General Versus Regional Anaesthesia for Caesarean Section Indicated for Acute Foetal Distress: A Retrospective Cohort Study

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Acute foetal distress (AFD) is a life-threatening foetal condition complicating 2% of all pregnancies and accounting for 8.9% of caesarean sections (CS) especially in developing nations. Despite the severity of the problem, no evidence exists as to the safest anaesthetic technique for the mother and foetus couple undergoing CS for AFD. We aimed to compare general anaesthesia (GA) versus regional (spinal and epidural) anaesthesia in terms of their perioperative maternal and foetal outcomes.

Methods

We carried out a retrospective cohort study by reviewing the medical records of all women who underwent CS indicated for AFD between 2015 to 2018 at the Douala General Hospital, Cameroon. Medical records of neonates were also reviewed. We sought to investigate the association between GA, and regional anaesthesia administered during CS for AFD and foetal and maternal outcomes. The threshold of statistical significance was set at 0.05.

Results

We enrolled the medical records of 117 pregnant women who underwent CS indicated for AFD. Their mean age and mean gestational age were 30.5 ± 4.8 years and 40 weeks respectively. Eighty-three (70.9%), 29 (24.8%) and 05 (4.3%) pregnant women underwent CS under SA, GA and EA respectively. Neonates delivered by CS under GA were more likely to have a significantly low APGAR score at both the 1st (RR = 1.93, p = 0.014) and third-minute (RR = 2.52, p = 0.012) and to be resuscitated at birth (RR = 2.15, p = 0.015). Past CS, FHR pattern on CTG didn’t affect these results in multivariate analysis. Adverse maternal outcomes are shown to be higher following SA when compared to GA.

Conclusion

The study infers an association between CS performed for AFD under GA and fetal morbidity. This, however, failed to translate into a difference in perinatal mortality when comparing GA vs RA. This finding does not discount the role of GA, but we emphasize the need for specific precautions like adequate anticipation for neonatal resuscitation in order to reduce neonatal complications associated with CS performed for AFD under GA.

Background

Acute foetal distress (AFD) is defined as sudden lack or shortage of oxygen supply via the bloodstream to the foetus, leading to foetal hypoxia, hypercarpnia and metabolic acidosis either intra-uterinely or during childbirth (1,2). It is a non-specific term which engulfs abnormal clinical findings suggestive of a compromised foetal wellbeing most often seen during the intra-partum period. AFD clinically manifests with an abnormal foetal heart rate (tachycardia ≥ 160 beats/minutes or bradycardia ≤ 110 beats/minutes) on cardiotocography (CTG), intermittent doppler or hand-held foetoscope auscultation. Reduced foetal movements in-utero can be felt by the mother and/or reduced foetal biophysical or a resistance in umbilical cord circulation on obstetrical ultrasound scan (4). Furthermore, the intrauterine stress of the foetus during AFD leads to emission of fresh meconium into the amniotic fluid. Meconium is slightly corrosive to the airways and although sterile, is a culture media for bacteria. This subsequently could lead to respiratory distress due to Meconium Aspiration Syndrome, if meconium stained amniotic fluid is inhaled intra-uterinely or during delivery (1)(5). AFD is a foetal and obstetrical emergency, complicating up to 2% (6) of all pregnancies and accounting for 8.9% of births due to caesarean section (CS) especially in developing countries (7). Mortality still remains high at 31.25 per 1000 deliveries, especially when the interval between the start of AFD and childbirth exceeds 30 minutes (7)(5). The management of AFD requires the safest and fastest possible route of delivery to prevent avert perinatal morbidity and mortality compounded after delivery by neonatal asphyxia (NA) or hypoxic ischemic encephalopathy (4).

However, there is an on-going debate on the safest anaesthetic technique for CS indicated for AFD in anaesthesiology. This is more challenging in low-income countries (LICs), due to insufficient health infrastructure, unfunded and unstaffed healthcare systems (8). Comparing regional (spinal and epidural) to general techniques of anaesthesia, although general anaesthesia (GA) has the merit of rapidity in induction of anaesthesia which is invaluable for this obstetrical emergency, (AFD), when compared to regional anaesthesia techniques (RATs) (9)(10) GA could have deleterious and potentially lethal consequences to neonates born through CS performed under GA. This is due to the trans-placental passage of hypnotics, and opioids derivatives which can lead to depression of cardiovascular, respiratory and neurological functions of the neonate (11). This later could be associated with neonatal resuscitation and neonatal intensive care unit admission. The neonates with birth asphyxia resuscitated at birth are predisposed to nosocomial infections which may increase neonatal mortality. RATs, though associated with better APGAR scores both in the 1st and 5th minutes following delivery take a longer time to be realized, a factor non-desirable in women undergoing CS indicated for AFD (12). This delay is thought to be possibly lethal as increased induction time for a foetus in acute distress may worsen the consequences of AFD such as hypoxic ischemic encephalopathy, cerebral palsy, neonatal anaemia, metabolic acidosis in the newborn and ultimately, death. However, studies are yet to prove this hypothesis if true. Also, RATs have been shown to be associated with less maternal blood loss and greater postoperative satisfaction [9]. This however, is shown to be true in elective CS, but not in emergency CS, especially in the case of AFD (10). A systematic review of 22 randomized and quasi-randomized controlled studies by the Cochrane Group assessed the effects of RATs versus GA on maternal and neonatal outcomes following CS (10). However, most studies included in the review involved elective CS with only two studies involving emergency CS for AFD. Their findings therefore, cannot be readily applied to women undergoing anaesthesia indicated for emergency CS for AFD. There is, therefore, a need for more studies comparing both RAT and GA for CS indicated for AFD to generate more evidence required for decision making in daily clinical practice.

Against this background, we sought to compare the maternal and neonatal outcomes of women undergoing emergency CS for AFD under either RATs or GA. The research goal was to contribute in providing information necessary to generate evidence for the safest anaesthetic technique to be used in the case of this emergency.
Methods

Study design and setting

The study was carried out and reported in accordance to the STROBE checklist for cohort studies. This was a retrospective cohort study conducted at the Douala General Hospital (DGH), Douala, Cameroon. Douala is an urban zone and the economical capital of Cameroon with a population 3 million inhabitants [10]. The DGH is a university teaching hospital and one of the major reference hospitals in Cameroon. It has an Obstetrics and Gynaecology department, a Neonatal unit and an Anaesthesiology and Intensive Care department. It’s neonatal unit serves as the main referral neonatal unit for all health centres in Douala and its environs. Every year, an average of 1100 childbirths occur in its Obstetrics and Gynaecology department [9] some within the delivery room (in case of vaginal delivery) and others within the operating room of the department of Anaesthesiology and Intensive Care.

Sampling and study participants

We performed a chart review of the obstetrical and anaesthesiology records of all consecutive parturients who underwent an emergency CS indicated for AFD between January 01, 2015, to August 31, 2018. We also reviewed the records of the neonates of these women who delivered via emergency CS. We excluded parturients with contraindications for regional anaesthesia (coagulation abnormalities, infection at the point of lumbar puncture, and haemodynamic instability, pre-existing neurological pathologies such as epilepsy, space occupying lesions or radiculopathies) as well as cases of extreme emergencies such as cord prolapse.

Variables studied:

Data extracted from the obstetrical and anaesthesiology records of parturients and neonates included maternal age, past history (parity, gravidity, comorbidities and previous CS), the anaesthesia technique whether regional (spinal or epidural) or general. Parameters specific to anaesthesiology consultation included ASA score and intubability criteria namely the mallampati score. Information on perioperative complications (immediate and late) such as post-partum haemorrhage (PPH), post-dural puncture headache (PDPH), post-operative wound infection and duration of hospitalisation were also collected. Pathologic cardiotocographic (CTG) tracings were used to group patients into two groups of foetal heart rate pattern; non-reassuring and abnormal group, according to the NICE guidelines on intra-partum care (13) Those with at least 2 non reassuring features were under the ‘non-reassuring group’ and those with an abnormal feature under the "abnormal group." Neonatal parameters collected from hospital files of newborns included gestational age, birth weight, APGAR scores at 1st, 3rd and 5th minutes after delivery, neonatal resuscitation and clinical diagnosis of neonatal asphyxia according to the Sarnat classification (14). Hospitalization in the neonatal unit as well as its duration was noted. Other maternal parameters included maternal age, gestational age and referral or not to the DGH.

Data analysis

Data was extracted from the clinical records of the participants into a pilot-tested structured data collection sheet. The data was entered into Epi-info version 7 and exported to STATA 14 for analysis. The primary exposure of interest was the type of anaesthesia administered, whether regional (spinal, epidural) or general anaesthesia(GA). The primary outcomes of interest were the foetal outcomes after delivery which included: APGAR score at the 1st, 3rd and 5th minutes, a clinical diagnosis of neonatal asphyxia according to the Sarnat classification (14), neonatal resuscitation, We conducted univariable analysis of the association between the outcomes of interest and other exposure variables namely: American Society of Anaesthesia (ASA) score, parity, gravidity, type of foetal heart rate (FHR) abnormality, referral, maternal age, prematurity (gestational age less than 37 weeks), low birth weight, previous CS, and fever. Furthermore, we conducted multivariable analysis of the association between the primary outcomes and type of anaesthetic technic considering confounders such as foetal heart rate pattern,past caesarean section and whether paturiant was refered or not. Each variable within the dataset was explored for missing values and consistency. There were no missing data for the main exposure and outcomes of interest. Variables with missing data precluding meaningful analyses were excluded. Descriptive statistics were calculated for each variable. In univariate analysis, each exposure was tested for association with the outcome using generalised linear models. Crude risk ratios (CRR) p-values and 95% confidence intervals (CI) were read-off. P-values of less than 0.05 were considered statistically significant.

Results

Socio-demographic characteristics of parturients

A total of 117 women met the eligibility criteria and were included into the study. The mean age was 30.5 ± 4.8 years (range: 18 to 42 years). Among the women included in the study, 18 (15.4%) were referred from other health facilities to DGH for CS delivery. The main reasons for referral included: stationary labour, post-term delivery, acute foetal distress (AFD), pre-eclampsia and preterm labour. The gestational age of pregnancy ranged from 30 to 42 weeks, with a median gestational age of 40 weeks (IQR: 39 – 40 weeks). The gravidity of participants ranged from 1 to 8 with a median gravidity of 2 (IQR = 1 to 4). Few women, 16 (13.68%) had undergone a previous CS.

Neonatal characteristics

Most of the babies born to the participants were males (61.11%). All the neonates were born alive. The APGAR score at birth ranged from 2 to 10, with a median of 8 (IQR 6 to 8). Table 1 summarizes the APGAR scores of newborns at birth and after the 3rd and 5th minutes of life. (Table 1 here)
Amongst the newborns, 42 were diagnosed of neonatal asphyxia giving a cumulative incidence of 35.9%. About two thirds (64.3%) of the new-borns with neonatal asphyxia were classified as Sarnat class 1, meanwhile 21.4% and 14.3% were Sarnat class 2 and 3 respectively. The duration of hospitalization of the newborns in the neonatal unit ranged from 2 to 43 days with a median of 4 days (IQR: 2 to 21 days). A total of 29 neonates (24.8%) were resuscitated at birth. Table 2 summarizes the characteristics of the new-borns.

(Table 2 here)

### Table 2: Summary of new-born characteristics

| Variable                  | Category | Number (%) | Percentage (%) |
|---------------------------|----------|------------|----------------|
| Neonatal asphyxia         | Yes      | 42         | 35.9           |
|                           | No       | 75         | 64.1           |
| Sarnat classification     | Sarnat 1 | 27         | 64.3           |
|                           | Sarnat 2 | 9          | 21.4           |
|                           | Sarnat 3 | 6          | 14.3           |
| Birth Weight              | Low      | 16         | 15.4           |
|                           | Normal   | 88         | 84.6           |
| Immediate cry             | Yes      | 27         | 23.1           |
|                           | No       | 90         | 76.9           |
| Resuscitation             | No       | 88         | 75.2           |
|                           | Yes      | 29         | 24.8           |
| Apgar at birth            | Low      | 36         | 30.8           |
|                           | Normal   | 81         | 69.2           |
| Apgar at 3 minutes        | Low      | 22         | 18.8           |
|                           | Normal   | 95         | 81.2           |
| Apgar at 5 minutes        | Low      | 8          | 6.8            |
|                           | Normal   | 109        | 93.2           |
| Sex                       | Male     | 66         | 61.1           |
|                           | Female   | 42         | 38.9           |

### Clinical Parameters of parturients

Upon hospital presentation, most of the parturients had a good general state 112 (95.7%). The ASA score was II in 75 (64.10%), III in 38 (32.48%) and IV in 4 (3.42%) of the parturients. Fever was present in 18 (15.4%) of participants.

### Type of anaesthetic technique used for emergency caesarean section indicated for AFD

More than two thirds 83 (70.9%) of the participants underwent CS for AFD under spinal anaesthesia (SA); 29 (24.8%) under general anaesthesia; and five (4.3%) under epidural anaesthesia (EA). Parturients who underwent emergency CS for AFD under epidural anaesthesia had the epidural catheter placed before delivery for obstetrical analgesia. This was converted to obstetrical anaesthesia immediately within the operating room when CS was indicated for AFD. Among patients administered GA, the most used hypnotic for induction was propofol 24 (82.8%). Thiopental and ketamine were used in 3 and 2 parturients respectively. Bupivacaine (Bupi) with fentanyl as adjuvant was used in 79 (95.2%) of patients operated under SA. Bupivacaine only and combinations of Bupi+morphine or Bupi+morphine+Fentanyl were used in two, one and one cases respectively. Bupivacaine was used for epidural anaesthesia. Hypotension during regional anaesthesia was managed with the use of ephedrine in 32 (27.3%) of parturients.

### Maternal outcome after surgery
Immediate postoperative complications were few. In the GA group, we had one case of Post-partum haemorrhage (PPH). In the SA group, there were 2 cases of PPH, one of the cases being complicated by maternal death. Furthermore, one case of severe hypotension was noted. No maternal complications were noted in the epidural anaesthesia group. Duration of hospitalisation of mothers ranged from 3 to 13 days with a mean of 5 days. Mean duration of hospitalization for women who underwent CS under SA was 4.5 days and 4.7 days for GA (p = 0.5154). Late complications observed during hospitalization were seen mostly in postpartum women who underwent SA. These included four cases of post-dural puncture headaches, two cases of endometritis, one case of malaria and one case surgical site infection.

Univariable analysis

Association of predictor variables with APGAR at the first minute

In univariable analysis, babies born of women who received GA had two-fold increase risk of having a low APGAR score at the first minute compared to babies of women who received SA (RR = 2.00, p = 0.011). Furthermore, neonates born of women with fever almost had a double likelihood of having a low APGAR score at the first minute compared to babies born of women without fever (RR = 1.83, p = 0.035). On the other hand, gravidity, the type of FHR pattern, use of epinephrine, gestational age, birth weight and previous CS were not associated with low APGAR in univariable analysis. Table 3 shows the association between the exposure variables and APGAR at the first minute in univariable analysis.

| Exposure                              | Categories   | APGAR at birth | RR    | p value | 95% CI     |
|---------------------------------------|--------------|----------------|-------|---------|------------|
|                                       |              | ≥ 7 (%) | < 7 (%) |        |            |
| Type of Anaesthesia administered      | Spinal       | 63 (80.7) | 20 (58.8) | 1 | -         |
|                                       | General      | 15 (19.2) | 14 (41.2) | 2.00 | 0.011 | 1.17 - 3.42 |
| Gravidity                             | Multi-Gravida | 60 (74.1) | 26 (72.2) | 1 | -         |
|                                       | Primi-gravida | 21 (25.9) | 10 (27.8) | 1.06 | 0.833 | 0.58 - 1.95 |
| Type of FHR                           | Abnormal     | 70 (86.4) | 29 (80.6) | 1 | -         |
|                                       | Non-Reassuring | 11 (13.6) | 7 (19.4) | 1.32 | 0.396 | 0.69 - 2.55 |
| Referral                              | Not referred | 69 (85.2) | 30 (83.3) | 1 | -         |
|                                       | Referred     | 12 (14.8) | 6 (16.7) | 1.10 | 0.795 | 0.53 - 2.26 |
| Use of Ephedrine                      | No           | 57 (70.4) | 28 (77.8) | 1 | -         |
|                                       | Yes          | 24 (29.6) | 8 (22.2) | 0.76 | 0.421 | 0.39 - 1.49 |
| Gestational age                       | Term         | 81 (63.0) | 21 (58.3) | 1 | -         |
|                                       | Premature    | 6 (7.4)   | 7 (19.5) | 1.85 | 0.052 | 0.99 - 3.43 |
|                                       | Post term    | 24 (29.6) | 8 (22.2) | 0.86 | 0.666 | 0.42 - 1.72 |
| Birth Weight                          | Normal or high | 65 (86.7) | 23 (79.3) | 1 | -         |
|                                       | Low          | 10 (13.3) | 6 (20.7) | 1.43 | 0.328 | 0.69 - 2.96 |
| Previous CS                           | No           | 66 (81.5) | 35 (97.2) | 1 | -         |
|                                       | Yes          | 15 (18.5) | 1 (2.8) | 0.18 | 0.080 | 0.03 - 1.22 |
| Fever                                 | No           | 72 (88.9) | 27 (75.0) | 1 | -         |
|                                       | Yes          | 9 (11.1)  | 9 (25.0) | 1.83 | 0.035 | 1.04 - 3.22 |

Association of exposure variables with APGAR at the third minute

Babies born of women who underwent GA had almost three times the risk of having a low APGAR score at the third minute compared to babies of women who underwent SA (RR = 2.86, p = 0.007). Furthermore, neonates delivered by women with fever had three times the risk of having a low APGAR score at the third minute compared to babies born of women without fever (RR = 3.14, p = 0.002). On the other hand, gravidity, the type of FHR, use of epinephrine, gestational age, birth weight and previous CS were not associated with a low APGAR score at the third minute. Table 4 shows the association between the exposure variables and APGAR score at the third minute.

Table 4: Association between exposure variables and APGAR at third minute
Association of exposure variables with APGAR at the fifth minute

The type of anaesthesia administered, maternal fever, gravidity, the type of FHR, use of epinephrine, gestational age, birth weight and previous CS were not significantly associated with low APGAR at the fifth minute. Table 5 shows the association between the exposure variables and APGAR at the fifth minute. (Table 5 here)

Table 5: Association between exposure variables with APGAR at fifth minute
| Exposure                               | Category          | APGAR at 5th minute |   |   |   |
|---------------------------------------|-------------------|---------------------|--|--|--|
|                                       |                   | ≥ 7(%) ≤ 7(%)       | RR | p value | 95% CI |
| **Type of Anaesthesia administered**  |                   |                     |   |   |   |
| Spinal                                | 79 (76.0)         | 4 (50.0)            | 1 | - | - |
| General                               | 25 (24.0)         | 4 (50.0)            | 2.86 | 0.118 | 0.76 - 10.71 |
| **Gravidity**                         |                   |                     |   |   |   |
| Multi-Gravida                         | 82 (75.2)         | 4 (50.0)            | 1 | - | - |
| Primi-gravida                         | 27 (24.8)         | 4 (50.0)            | 2.77 | 0.131 | 0.74 - 10.42 |
| **Type of FHR**                       |                   |                     |   |   |   |
| Abnormal                              | 92 (84.4)         | 7 (87.5)            | 1 | - | - |
| Non-Reassuring                        | 17 (15.6)         | 1 (12.5)            | 0.79 | 0.816 | 0.10 - 6.01 |
| **Referral**                          |                   |                     |   |   |   |
| Not referred                          | 93 (85.3)         | 6 (75.0)            | 1 | - | - |
| Referred                              | 16 (14.7)         | 2 (25.0)            | 1.83 | 0.434 | 0.40 - 8.38 |
| **Use of Ephedrine**                  |                   |                     |   |   |   |
| No                                    | 79 (72.5)         | 6 (75.0)            | 1 | - | - |
| Yes                                   | 30 (27.5)         | 2 (25.0)            | 0.88 | 0.878 | 0.19 - 4.16 |
| **Gestational age**                   |                   |                     |   |   |   |
| Term                                  | 66 (60.6)         | 6 (75.0)            | 1 | - | - |
| Premature                             | 13 (11.9)         | 0 (0.0)             | - | - | - |
| Post term                             | 30 (27.5)         | 2 (25.0)            | 0.75 | 0.715 | 0.16 - 3.52 |
| **Birth Weight**                      |                   |                     |   |   |   |
| Normal or high                        | 83 (84.7)         | 5 (83.3)            | 1 | - | - |
| Low                                   | 15 (15.3)         | 1 (16.7)            | 1.1 | 0.928 | 0.14 - 8.80 |
| **Previous CS**                       |                   |                     |   |   |   |
| No                                    | 93 (85.3)         | 8 (100.0)           | 1 | - | - |
| Yes                                   | 16 (14.7)         | 0 (0.0)             | - | - | - |
| **Fever**                             |                   |                     |   |   |   |
| No                                    | 93 (85.3)         | 6 (75.0)            | 1 | - | - |
| Yes                                   | 16 (14.7)         | 2 (25.0)            | 1.83 | 0.434 | 0.40 - 8.38 |

*Association of exposure variables and neonatal resuscitation*

Newborns of women who underwent GA were twice at risk of being resuscitated compared to those born of women who received spinal anaesthesia (P=0.015). Table 6 shows the association between the exposure variables and neonatal resuscitation. (Table 6 here )

Table 6: Association between exposure variables and neonatal resuscitation
| Exposure                          | Category        | Resuscitation | RR   | p value     | 95% CI      |
|----------------------------------|-----------------|---------------|------|-------------|-------------|
|                                  |                 | Yes (%)       | No (%)|             |             |
| Type of Anaesthesia administered | Spinal          | 16 (57.1)     | 67 (79.8) | 1           | -           |
|                                  | General         | 12 (42.9)     | 17 (20.2)  | 2.15        | 0.015       | 1.16 - 3.98 |
| Gravidity                        | Multi-Gravida   | 21 (72.4)     | 65 (73.9)  | 1           | -           |
|                                  | Primi-gravida   | 8 (27.6)      | 23 (26.1)  | 1.06        | 0.878       | 0.52 - 2.13 |
| Type of FHR                      | Abnormal        | 25 (86.2)     | 74 (84.1)  | 1           | -           |
|                                  | Non-Reassuring  | 4 (13.8)      | 14 (15.9)  | 0.88        | 0.787       | 0.35 - 2.23 |
| Referral                         | Not referred    | 28 (96.6)     | 71 (80.7)  | 1           | -           |
|                                  | Referred        | 1 (3.4)       | 17 (19.3)  | 0.19        | 0.98        | 0.03 - 1.35 |
| Use of Ephedrine                 | No              | 23 (79.3)     | 62 (70.5)  | 1           | -           |
|                                  | Yes             | 6 (20.)       | 26 (29.5)  | 0.69        | 0.370       | 0.31 - 1.54 |
| Gestational age                  | Term            | 20 (69.0)     | 52 (59.1)  | 1           | -           |
|                                  | Premature       | 2 (6.9)       | 11 (12.5)  | 0.55        | 0.383       | 0.15 - 2.09 |
|                                  | Post term       | 7 (24.1)      | 25 (28.4)  | 0.79        | 0.534       | 0.37 - 1.67 |
| Birth Weight                     | Normal or high  | 20 (83.3)     | 68 (85.0)  | 1           | -           |
|                                  | Low             | 4 (16.7)      | 12 (15)    | 1.1         | 0.841       | 0.43 - 2.79 |
| Previous CS                      | No              | 26 (89.7)     | 75 (85.2)  | 1           | -           |
|                                  | Yes             | 3 (10.3)      | 13 (14.8)  | 0.73        | 0.562       | 0.25 - 2.13 |
| Fever                            | No              | 23 (79.3)     | 76 (86.4)  | 1           | -           |
|                                  | Yes             | 6 (20.7)      | 12 (13.6)  | 1.43        | 0.342       | 0.68 - 3.02 |

**Association of exposure variables with neonatal asphyxia (NNA)**

In univariable analysis, the type of anaesthesia administered was not significantly associated with the clinical diagnosis of NNA. Furthermore, gravidity, the type of FHR pattern, gestational age, birth weight, previous CS, the use of epinephrine and the presence of postoperative fever were not associated with NNA in univariable analysis. Table 7 shows the association between the exposure variables and NNA. (Table 7 here)

Table 7: Association between exposure variables with NNA
Association of exposure variables and new-born hospitalization in the neonatal unit

There was no significant difference in the chances of neonates being hospitalised in the neonatal unit for both SA and GA. However, post term newborns were about 50% less likely to be hospitalized in the neonatal unit compared to neonates born at term (P=0.035). Also, babies with low birth weights were about twice as likely to be hospitalised (P=0.001). Table 8 shows the association of exposure variables with hospitalization of newborns in the neonatal unit.

Table 8: Association between exposure variables and neonatal unit admission
| Exposure                           | Category          | Hospitalization in the neonatal unit |
|-----------------------------------|-------------------|--------------------------------------|
|                                   |                   | Yes (%) | No (%) | RR | p value | 95% CI    |
| Type of Anaesthesia administered  | Spinal            | 43 (70.5) | 40 (78.4) |   |        | -         |
|                                   | General           | 18 (29.5) | 11 (21.6) | 1.20 | 0.314   | 0.84 - 1.70 |
|                                   | Gravidity         |          |         |    |         |           |
|                                   | Multi-Gravida     | 44 (68.8) | 42 (79.3) |   |        | -         |
|                                   | Primi-gravida     | 20 (31.2) | 11 (20.7) | 1.26 | 0.172   | 0.90 - 1.76 |
|                                   | Type of FHR       |          |         |    |         |           |
|                                   | Abnormal          | 53 (82.8) | 46 (86.8) |   |        | -         |
|                                   | Non-Reassuring    | 11 (17.2) | 7 (13.2)  | 1.14 | 0.529   | 0.76 - 1.72 |
|                                   | Referral          |          |         |    |         |           |
|                                   | Not referred      | 52 (81.2) | 47 (88.7) |   |        | -         |
|                                   | Referred          | 12 (18.8) | 6 (11.3)  | 1.27 | 0.215   | 0.87 - 1.85 |
|                                   | Use of Epinephrine|          |         |    |         |           |
|                                   | No                | 49 (76.6) | 36 (67.9) |   |        | -         |
|                                   | Yes               | 15 (23.4) | 17 (32.1) | 0.81 | 0.324   | 0.54 - 1.23 |
|                                   | Gestational age   |          |         |    |         |           |
|                                   | Term              | 43 (67.2) | 29 (54.7) |   |        | -         |
|                                   | Premature         | 10 (15.6) | 3 (5.7)   | 1.29 | 0.160   | 0.90 - 1.83 |
|                                   | Post term         | 11 (17.2) | 21 (39.6) | 0.57 | 0.035   | 0.34 - 0.96 |
|                                   | Birth Weight      |          |         |    |         |           |
|                                   | Normal or high    | 40 (74.1) | 48 (96.0) |   |        | -         |
|                                   | Low               | 14 (25.9) | 2 (4.0)   | 1.92 | < 0.001 | 1.43 - 2.58 |
|                                   | Previous CS       |          |         |    |         |           |
|                                   | No                | 57 (89.1) | 44 (83.0) |   |        | -         |
|                                   | Yes               | 7 (10.9)  | 9 (17.0)  | 0.77 | 0.391   | 0.43 - 1.39 |
|                                   | Fever             |          |         |    |         |           |
|                                   | No                | 53 (82.8) | 46 (86.9) |   |        | -         |
|                                   | Yes               | 11 (17.2) | 7 (13.2)  | 1.14 | 0.529   | 0.76 - 1.72 |

**Association of exposure variables and duration of neonatal unit hospitalization**

Neonates born following GA were likely to have a longer mean duration of hospitalisation in the neonatal unit compared to those born under SA 4.7 days versus 4.5 days. However, the difference in mean was not statistically significant (p = 0.515).

**Multivariable Analysis**

After accounting for foetal heart rate patterns on CTG, past caeserian scar and whether or not paturients were refered from another hospital, SA remained significantly associated with better APGAR scores in the first and 3rd minute following Caeserean section, and with lesser risks of rescusiation of newborns (P<0.05). Table 9 shows the association between anaesthesia technic and main outcome variables in multivariable analysis. (Table 9 here).

**Table 9: Association between Anesthesia technic and outcome Variables in Multivariate Analysis**
| Exposure                  | ARR   | CI          | P-Value |
|--------------------------|-------|-------------|---------|
| **APGAR at birth**       |       |             |         |
| Type of anaesthesia*     |       |             |         |
| Regional                 | 1     | -           | 0.016   |
| General                  | 1.86  | 1.12 – 3.08 |         |
| Yes                      | 0.212 | 0.03 – 1.44 |         |
| **APGAR 3rd minute**     |       |             |         |
| Type of anaesthesia*     |       |             |         |
| Regional                 | 1     | -           | 0.025   |
| General                  | 2.33  | 1.11 – 4.86 |         |
| **APGAR at 5th minute**  |       |             |         |
| Type of anaesthesia*     |       |             |         |
| Regional                 | 1     | -           | 0.124   |
| General                  | 2.81  | 0.75 – 10.53|         |
| **Resuscitation**        |       |             |         |
| Type of anaesthesia*     |       |             |         |
| Regional                 | 1     | -           | 0.041   |
| General                  | 1.90  | 1.02 – 3.51 |         |
| **Neonatal Asphyxia**    |       |             |         |
| Type of anaesthesia*     |       |             |         |
| Regional                 | 1     | -           | 0.765   |
| General                  | 1.08  | 0.63 – 1.88 |         |

**Discussion**

The aim of our study was to assess the effects of regional versus general anaesthesia on foetal and maternal outcomes following caesarean section for acute foetal distress, in order to determine the safest anaesthetic technique to use in the case of this emergency. We also sought to analyse the influence of other maternal and foetal factors on foetal and maternal outcomes. We found that unlike SA, GA was associated with lower APGAR scores in the 1st 3rd and 5th minutes following CS. However, this finding was significant for the 1st and 3rd minutes only.

Our findings are consistent with those of several other studies in Africa, Europe and the USA, where GA was seen to be associated with lower APGAR scores, following anaesthesia for AFD. However, unlike our study, their results showed that lower APGAR scores following GA was significant even at the 5th minute following delivery (15),(16),(17). GA is shown in our study to be associated with significantly higher chances of neonatal resuscitation when compared to SA. We therefore might have thought that neonatal admission and morbidity would have consequently been increased. However, this was not the case in our study as expected. Thangaswamy et al. showed that in Category 1 CS, GA was significantly associated with greater frequency of neonatal unit admissions and mortality (15). Several studies have shown that neonatal resuscitated babies have higher morbidity and sequelae of neonatal asphyxia(18)(19). Failure of our study to tie with these findings may infer better resuscitative techniques in the context of DGH for babies born by caesarean section.

Confounders studied in the current study included previous CS, foetal heart rate pattern on CTG, and patients referral from a different hospital. None of these were found to influence the choice of anaesthetic technique. We noticed that, whether patients were referred or not, and no matter the degree of heart rate abnormality, or whether they had had a past caesarean section, foetal outcome were still better if SA and not GA was used for CS. This finding is consistent with previously reported studies(15) (17). Our study also went further to examine the association of other exposures such as gestational age, birth weight, gravidity, the use of ephedrine and fever on neonatal outcomes. Maternal fever was consistently shown to be associated be associated with lower APGAR scores, significantly so, in the first and third minutes following delivery. These results are not surprising and have been confirmed by other studies showing the impact of maternal fever on neonatal outcome(20), (21), (22). Mothers presenting with fever should therefore be aggressively resuscitated in the perinatal wards prior to delivery to reduce the risks of poor foetal outcomes.

Maternal outcomes in our study surprisingly show that, women presenting with AFD who were operated, were likely to have a more favourable outcome if GA instead of SA was the technique of anaesthesia used. This is contrary to findings of other studies. Where regional anaesthesia is found to be associated with better maternal outcomes (23). Thangaswamy et al. revealed that ICU admission and maternal mortality were also comparable between GA and SA(15). However further studies will be needed to conclude on these observations.

The present study should also be interpreted in the context of its limitations. Firstly, we were not able to assess some factors such as the interval between the induction of anaesthesia and delivery of the neonate as this is a paramount factor influencing neonatal outcome with respect to anaesthetic technique. Secondly, maternal factors such as blood loss and postoperative pain were not studied. This was due to the retrospective nature of our study as this data was very inconsistently written in the medical records. However, using robust methods, we have contributed to the scarcity of data on the safest anaesthesia technique for CS indicated for AFD. These findings should contribute in informing decision making by anaesthesiologists, who are often confronted with the dilemma of which technique of anaesthesia to choose in this emergency situation. It has been a common clinical anaesthesia practice to perform GA in this situation. The current study shows that SA is safer than the traditional GA often used.
Conclusion

The study infers associations between GA for CS indicated for AFD and neonatal morbidity on one hand and between SA and maternal morbidity and mortality on the other hand. This, however failed to translate into a difference in perinatal mortality. These results do not discount the role of GA in low-income settings, but we emphasise the need for specific precautions like close monitoring of labour for AFD and adequate anticipation of neonatal resuscitation when GA is used for CS in the case of AFD. Proper anticipation of maternal morbidity and mortality following SA is also warranted.

Abbreviations

AFD: Acute foetal distress
CTG: Cardiotocography
CS: Caesarean section
GA: General Anaesthesia
SA: Spinal Anaesthesia
LICs: Low-income countries
RATs: Regional anaesthesia techniques
NNA: Neonatal asphyxia
DGH: Douala General Hospital
PDPH: Post-dural puncture headache
ASA: American Society of Anaesthesia
FHR: Fœtal Heart Rate
CRR: Crude risk ratios
CI: Confidence Interval
IQR: Interquartile Range
PPH: Post-partum haemorrhage

Declarations

Ethics approval and consent to participate: The study was approved by the Institutional Review Board of the Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon. Administrative authorizations were equally obtained from the directorate of Douala General Hospital prior to the beginning of the study. Being a retrospective study, written informed consent from participants to partake into the study was not necessary. hence, we obtained an informed consent waiver from both aforementioned ethical committee.

The study protocol is performed in accordance with the STROBE checklist for cohort studies.

Consent for publication: Not applicable

Availability of data and materials: The dataset analysed in this study are not publicly available because they are currently being analysed for a second research article. Nonetheless, they are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions:

JAMM and EBN: Study conception and design, acquisition of data, data analysis and interpretation of results, manuscript writing and critical revisions. TTN, BAN, CAA and JNT: acquisition of data, data analysis interpretation of results and critical revisions. JZM: interpretation of results, manuscript writing and critical revisions of the manuscript for intellectual content. All authors read and approved the final manuscript.

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