

# Perinatal outcome of preterm cesarean section in a resource-limited centre: A comparison between general anaesthesia and subarachnoid block

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## Abstract

**Background:** The relationship between perinatal outcome and anesthetic technique for preterm cesarean sections has not been explored in South Eastern, Nigeria.

**Objective:** The objective of the following study is to evaluate perinatal outcome in preterm cesarean sections conducted under general anesthesia (GA) and subarachnoid block (SAB) with the aim to ascertain any difference in outcome between the two methods.

**Materials and Methods:** A retrospective observational study of consecutive preterm cesarean deliveries at the University of Nigeria Teaching Hospital from May 1999 to April 2008. Data entry and statistical analysis utilized the SPSS statistical package for the social sciences, 2008 version 15.0 for windows (SPSS Inc, Chicago IL, USA). Chi-square test was done to determine statistical significance and  $P \leq 0.05$  were considered to be significant at 95% confidence interval. The delivery characteristics were compared by logistic regression analysis to ascertain any associated confounding effect on perinatal outcome in those exposed to either anesthetic technique.

**Results:** There were 7568 deliveries and 1961 cesarean sections giving a cesarean section rate of 25.9%. A total of 236 cesarean sections were for preterm deliveries giving a preterm cesarean section rate of 3.1%. Of these, 151 women delivered under GA while SAB was used in 85 cases. The mean gestational ages for preterm cesarean sections were  $33.2 \pm 2.6$  weeks and  $33.8 \pm 2.2$  weeks for those who had GA and SAB respectively. The mean Apgar scores were  $6.4 \pm 3.1$  and  $7.6 \pm 3.1$  at 5 min for GA and SAB respectively. There were 24 stillbirths (15.9%) in cesarean deliveries done under GA and 7 stillbirths (8.2%) in women who had SAB ( $P = 0.09$ ). Twenty-two (14.6%) babies delivered through GA and 14 (16.4%) delivered under SAB, died within 1 week of delivery ( $P = 0.7$ ). There were more babies with low Apgar scores in parturient delivered under GA ( $P = 0.0004$ ). More preterm babies delivered under SAB were discharged from the New Born Special Care Unit within 10 days of delivery ( $P = 0.006$ ). Hypertensive disorders, though not statistically significant was the most common indication for preterm cesarean delivery among those with GA and SAB. No maternal death occurred during the study period.

**Conclusion:** The study infers a strong association between anesthetic technique and immediate Apgar scores and outcome of resuscitation following preterm cesarean section. This however, failed to translate into higher differences in perinatal mortality.

**Key words:** General anesthesia, perinatal-outcome, preterm cesarean section, subarachnoid block

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## Introduction

Preterm delivery (delivery before 37 completed weeks of gestation),<sup>[1]</sup> constitutes a large number of deliveries world-wide and are a significant cause of perinatal morbidity and mortality.<sup>[2,3]</sup> The survival of the preterm infant is known

to be related to birth weight and gestational age. Gestational age although at times, not accurately available is generally a better predictor of maturation and chance of survival

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than birth weight.<sup>[4]</sup> Preterm cesarean section is cesarean delivery performed between the age of viability and 37 weeks of gestation. In this institution, both general and regional anesthesia is performed for preterm cesarean sections.

In deciding the ideal anesthetic technique for cesarean section, both Anesthetist and Obstetrician must consider the technique with the least adverse effect on materno-fetal well-being. There has been a great deal of concern about the effects of drugs administered during delivery on the infant. Preterm babies are particularly susceptible to maternally administered drugs due to the immaturity of their enzyme systems, their incomplete blood-brain-barrier and low availability of serum protein for drug binding.<sup>[5]</sup> Various anesthetic agents have resulted in a wide array of effects on the baby at birth.<sup>[5]</sup> Most general anesthesia (GA) agents, with the exception of Suxamethonium and other muscle relaxants, cross the placenta and depress the fetal central nervous system if large doses are administered.<sup>[6,7]</sup> The effect of local anesthetic agents used during subarachnoid block (SAB) on the neonate is related to the concentration of the drug that reaches the fetus and it is associated with low maternal and fetal blood drug levels.<sup>[8]</sup> They however cause substantial drop in maternal blood pressure which may affect both the mother and fetus.

The traditional method for evaluating neonatal condition at birth, the Apgar scoring system,<sup>[9]</sup> is a practical method of systematically assessing newborn infants immediately after birth to identify those requiring resuscitation and to predict survival in the neonatal period.<sup>[10]</sup> At 5-min score indicate responsiveness to therapy and can also identify babies at high risk for further problems in the immediate neonatal period. In assessing the significance of the 5-min Apgar score for predicting survival during the first 28 days of life, Casey *et al.* found that low 5-min scores were comparably predictive of neonatal death in the preterm infant,<sup>[11]</sup> concluding that the Apgar scoring system is as relevant for the prediction of neonatal survival today as it was almost 50 years ago.<sup>[11]</sup>

Fewer studies from developed nations have compared the effects of GA and SAB on neonatal outcome, especially in preterm cesarean section deliveries.<sup>[12]</sup> Extensive review of existing literature from the developing world showed no studies evaluating perinatal outcome for preterm cesarean section following both anesthetic techniques, hence, the motivation for this study.

This study aims to evaluate perinatal outcome in preterm cesarean sections conducted under GA and SAB in order to ascertain any difference in outcome between the two methods.

## Materials and Methods

This retrospective observational study was approved by the Ethics and Research committee of the institution.

Consecutive preterm cesarean sections at the University of Nigeria Teaching Hospital Enugu were reviewed from May 1999 to April 2008. This is a tertiary health institution that provides full scale antenatal services. It has well-equipped labor ward with 24 h doctor's coverage and dedicated obstetrics theatre. The institution has all cadres of Surgeons and Anesthetists, from junior resident doctors to senior consultants and Professors. The newborn special care unit of the hospital is well-equipped and has dedicated team of neonatologists. The hospital has capacity to perform both elective and emergency cesarean sections any time in the obstetrics theater.

The choice of anesthesia in this hospital is primarily determined by the clinical condition of the mother and the fetus. However, maternal preferences and the proficiency of the Anesthetist also influence this choice.

For patients undergoing GA pre-medication was done with intravenous injection of ranitidine 50 mg. Following 3 min of pre-oxygenation, rapid sequence induction was achieved using intravenous sodium thiopentone 5 mg/kg while muscle relaxation was achieved by use of intravenous Suxamethonium 1.5 mg/kg. Cricoid pressure was maintained until intubation and satisfactory confirmation of endotracheal placement of endotracheal tube using chest auscultation and capnography. Initial analgesia before delivery of the baby was achieved by use of analgesic dose of ketamine 0.1 mg/kg. Following delivery of the baby, intravenous injection of Tramadol 100 mg was given to maintain analgesia. Patients also received 0.5 volume percent halothane as part of maintenance of anesthesia. For SAB 0.5% hyperbaric bupivacaine was the agent of choice.

Research proforma for recording data on socio-demographic characteristics, gestational age at delivery, indication for delivery, type of cesarean section, anesthetic technique, Apgar scores at one and 5 min, new born special care unit admission and perinatal outcome was utilized. The gestational ages of the pregnancies were determined using Naegele's rule and ultrasonography.

The exclusion criteria were preterm cesarean deliveries for multiple pregnancies and ruptured uterus. Preterm cesarean section in this study referred to those performed between 28 and 36 weeks of gestation. All the cesarean sections were transverse lower segment cesarean sections. The abdominal incisions were either sub-umbilical midline or Pfannestiel. Data entry and analysis were carried out using SPSS statistical package for the social sciences 2008 version 15 for windows (SPSS Inc, Chicago IL, USA). Chi-square test was done for the determination of statistical significance.  $P \leq 0.05$  was considered to be statistically significant. Delivery characteristics were included in a single step entry into logistic regression to ascertain any association of these factors as confounders to anesthetic methods in perinatal outcome.

## Results

There were 7568 deliveries and 1961 caesarean sections giving a caesarean section rate of 25.9%. A total of 236 caesarean sections were for preterm deliveries resulting in a preterm caesarean section rate of 3.1%. Of these, 151 (64%) women delivered under GA while SAB was used in 85 (36%) cases. The mean gestational ages for preterm caesarean sections were  $33.2 \pm 2.6$  and  $33.8 \pm 2.2$  weeks for those who had GA and SAB respectively while the mean ages of the mothers were  $30.8 \pm 5.4$  and  $31.7 \pm 5.4$  years for GA and SAB respectively. The mean Apgar scores were  $4.9 \pm 2.7$  and  $6.5 \pm 2.9$  at 1 min; and  $6.4 \pm 3.1$  and  $7.6 \pm 3.1$  at 5 min for GA and SAB respectively.

Table 1 shows indications for the caesarean section in preterm delivery and maternal characteristics. 157 (66.5%) women with preterm caesarean sections booked for antenatal care while 79 (33.5%) were unbooked. 96 (63.6%) and 61 (71.8%) of the women that had GA and SAB respectively for preterm caesarean sections were booked, while 55 (36.4%) and 24 (28.2%) of those that had GA and SAB were unbooked. Multiparous women constituted greatest number among those that had GA 106 (70.2%) and SAB 52 (61.2%) for preterm caesarean deliveries. Tertiary education was most prevalent among those that had GA 106 (70.2%) and SAB 52 (61.2%). Number of women who had preterm caesarean delivery for hypertension, malpresentation with preterm rupture of membranes and previous caesarean sections did not differ between the two anaesthetic techniques.

Table 2 shows adverse perinatal outcomes following preterm caesarean delivery. 47 (31.1%) preterm babies delivered with GA and seven preterm babies (8.2%) delivered with SAB had low 5-min Apgar scores (1-6), ( $P = 0.0004$ ). The mortality patterns for preterm babies delivered with SAB and GA were not statistically significant. Significant number of preterm babies delivered under SAB 32 (37.7%) were discharged from the New Born Special Care Unit within 10 days of delivery when compared with 19 (12.6%) delivered under GA ( $P = 0.006$ ).

Table 3 shows the relationship between intrapartum death, low 5-min Apgar scores (1-6) and the indication for preterm caesarean section. Compared with SAB, GA was associated with a higher frequency of low 5-min Apgar scores (0-6) in preterm deliveries due to hypertensive disorders, previous caesarean sections and severe oligohydramnios. 63 (48.5%) emergency preterm caesarean sections under GA and 9 (15.5%) under SAB were associated with low 5-min Apgar scores 0-6 ( $P = 0.00002$ ).

Table 4 shows the relationship between the maternal and delivery characteristics and low 5 min Apgar scores following

**Table 1: Indications for the caesarean section in preterm delivery and maternal characteristics**

Maternal characteristics	Total deliveries (n=236) (%)	General anaesthesia (n=151) (%)	Spinal anaesthesia (n=85) (%)	P value
Age (years)				
<29	91 (38.6)	60 (39.7)	31 (36.5)	0.6
30-39	129 (54.7)	83 (55.0)	46 (54.1)	0.9
≥40	16 (6.7)	8 (5.3)	8 (9.4)	0.2
Parity				
Nulliparous (para 0)	29 (12.3)	21 (13.9)	8 (9.4)	0.3
Multiparous (para 1-4)	171 (72.5)	106 (70.2)	65 (76.5)	0.3
Grandmultiparous (para ≥5)	36 (15.2)	24 (15.9)	12 (14.1)	0.7
Educational attainment				
Primary	16 (6.8)	11 (7.3)	5 (5.9)	0.7
Secondary	62 (26.3)	34 (22.5)	28 (32.9)	0.08
Tertiary	158 (66.9)	106 (70.2)	52 (61.2)	0.2
Occupation				
Housewife	87 (36.9)	63 (41.7)	24 (28.2)	0.04
Petty traders	27 (11.4)	14 (9.3)	13 (15.3)	0.2
Students	39 (16.5)	23 (15.2)	16 (18.8)	0.5
Civil servants	83 (35.2)	51 (33.8)	32 (37.7)	0.5
Booking status				
Booked	157 (66.5)	96 (63.6)	61 (71.8)	0.2
Unbooked	79 (33.5)	55 (36.4)	24 (28.2)	0.2
Indications				
Hypertensive diseases	101 (42.8)	66 (43.7)	35 (41.2)	0.7
Malpresentation with preterm rupture of membranes	16 (6.8)	11 (7.3)	5 (5.9)	0.09
Previous caesarean section	35 (14.8)	18 (11.9)	17 (20.0)	0.09
Antepartum haemorrhage	49 (20.8)	43 (28.5)	6 (7.1)	0.001
Oligohydramnios	24 (10.1)	9 (6.0)	15 (17.6)	0.004
Malpresentation with preterm labour	11 (4.7)	4 (2.6)	7 (8.2)	0.05
Gestational age (weeks)				
<30	43 (18.2)	34 (22.5)	9 (10.6)	0.02
31-32	37 (15.7)	20 (13.3)	17 (20.0)	0.17
33-34	58 (24.6)	39 (25.8)	19 (22.4)	0.55
35-36	98 (41.5)	58 (38.4)	40 (47.0)	0.00001

preterm caesarean section. The prevalence of low Apgar score in preterm caesarean section reduced with gestational age in both groups of babies and was most marked in the more mature babies 35-36 weeks gestation. Emergency preterm caesarean sections and preterm operations by junior residents were other important confounding factors for poor Apgar score.

Table 5 shows logistic regression analysis of maternal and preterm delivery characteristics and low Apgar score. Anesthetic technique had a significant contribution to low Apgar score. The co-efficient of SAB was statistically significant ( $P = 0.001$ ). The relative odds of 0.211; 95% CI: 0.097-0.462 indicated that SAB was 0.211 times as likely to cause low Apgar scores as GA. Gestational age of 31-32 weeks was a significant confounder. The indications for the delivery, rank of the Surgeon, rank of the Anesthetist, booking status and type of cesarean section were not significant confounders to low Apgar score.

### Discussion

GA was found to be the predominant anesthetic technique for preterm cesarean sections for this study period at our institution, with SAB performed in just 36% of the preterm cesarean sections. Both GA and SAB are anesthetic methods of choice for cesarean delivery. Several factors such as the indication for the delivery, maternal medical condition and gestational age at delivery, type of cesarean section, experience of the surgeon and proficiency of the anesthetist may influence the preference for a particular anesthetic technique. In this study, the prevalence of low Apgar score reduced with increasing gestational age in both groups and was most marked in babies 35-36 weeks. Emergency cesarean section and operations done by junior doctors were important confounding factors for poor Apgar score. However, overall low Apgar score was significantly

less in babies delivered by cesarean section under SAB than GA ( $P = 0.00004$ ). In a large population-based prospective cohort study of very preterm infants and comparing three anesthetic techniques (GA vs. SAB vs. epidural) for their deliveries, Laudenbach *et al.* found that SAB had more risk of neonatal mortality than GA,<sup>[12]</sup> with severe hypotension and subsequent excessive use of ephedrine implicated. This is in contradiction to the findings in this study. Ketamine has minimal effect on central respiratory drive, although a transient decrease in ventilation can occur after bolus administration.<sup>[13]</sup> It improves pulmonary compliance and is as effective as halothane in preventing bronchospasm. The use of analgesic dose of ketamine before delivery of the baby under GA has been found not to have any significant influence on the Apgar score.<sup>[6,13,14]</sup> We surmise that the lower 5-min Apgar scores following GA for preterm cesarean section may not be unconnected with the anesthetic agents used.

In the study period, thiopentone, low dose volatile anesthetic agent and medical air were most commonly used for GA while 0.5% hyperbaric bupivacaine was the agent of choice for SAB. Thiopentone which is a barbiturate has high lipid solubility with a significantly larger volume of distribution in the infant.<sup>[11]</sup> It rapidly diffuses out of the brain and other highly vascular tissues and is redistributed to fat and muscle. However, due to low body fat and muscle content in the preterm infants less thiopentone is distributed to these tissues leading to high concentration in the central nervous system.<sup>[15,16]</sup> All inhaled anesthetics are respiratory depressants and preterm infants are particularly susceptible to their depressant effects.<sup>[15,17]</sup> This may be due to their underdeveloped and often immature lungs and immature central respiratory drive.<sup>[4]</sup> The smaller blood and tissue volumes into which the drugs are distributed result in an earlier rise in brain partial pressures.<sup>[17]</sup> Thiopentone is a potent respiratory depressant<sup>[15]</sup> and also causes cardiovascular depression.<sup>[18]</sup> It has been found to facilitate the actions of Gamma-Amino Butyric Acid which is the major inhibitory neurotransmitter in the central nervous system.<sup>[18]</sup> Further more due to the poorly developed drug-handling processes in preterm infants, the half-life of thiopentone is longer leading to relatively higher blood level

**Table 2: Adverse perinatal outcomes following preterm caesarean delivery**

Perinatal outcome	General anaesthesia (n=151) (%)	Spinal anaesthesia (n=85) (%)	P value
Low 5-Apgar (1-6)	47 (31.1)	7 (8.2)	0.00004
Stillbirth	24 (15.9)	7 (8.2)	0.09
Death within 1 week	22 (14.6)	14 (16.5)	0.7
Prolonged new born hospitalization (> 10 days)	39 (25.8)	25 (29.4)	0.6
Discharged from new born <10 days	19 (12.6)	32 (37.7)	0.006

**Table 3: The relationship between intrapartum death, low 5-min Apgar scores (1-6) and the indications for preterm caesarean section**

Indication for caesarean section	Total deliveries (%)		Apgar scores 0-6 (%)		P value
	General anaesthesia (n=151)	Spinal anaesthesia (n=85)	General anaesthesia (n=71)	Spinal anaesthesia (n=14)	
Hypertensive diseases	66 (43.7)	35 (41.2)	29 (40.8)	6 (42.9)	0.007
Malpresentation with preterm rupture of membranes	11 (7.3)	5 (5.9)	5 (7.0)	3 (21.4)	0.6
Previous caesarean section	18 (12.0)	17 (20.0)	8 (11.3)	2 (14.3)	0.03
Antepartum haemorrhage	43 (28.4)	6 (7.1)	21 (29.6)	1 (7.1)	0.14
Oligohydramnios	9 (6.0)	15 (17.6)	7 (9.9)	2 (14.3)	0.002
Malpresentation with preterm labour	4 (2.6)	7 (8.2)	1 (1.4)	0 (0.0)	0.17

**Table 4: Relationship between maternal and delivery characteristics and low 5-min Apgar score in preterm caesarean section**

Characteristics	Total deliveries		General anesthesia (n=48) (%)	Spinal anesthesia (n=7) (%)	P value
	Anesthesia				
	General (n=151)	Spinal (n=85)			
Gestational age					
≤30	34	9	16 (47.1)	2 (22.2)	0.2
31-32	20	17	5 (25.0)	2 (11.8)	0.3
33-34	39	19	10 (25.6)	2 (10.5)	0.2
35-36	58	40	17 (29.3)	1 (2.5)	0.0008
Type of surgery					
Elective	21	27	6 (28.6)	5 (18.5)	0.4
Emergency	130	58	42 (32.3)	2 (3.4)	0.00002
Rank of surgeon					
Junior resident	6	2	3 (50.0)	1 (50.0)	1.0
Senior registrar	109	59	34 (31.2)	4 (6.8)	0.0003
Consultant	36	24	11 (30.6)	2 (8.3)	0.04
Rank of anesthetist					
Junior resident	30	8	10 (33.3)	0	0.06
Senior registrar	106	73	32 (30.2)	7 (9.6)	0.001
Consultant	15	4	6 (40.0)	0	0.1

of the drugs and increased depressant effect on the baby.<sup>[4,19]</sup> Bupivacaine used in spinal anesthesia is more cardiotoxic than other local anesthetic agents, but the maternal blood level following spinal anesthesia is usually insignificant,<sup>[20]</sup> explaining its little fetal effect.

There was no significant difference in perinatal mortality between the two groups of babies studied. However, babies delivered to women for hypertensive diseases, oligohydramnios and previous caesarean sections had significantly fewer poor 5 min Apgar score following SAB than GA. Apart from oligohydramnios and antepartum hemorrhage there was little or no selection bias in either methods of anesthesia in women observed ( $P > 0.05$ ). In a population based study conducted in Australia, infants already compromised in utero with fetal distress had the worst outcomes following GA.<sup>[21]</sup> Cohorts of caesarean section by indication showed that deliveries performed under GA when compared with those performed under SAB were associated with lower 5-min Apgar scores for elective caesarean section. Similar outcome was found in unplanned caesarean sections done for fetal distress and poor progress of labor. Some studies suggest that emergency caesarean sections irrespective of type of anesthesia are associated with increased risk of adverse

**Table 5: Logistic regression analysis of maternal and preterm delivery characteristics and low Apgar score**

Characteristics	B	SE	Wald	df	Significant	Exp (B)	95% CI for Exp (B)	
							Lower	Upper
Age group (years)								
<20					Referent			
20-24 (1)	-19.394	28195.915	0.000	1	0.999	0.000	0.000	
25-29 (2)	-20.298	28195.915	0.000	1	0.999	0.000	0.000	
30-34 (3)	-19.123	28195.915	0.000	1	0.999	0.000	0.000	
35-39 (4)	-19.444	28195.915	0.000	1	0.999	0.000	0.000	
40-44 (5)	-18.658	28195.915	0.000	1	0.999	0.000	0.000	
45-49 (6)	-20.003	28195.915	0.000	1	0.999	0.000	0.000	
Type of anesthesia								
General anesthesia					Referent			
Subarachnoid block (1)	-1.554	0.399	15.193	1	0.001	0.211	0.097	0.462
Gestational age (weeks)								
<30					Referent			
31-32 (1)	-1.530	0.489	9.783	1	0.002	0.216	0.083	0.565
33-34 (2)	-0.652	0.485	1.811	1	0.178	0.521	0.201	1.347
35-36 (3)	-0.006	0.426	0.000	1	0.989	0.994	0.432	2.290
Booking status								
Booked					Referent			
Unbooked (1)	0.686	0.358	3.662	1	0.056	1.986	0.984	4.009
Indications								
Hypertensive diseases					Referent			
Antepartum hemorrhage (1)	1.225	0.819	2.238	1	0.135	3.403	0.684	16.927
Malpresentation with preterm rupture of membranes (2)	0.644	0.835	0.594	1	0.441	1.904	0.370	9.787
Previous caesarean section (3)	1.312	1.018	1.661	1	0.197	3.712	0.505	27.274
Oligohydramnios (4)	0.585	0.841	0.484	1	0.486	1.795	0.345	9.333
Malpresentation with preterm labor (5)	0.817	0.945	0.748	1	0.387	2.264	0.355	14.421

Contd...

**Table 5: Contd...**

Characteristics	B	SE	Wald	df	Significant	Exp (B)	95% CI for Exp (B)	
							Lower	Upper
Type of caesarean section								
Elective					Referent			
Emergency (1)	0.375	0.386	0.946	1	0.331	1.455	0.683	3.099
Rank of surgeon								
Registrar					Referent			
Senior registrar (1)	-1.308	0.867	2.279	1	0.131	0.270	0.049	1.478
Consultant (2)	-0.373	0.420	0.786	1	0.375	0.689	0.302	1.570
Anesthetist								
Registrar					Referent			
Senior registrar (1)	0.695	0.689	1.017	1	0.313	2.004	0.519	7.739
Consultant (2)	0.577	0.609	0.898	1	0.343	1.781	0.540	5.873

SE=Standard error; CI=Confidence interval; df= Degree of freedom

neonatal outcomes.<sup>[22]</sup> Forty-two (87.5%) emergency cesarean section done under GA compared with 2 (28.6%) done under SAB were associated with Apgar scores below 7 ( $P = 0.003$ ). From these findings it may be reasonable to infer that for babies requiring emergency cesarean section who are often more compromised than babies of elective cesarean section delivery, SAB has a less depressive effect than GA.

An important study limitation is the retrospective nature of this study. A prospective randomized study would be better in determining if post-operative perinatal morbidity was greater in babies delivered preterm with GA than with SAB, particularly in unplanned cesarean sections. Another limitation is that confounding factors could not be controlled for, leading to measurement bias. The study however, infers a strong association between anaesthetic technique and immediate Apgar scores and outcome of resuscitation following preterm cesarean section. This however, failed to translate into higher differences in perinatal mortality. We recommend SAB in preterm cesarean sections where facilities for post-operative resuscitation are not optimal.

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