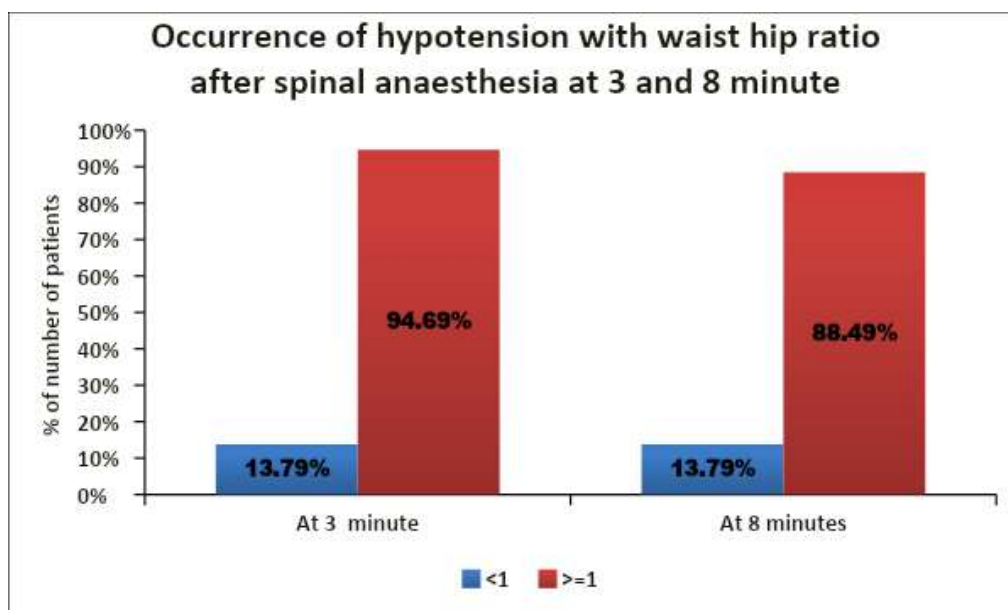


Figure 7:- Occurrence of hypotension with waist hip ratio after spinal anaesthesia at 3 and 8 minute.

Occurrence of hypotension was seen in 12 out of 87 patient and 12 out of 87 patient with waist hip ratio <1, 107 out of 113 patient and 100 out of 113 patient at 3 minute and 8 minute after spinal anaesthesia. It is shown in table 7 and figure 7.

After 12 minutes of delivery			
Mean ± SD	63.75 ± 6.59	59.74 ± 9.78	0.0007*
Median(25th-75th percentile)	65(60-69)	62(48-69)	
Range	48-78	48-77	

* Independent t test

Table 9:-Association of spinal level with waist hip ratio.

Spinal level	<1(n=87)	>=1(n=113)	Total	P value
T4	4 (4.60%)	40 (35.40%)	44 (22%)	<.0001†
T5	3 (3.45%)	46 (40.71%)	49 (24.50%)	
T6	49 (56.32%)	21 (18.58%)	70 (35%)	
T7	20 (22.99%)	4 (3.54%)	24 (12%)	
T8	11 (12.64%)	2 (1.77%)	13 (6.50%)	
Total	87 (100%)	113 (100%)	200 (100%)	

† Chi square test

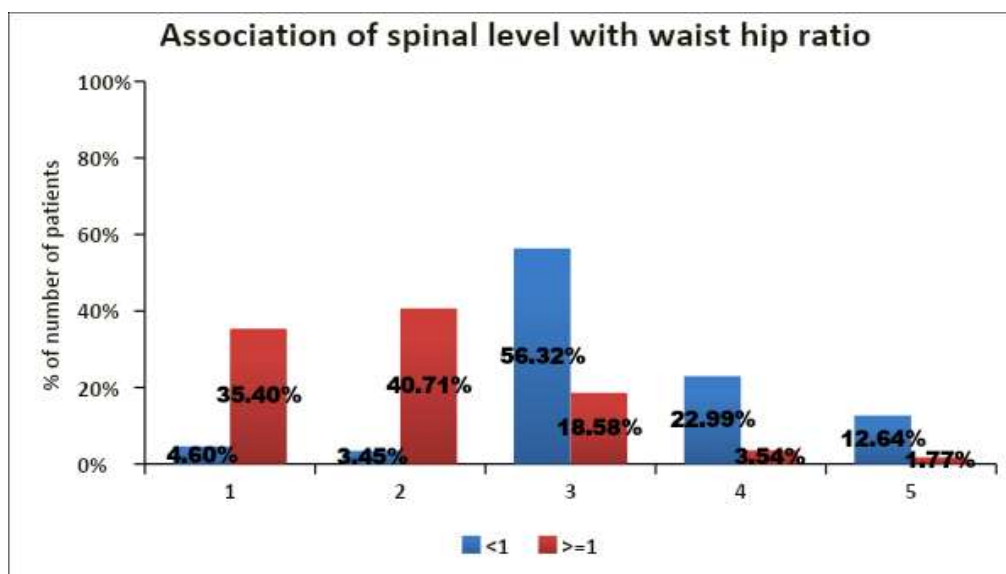


Figure 9:-Association of spinal level with waist hip ratio.

Distribution of spinal level was comparable between waist hip ratio(<1 and >=1). (T4:- 4.60% vs 35.40% respectively, T5:- 3.45% vs 40.71% respectively, T6:-56.32% vs 18.58% respectively, T7:- 22.99% VS 3.54% respectively, T8:-12.64% vs 1.77% respectively) (p value=0.0001). It is shown in table 9, figure 9.

Table 17:- Occurrence of bradycardia with body mass index(kg/m²) After spinal anaesthesia at 3 and 8 minutes.

Time of occurrence of bradycardia	<30	>=30	p-value
At 3 minute	1 (1.17%)	16 (13.91%)	0.285
At 8 minutes	1 (1.17%)	12 (10.43%)	

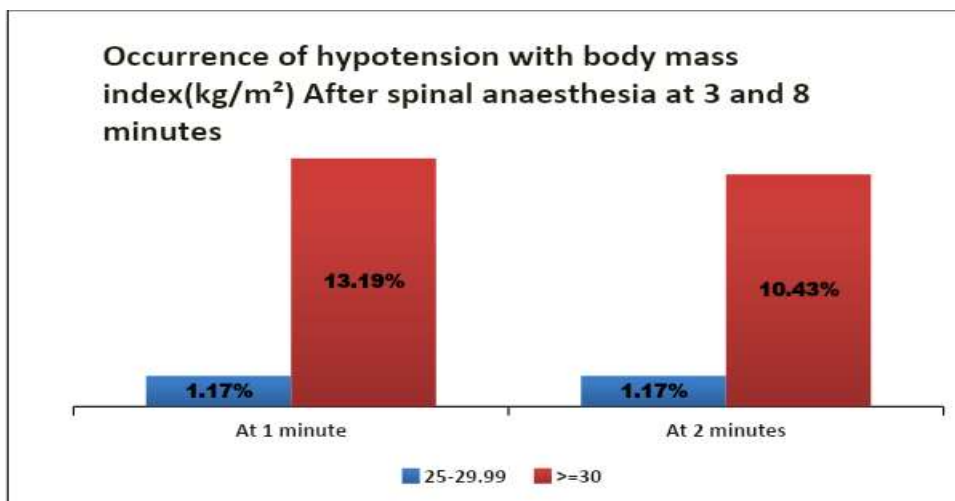


Figure 17:- Occurrence of bradycardia with body mass index(kg/m²) After spinal anaesthesia at 3 and 8 minutes.

Occurrence of bradycardia was seen in 1 out of 85 patient and 1 out of 85 patient with BMI<30,16 out of 115 patient and 12 out of 115 patient of BMI>30 at 3 minute and 8 minute after spinal anaesthesia. It is shown in table 17figure 17.

Table 19:- Occurrence of hypotension with body mass index(kg/m²) After spinal anaesthesia at 3 and 8 minutes.

Time of occurrence of hypotension	25-29.99	≥30	p-value
At 1 minute	10 (11.76%)	109(94.78%)	0.379
At 2 minutes	10 (11.76%)	102 (88.69%)	

† Fisher's exact test

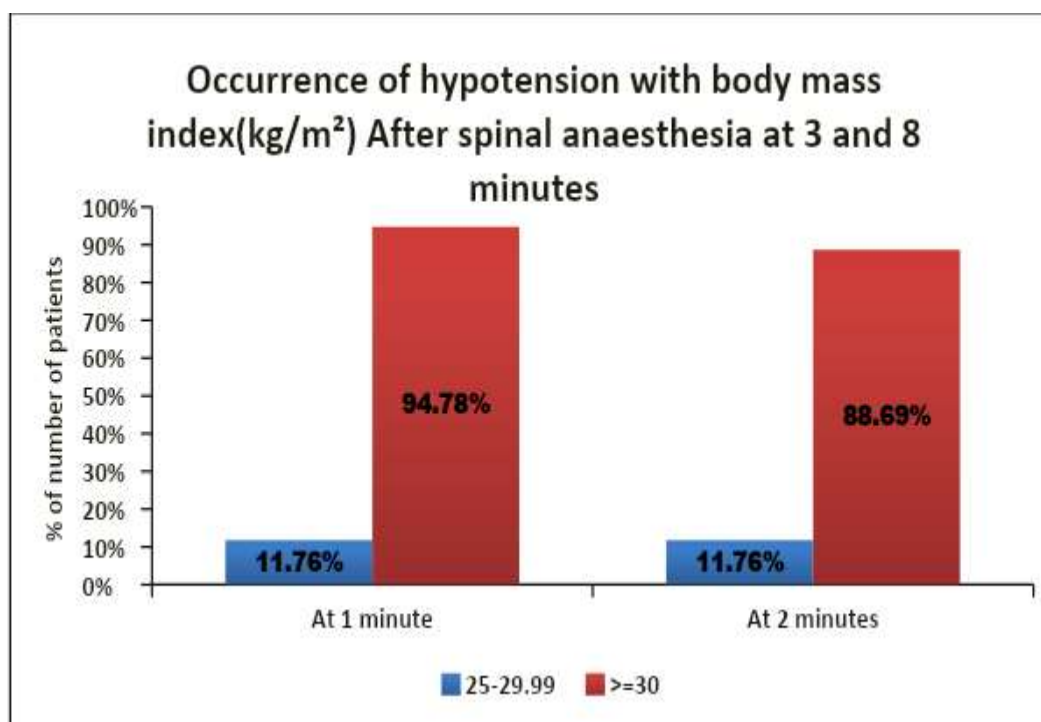


Figure 19:- Occurrence of hypotension with body mass index(kg/m²) After spinal anaesthesia

at 3 and 8 minutes.

Occurrence of hypotension seen in 10 out of 85 patient each at 3 min and 8 min with BMI<30,109 out of 115 patient and 102out of 115 patient with BMI>30 at 3 minute and 8 minute after spinal anaesthesia. It is shown in table 19figure 19

Table 21:-Association of spinal level with body mass index(kg/m²).

Spinal level	<30(n=85)	>=30(n=115)	Total	P value
T4	2 (2.35%)	42 (36.52%)	44 (22%)	<.0001 [†]
T5	3 (3.53%)	46 (40%)	49 (24.50%)	
T6	49 (57.65%)	21 (18.26%)	70 (35%)	
T7	20 (23.53%)	4 (3.48%)	24 (12%)	
T8	11 (12.94%)	2 (1.74%)	13 (6.50%)	
Total	85 (100%)	115 (100%)	200 (100%)	

[†] Chi square test

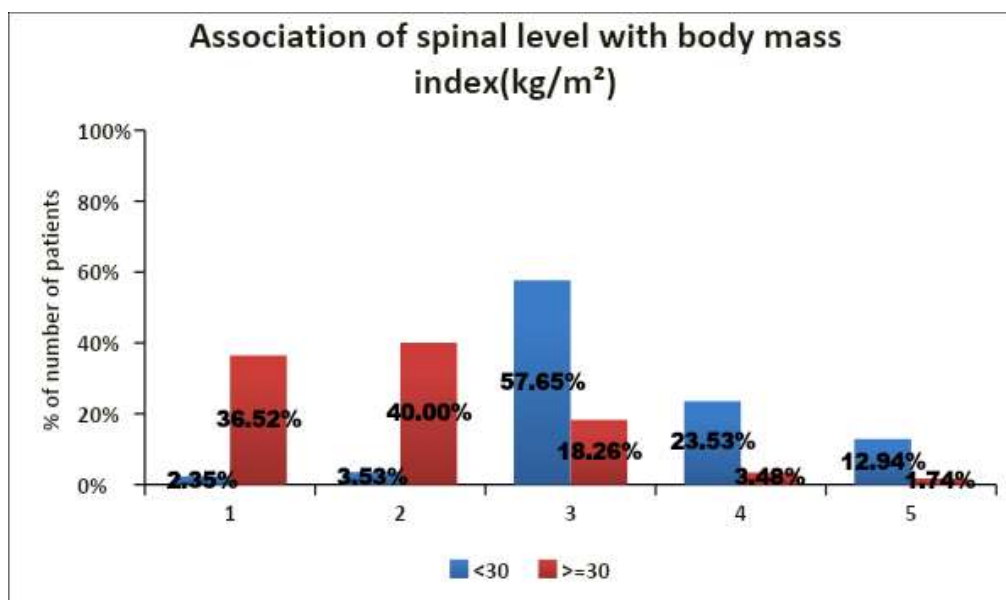


Figure 21:-Association of spinal level with body mass index(kg/m²).

Distribution of spinal level was comparable between BMI(<30 AND >=30). (T4:- 2.35% vs 36.52% respectively, T5:- 3.53% vs 40% respectively,T6:-57.65%vs18.26% respectively,T7:-23.53% VS 3.48% respectively.,T8:-12.94%vs6.50% respectively) (p value=0.0001).

It is shown in table 21, figure 21.

DISCUSSION

The characteristics we included in our study weight, height for BMI calculation, waist circumference and hip circumference for waist- hip ratio calculation. In haemodynamic parameters systolic blood pressure ,diastolic blood pressure ,heart rate and height of neuraxial block considered.

Our study found a strong positive correlation between high BMI ,high waist hip ratio with hypotension and more cephaled spread of neuraxial block.

Some of the previous studies showed higher level of sensory block with high BMI, waist hip ratio and uterine size .they studied relationship between body mass index and spread of spinal anaesthesia in pregnant women in a randomized controlled double blind trial, 405 women undergoing elective

cesarean delivery were allocated to group S (BMI <25), group M (25 ≤BMI <30), or group L (BMI ≥30). Women in each group were further assigned to receive 7, 8, 9, 10, 11, 12, 13, 14, or 15 mg of spinal ropivacaine. The ED50 and ED95 values of ropivacaine were 9.487 mg and 13.239 mg in Group S, 9.984 mg and 13.737 mg in Group M, and 9.067 mg and 12.819 mg in Group L. There were no significant differences among the 3 groups (p=0.915). Group L had a higher incidence of hypotension and a greater change in MAP after spinal anesthesia compared to the other 2 groups, and also required more doses of ephedrine than the other 2 groups when a dose of 15 mg ropivacaine was used. The incidence of hypotension had a positive correlation with the dose of ropivacaine (OR=1.453, p<0.001) and gestational age (OR=1.894, p<0.001). They concluded that spinal ropivacaine dose requirements were similar in the normal BMI range. However, higher doses of spinal ropivacaine were associated with an increased incidence and severity of hypotension in obese patients compared with that in non-obese patients.

A study on the effects of anthropometric measurements on spinal anesthesia block characteristics and hemodynamics. Weight, length, body surface area, and body mass index, abdominal, waist, and hip circumferences of 50 patients were measured. Spinal anesthesia was applied while the patient was sitting position. In this study hypotension was observed in 54% of patients and it was determined that the prevalence of hypotension increased in patients with a shorter height, larger abdominal circumference, higher body mass index, lower body surface area and a higher waist/hip ratio. It was found that the prevalence of bradycardia increased in patients with a shorter height, higher body mass index, lower body surface area and a higher waist/hip ratio. This study also determined a positive correlation between the values of height, weight and body surface area and the time of sensorial block to reach the T4 dermatome; and a positive correlation between body mass index and the dermatome area of the maximum sensorial block. Agnes M Lamon et al(2017) in their retrospective study assessed the impact of body mass index on the risk of high spinal block in parturients undergoing cesarean delivery: The primary outcome was high spinal block defined as need to convert to general anesthesia within 20 min of spinal placement as a result of altered mental status, weakness, or respiratory distress resulting from the high block, or a recorded block height >T1. The analysis included 5015 women. High spinal blocks occurred in 29 patients (0.6%). The risk of high spinal was significantly different according to BMI (p = 0.025). In a multivariate model, BMI (p = 0.008) and cesarean delivery priority (p = 0.009) were associated with high blocks. BMI >50 kg/m² was associated with greater odds of high block compared to BMI <30 kg/m² [odds ratio (95% confidence interval): 6.3 (2.2, 18.5)]. Scheduled cesarean delivery was also associated with greater odds of high block compared with unscheduled delivery. They concluded that at standard spinal doses of hyperbaric bupivacaine used in our practice (>10.5 mg), there were greater odds of high block in those with BMI >50 kg/m². Ngaka et al(2016) studied the influence of body mass index on sensorimotor block and vasopressor requirement during spinal anesthesia for elective cesarean delivery. The primary outcomes were phenylephrine requirement in the first 30 minutes after SA, and maximum block height, measured by the sensation of touch and cold. Secondary outcomes were total phenylephrine dose required, changes in hand grip strength, and peak flow rate. They concluded that only a minor increase in block height as assessed by temperature occurred in group O at 25 minutes. Vasopressor requirements during the first 30 minutes of SA were equivalent. Time for regression of SA block level was longer in the group O, which may be beneficial considering the longer surgical time. A dose of spinal bupivacaine 10 mg for single-shot SA should not be reduced in morbidly obese parturients.

BIBLIOGRAPHY

1. S Hogan QH, Prost R, Kulier A, et al. Magnetic resonance imaging of cerebrospinal fluid volume and the influence of body habitus and abdominal pressure. *Anesthesiology*. 1996;84:1341-9
2. Richardson MG, Wissler RN. Density of lumbar cerebrospinal fluid in pregnant and

- nonpregnant humans. *Anesthesiology*. 1996;85:326–30.
3. Hirabayashi Y, Shimizu R, Fukuda H, et al. Anatomical configuration of the spinal column in the supine position: Comparison of pregnant and non-pregnant women. *Br J Anaesth*. 1995;75:6–8.
 4. Fassoulaki A, Gatzou V, Petropoulos G, Siafaka I. Spread of subarachnoid block, intraoperative local anaesthetic requirements and postoperative analgesic requirements in Caesarean section and total abdominal hysterectomy. *Br J Anaesth*. 2004;93:678–82.
 5. Ni TT, Zhou Y, Yong AC, Wang L, and Zhou QH, “Intra-abdominal pressure, vertebral column length, and spread of spinal anesthesia in parturients undergoing cesarean section: an observational study. *PLoS one* 2018; 13
 6. Zhang N, He L, and Ni JX, Level of sensory block after spinal anesthesia as a predictor of hypotension in parturient. *Medicine (Baltimore)*, 2017 96; e7184 .
 7. Organization WH. Obesity: preventing and managing the global epidemic. 2000:World Health Organization.
 8. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. *JAMA*. 2010;303(3):235-41.
 9. Bergholt T, Lim LK, Jørgensen JS, Robson MS. Maternal body mass index in the first trimester and risk of cesarean delivery in nulliparous women in spontaneous labor. *Am J Obstet And Gynecol*. 2007;196(2):163. e1-163. e5.
 10. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *The Lancet*. 2006;368(9542):1164-70.
 11. Rodrigues FR, Brandão MJN. Regional anaesthesia for cesarean section in obese pregnant women: A retrospective study. *Braz J Anaesthesiol*. 2011;61(1):13-20.
 12. Nucci LB, Schmidt MI, Duncan BB, Fuchs SC, Fleck ET, Maria Margarida Santos Britto MMS. Nutritional status of pregnant women: prevalence and associated pregnancy outcomes. *Revista De Saude Publica*. 2001;35(6):502-07.
 13. Vallejo MC. Anaesthetic management of the morbidly obese parturient. *Curr Opin in Anaesthesiol*. 2007;20(3):175-80.
 14. Chu SY, Kim SY, Schmid CH, Dietz PM, Callaghan WM, Lau J, et al. Maternal obesity and risk of cesarean delivery: a meta-analysis. *Obesity Reviews*. 2007;8(5):385-94.
 15. Nani FS, Torres MLA. Correlation between the body mass index (BMI) of pregnant women and the development of hypotension after spinal anesthesia for cesarean section. *Braz J Anaesthesiol*. 2011;61(1):21-30.
 16. Mitra J. Prevention of hypotension following spinal anesthesia in [10] caesarean section-then and now. *Kathmandu University Medical J*. 2012.8(4):415-19.
 17. Gupta S. Vasopressors and tight control of maternal blood pressure during [11] cesarean delivery: a rocky alliance. *J of Anaesthesiology. Clin Pharmacol*. 2013;29(1):1.
 18. Miller RD, Pardo M. Basics of Anaesthesia E-Book. 2011: Elsevier Health [12] Sciences.
 19. 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: 856–63
 20. Arzola C, Wiczorek PM: Efficacy of low-dose bupivacaine in spinal anesthesia for caesarean delivery: Systematic review and meta-analysis. *Br J Anaesth*, 2011; 107: 308–18
 21. Reyes M, Pan PH: Very low-dose spinal anesthesia for cesarean section in a morbidly obese preeclamptic patient and its potential implications. *Int J Obstet Anesth*, 2004; 13(2): 99–102
 22. Norris MC: Height, weight, and the spread of subarachnoid hyperbaric bupivacaine in the term parturient. *Anesth Analg*, 1988; 67: 555–58
 23. Carvalho B, Collins J, Drover DR et al: ED(50) and ED(95) of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery. *Anesth*, 2011; 114: 529–35

24. Magalhães E, Govêia CS, de Araújo Ladeira LC, Nascimento BG, Kluthcouski SM. Ephedrine versus phenylephrine: prevention of hypotension during spinal block for cesarean section and effects on the fetus. *Rev Bras Anesthesiol*. 2009 Jan-Feb;59(1):11-20.
25. Ronenson AM, Sitkin SI, Savel'eva IuV. Effect of intra-abdominal pressure in pregnant women on level of spina block and frequency of hypotension during cesarean section. *Anesteziol Reanimatol*. 2014 Jul-Aug;59(4):26-9.
26. Marshalov DV, Shifman EM, Salov IA, Petrenko AP. Correction of local anesthetic dosage in spinal anesthesia in pregnant women with obesity. *Anesteziol Reanimatol*. 2014 Nov-Dec;59(6):19-23.
27. Ozkan Seyhan T, Orhan-Sungur M, Basaran B, Savran Karadeniz M, Demircan F, Xu Z, Sessler DI. The effect of intra-abdominal pressure on sensory block level of single-shot spinal anesthesia for cesarean section: an observational study. *Int J Obstet Anesth*. 2015 Feb;24(1):35-40.
28. Polin CM, Hale B, Mauritz AA, Habib AS, Jones CA, Strouch ZY, Dominguez JE. Anesthetic management of super-morbidly obese parturients for cesarean delivery with a double neuraxial catheter technique: a case series. *Int J Obstet Anesth*. 2015 Aug;24(3):276-80.
29. Ngaka TC, Coetzee JF, Dyer RA. The influence of body mass index on sensorimotor block and vasopressor requirement during spinal anaesthesia for elective Caesarean section. *Anesth Analg*. 2016 Dec;123(6): 1527-34.
30. Baysal PK, Golboyu BE, Ekinci M, Güden M, Ahiskalioglu A, Celik EC. Effects of anthropometric measurements on spinal anaesthesia block characteristics and hemodynamics. *Medeniyet Med J*. 2016;31(1):23-31.
31. Kuok CH, Huang CH, Tsai PS, Ko YP, Lee SW, Hsu WY, Hung FY. Preoperative measurement of maternal abdominal circumference relates the initial sensory block level of spinal anesthesia for cesarean section: An observational study. *Taiwanese J Obstetr Gynecol*. 2016;55(6):810-4. Lamon AM, Einhorn LM, Cooter M, Habib AS. The impact of body mass index on the risk of high spinal block in parturients undergoing cesarean delivery: a retrospective cohort study. *J Anesth*. 2017 Aug;31(4):552-8.