

Impact of planning of pregnancy in women with epilepsy on seizure control during pregnancy and on maternal and neonatal outcomes

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Impact of planning of pregnancy in women with epilepsy on seizure control during pregnancy
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Abstract

Purpose: To investigate whether planning of pregnancy in women with epilepsy affects seizure control during pregnancy and to compare the maternal and neonatal outcomes in planned and unplanned pregnancies

Methods: This was a retrospective cohort study of 153 pregnant women with epilepsy who were treated at the University of Tsukuba Hospital and Hokkaido University Hospital between 2003 and 2011. Twenty-one pregnancies were excluded due to insufficient data. Data of patients followed by neurologists during their planned pregnancies (planned-pregnancy group, $n = 51$) were compared to those of patients referred to neurologists after conception for managing epilepsy during pregnancy (unplanned-pregnancy group, $n = 81$). The treatment profile for epilepsy, seizure control, and maternal and neonatal outcomes in both groups were compared using Chi-square test or Fisher's exact test and Mann-Whitney U test.

Results: Compared to the unplanned-pregnancy group, the planned-pregnancy group showed a significantly greater proportion of patients receiving monotherapy with antiepileptic drugs (80% vs. 61%; planned vs. unplanned, $P = 0.049$) and those not requiring valproic acid (77% vs. 56%, $P = 0.031$). Furthermore, the frequency of epileptic seizures (16% vs. 35%, $P = 0.018$) and changes in antiepileptic drugs (24% vs. 41%, $P = 0.042$) were significantly lower in the planned-pregnancy group than in the unplanned-pregnancy group. No significant intergroup differences were noted in the obstetric complications and neonatal outcomes, including congenital malformations.

Conclusion: For women with epilepsy, planning of pregnancy is associated with good seizure control during pregnancy and less fetal exposure to antiepileptic drugs.

Key words

Epilepsy, Planned pregnancy, Seizure control, Antiepileptic drugs, Monotherapy,

Neonatal/maternal outcome

1) Introduction

Population-based studies indicate that the prevalence of epilepsy in pregnant women is 0.7%, whereas registry-based studies suggest a range of 0.2–0.4%¹. Thus, obstetricians often encounter cases of pregnancy in women with epilepsy (WWE¹) and can be involved in the management of the pregnancies in these women as well as offer preconception counseling. In general, although the pregnancy outcomes in most WWE are favorable, epilepsy poses additional risks for the mother and fetus, including the potential effects of teratogenic antiepileptic drugs (AEDs²), the effects of maternal seizures on the fetus, and genetic risks, all of which contribute to a two- to three-fold increase in the risk of adverse outcomes². These adverse outcomes include major congenital malformation (MCM³) in the fetus and long-term developmental delay.

A maternal seizure can directly affect the fetus and cause fetal hypoxia and distress. Additionally, adverse effects on the mother include falls; superficial abdominal hematomas; burns or other accidents; and significant obstetric sequelae, such as placental abruption and premature labor and delivery. Various complications of pregnancy have been reported in WWE. These women are at an increased risk of spontaneous abortion, induction of labor, cesarean section, and postpartum hemorrhage⁴. Infants of WWE exposed to AEDs in utero are at a high risk of fetal growth restriction, preterm birth, low birth weight, and low Apgar scores⁴.

¹ WWE: Women with epilepsy

² AED: Antiepileptic drug

³ MCM: Major congenital malformation

The incidence of fetal MCM in women without epilepsy is 1.6–2.2%⁵⁻⁷, whereas that in WWE is higher, at 2.8–3.6%⁸⁻¹⁰ who take AEDs and at 4.2–6.7% who do not take AEDs^{5, 6 8-10}. Furthermore, the risk of fetal MCM increases with the number of AEDs administered^{6, 7, 10, 11}. In particular, treatment with valproic acid (VPA⁴) in combination with AEDs is associated with a high risk of fetal MCM¹². The teratogenic effects of most AEDs appear to be dose dependent^{8, 13}, and numerous reports have confirmed this dose dependency in the case of VPA^{8, 10, 11, 14-16}. Hence, transitioning from VPA to another AED should be considered before conception, and the lowest possible dose of the most appropriate AED should be administered before conception in WWE.

The Japanese guidelines for the management of WWE, as stipulated by the Societas Neurologica Japonica, recommend preconception counseling to provide detailed information about pregnancy and delivery in WWE and emphasize the importance of the medication during pregnancy, along with antenatal management involving the use of the lowest possible dose of the most appropriate AED, avoiding VPA, possibly withdrawing AED before conception, and supplementation with folic acid before and after conception to prevent neural tube defects¹⁷. International guidelines recommend monotherapy with lamotrigine owing to its low risk of teratogenicity; however, this treatment option is currently not permitted by the Japanese national health insurance policy¹⁷.

Although various guidelines recommend planned pregnancy for WWE, the effects of planning remain largely unclear. Preconception counseling for WWE has been reported to be

⁴ VPA: Valproic acid

effective for reducing fetal MCM in children born to WWE receiving AEDs¹⁸. However, the effects of a planned pregnancy on seizure control in WWE during pregnancy and maternal and neonatal peripartum outcomes have not been evaluated; in the present study, we aimed to evaluate these effects. Moreover, we aimed to compare the maternal and neonatal outcomes in planned and unplanned pregnancies in WWE.

2) Methods

We retrospectively reviewed the hospital records of 153 pregnancies in WWE who were treated at the University of Tsukuba Hospital (98 pregnancies) and Hokkaido University Hospital (55 pregnancies) between 2003 and 2011. Planned pregnancy was defined as the completed process of planning and preparing for pregnancy, during which the doses and numbers of AEDs and maternal physical health prior to conception were optimized by neurologists or neurosurgeons. According to the Japanese Healthcare system, all WWE taking AEDs should be followed up by their neurologists or neurosurgeons and not by general physicians, even if their seizures are well controlled, and some WWE who remain free of seizures without taking AEDs for a long duration are normally not followed by any medical doctor. Among WWE in the planned-pregnancy group, those who were regularly reviewed by their neurologists or neurosurgeons before conception received preconception counseling, epilepsy reassessment, AED dose adjustment; after successful execution of the planned pregnancy processes, their neurologists or neurosurgeons considered their conception appropriate. For WWE in the planned-pregnancy group who were not followed by medical doctors, neurologists or neurosurgeons consulted their conception, reviewed their condition, and considered pregnancy to be appropriate. The unplanned-pregnancy group included all the pregnancies not included in the planned-pregnancy group. WWE in the unplanned pregnancy group who were regularly followed up by their neurologists or neurosurgeons included those with unexpected pregnancies (for both WWE and medical doctors) and those in whom the

pregnancy had occurred during planning but not when conception was considered appropriate by the neurologists or neurosurgeons. The unplanned pregnancy group also included pregnancies of WWE who were not followed up by medical doctors and who did not consult neurologists or neurosurgeons about their pregnancy before conception. The planned pregnancy process was recorded on their medical chart or the introduction form administered at our hospital. The pregnancy was planned according to the discretion of the neurologist or neurosurgeon and was not structured, but it was in accordance with the guidelines for doctors authorized to treat patients under the Japanese government medical insurance system, as well as with the Japanese guidelines for the standard management of epilepsy. Data regarding the history of preconception treatment were unavailable in the case of 21 pregnancies, including medical letters from neurologists or neurosurgeons and medical interview forms; hence, these pregnancies were excluded from the study analysis. We classified the remaining 132 pregnancies on the basis of whether the pregnancy was planned or unplanned and compared the seizure control in pregnancy and maternal and neonatal outcomes in the 2 groups. Data were analyzed using the Chi-square test or Fisher's exact test and the Mann–Whitney *U* test, as appropriate. A *P* value of <0.05 was considered statistically significant.

The approval of the institutional review board and ethics committee was obtained at the University of Tsukuba Hospital (number: H23-62) and Hokkaido University Hospital (number: 011-0133). Informed consent was obtained from all patients.

3) Results

The planned-pregnancy group consisted of 51 pregnancies (39%), whereas the unplanned-pregnancy group comprised 81 pregnancies (61%).

Maternal backgrounds

Table 1 shows the patient demographics. Women in the planned-pregnancy group were significantly older (median age, 32 years; range, 17 – 42 years) than those in the unplanned-pregnancy group (median age, 28 years; range, 22–38 years; $P = 0.012$) (Table 1). The 2 groups showed no significant difference with respect to parity and gravidity (Table 1). Most women in both groups were Japanese. None of the women in the 2 groups had health conditions that were likely to affect maternal and neonatal peripartum outcomes, such as diabetes mellitus, hypertension, and hyperthyroidism. Only 1 woman in the unplanned-pregnancy group had asthma, which was well controlled. None of the women in the 2 groups had exposure to other teratogens except AEDs. Eight women in each group were overweight ($BMI > 25$), and the difference between the 2 groups in the proportion of overweight patients was not statistically significant ($P = 0.32$). Socio-economic statuses of the women in the 2 groups were not significantly different.

Treatment profile for epilepsy

Table 2 shows the epileptic treatments administered to the patients. Approximately 75% of WWE in both groups received some kind of AED during pregnancy. Compared to the unplanned-pregnancy group, the planned-pregnancy group showed a significantly higher proportion of WWE who received monotherapy with AEDs ($P = 0.049$). For monotherapy, phenobarbital (PB⁵) was the most common medication used in the planned-pregnancy group (10/31), followed by Carbamazepine (CBZ⁶) (8/31), VPA (8/31), clonazepam (3/31), diazepam (1/31), and primidone (1/31). In comparison, the primary drugs used for monotherapy in the unplanned-pregnancy group were VPA (17/37), CBZ (10/37), PB (3/37), phenytoin (PHT⁷) (3/37), clonazepam (2/27), clobazam (1/37), and zonisamide (1/37), in that order of frequency. Eight women required polytherapy in the planned-pregnancy group, of which 1 took VPA. In the unplanned-pregnancy group, 24 women required polytherapy, and 10 of them took VPA. VPA was required in significantly fewer cases in the planned-pregnancy group than in the unplanned-pregnancy group (9 vs. 27, $P = 0.031$). No significant intergroup difference was noted with regard to folic acid supplementation.

Seizure control and AEDs during pregnancy

A significantly high rate of seizures during pregnancy was recorded in the

⁵ PB: Phenobarbital

⁶ CBZ: Carbamazepine

⁷ PHT: Phenytoin

unplanned-pregnancy group than in the planned-pregnancy group (Table 3). Due to concerns of teratogenicity, changes in the AED schedule immediately after the diagnosis of pregnancy were required in 21 WWE who belonged to the unplanned-pregnancy group (Table 3). Of these 21 WWE, 8 requested the change themselves, whereas in 13 WWE, the change was recommended by neurologists. Eleven women (52.4%) had seizures even after altering the AED schedule. In particular, the rate of seizures was high (66.7%) in 12 women who took VPA before alteration of the AED schedule after pregnancy detection. With regard to these 12 women, seizures were noted in 1 of 3 women for whom VPA was switched to other AEDs, 1 woman whose VPA dosage was reduced, and 6 of 8 women for whom VPA was discontinued.

The rate of non-compliance with the AED treatment schedule was higher in the unplanned-pregnancy group than in the planned-pregnancy group (Table 3). In the planned-pregnancy group, 3 women opted to discontinue AEDs before conception of their own accord and then resumed these medications after completion of the high-risk period of fetal malformations according to the recommendations of their neurologists. They did not experience any seizure during the AED-free period. In the unplanned-pregnancy group, 13 women discontinued AEDs by themselves after the detection of pregnancy. Eight of them subsequently experienced seizures, which made it necessary to restart AED treatment, but 1 WWE refused to resume the AED treatment despite developing seizures. Of the remaining 5 women without seizures, 4 resumed AED treatment after the teratogenic period, whereas 1 did not resume AED treatment throughout the pregnancy, as per the advice of the neurologist.

The percentage of patients receiving stable antiepileptic treatment, i.e. no change in the type and dosage of AEDs or no additional requirement of AEDs, and was significantly higher in the planned-pregnancy group than in the unplanned-pregnancy group (Table 3). In the planned-pregnancy group, 12 women required medication adjustment, and all of them required an increase in the dosage of AEDs because of seizures (6/12), abnormal electroencephalogram findings (2/12), or for restarting previously withdrawn AEDs after the organogenetic period (4/12). In comparison, 33 women in the unplanned-pregnancy group required alterations in the AED schedule during pregnancy; the changes were required because of pregnancy detection in 21 of these women and because of seizures (increased dosage, 10 women) or for unknown reasons (increased dosage, 2 women) in 12 of them.

Peripartum outcomes

Peripartum outcomes are shown in Table 4. There was no significant difference in the frequency of preterm birth between the 2 groups (4/51 in planned vs. 8/81 in unplanned, $P = 0.77$). Similarly, no significant differences were noted in the frequency of termination of pregnancy and the modes of delivery.

Neonatal outcomes

Table 5 shows the neonatal outcomes. There was no significant difference in the birth weight and Apgar scores of the live-born neonates between the planned- and unplanned-pregnancy groups. The rates of congenital malformations were nearly identical in the 2 groups. In the planned-pregnancy group, the congenital malformations included 2 cases of ventricular septal defects (VSDs⁸), 1 case of cryptorchidism, and 1 case of congenital diaphragmatic eventration. Exposure to AEDs in utero was noted in 2 cases: one infant with VSD was exposed to VPA (600 mg) and clonazepam (10 mg), whereas the one with cryptorchidism was exposed to CBZ (400 mg). In the unplanned-pregnancy group, 6 neonates had congenital anomalies, with 1 case each of fetal hydantoin syndrome (exposure to VPA [500 mg], PB [30 mg], and PHT [100 mg]), stenosis of the external acoustic meatus (exposure to VPA [800 mg] and PB [90 mg]), choroid plexus cyst (exposure to PB [60 mg]), hypotonia with widely spaced nipples (exposure to VPA [400 mg]), duodenal atresia with hypospadias (no AED exposure), and VSD (no AED exposure). There was no significant intergroup difference in the neonatal complications.

⁸ VSD: ventricular septal defect

4) Discussion

In the present study, we investigated whether planned pregnancy in WWE affected seizure control in pregnancy and improved maternal and neonatal outcomes. We found that planning a pregnancy with alterations in the treatment regimen based on the currently accepted guidelines reduced the frequency of seizures during pregnancy and fetal exposure to AEDs, but did not significantly improve the maternal or neonatal outcomes.

Compared to the unplanned-pregnancy group, the planned-pregnancy group had a significantly higher rate of monotherapy and lower rate of VPA use, which reflects the clinical practice of the treating neurologists in adjusting the lowest possible dose of the most appropriate AED and switching from VPA to another AED according to the currently followed guidelines. Furthermore, compliance to medication was greater in the planned-pregnancy group than in the unplanned-pregnancy group; this may be partly attributed to the fact that the mothers were provided precise information about the risks of AEDs for the fetus and the necessity of taking AEDs to control seizure during the preconception counseling. Three women in the planned-pregnancy group chose to discontinue AEDs before conception, but restarted the AEDs according to the advice of their neurologists. Thus, preconception counseling and the active involvement of neurologists play important roles in improving seizure control in WWE during pregnancy.

In 21 cases in the unplanned-pregnancy group, the woman or the neurologist attempted to

change AEDs (5/21), decrease the dose of AEDs (5/21), or discontinue the AEDs (11/21) immediately after the detection of pregnancy because of concerns regarding the teratogenicity of AEDs, which led to seizures in 11 cases (52.4%). Seizures after changing the treatment schedule occurred particularly in women who had been taking VPA (66.7%). These cases were only observed in the unplanned-pregnancy group; it is possible that the seizures would have been avoided and the fetal exposure to AEDs would be minimized if the AEDs had been adjusted before conception in a carefully planned manner. If these 11 women had not had seizures, the rate of seizures during pregnancy in the unplanned-pregnancy group would be reduced to 21.0%, which is nearly equal to that in the planned-pregnancy group. Moreover, the absence of preconception counseling may have led to the non-compliance to AED intake noted in 13 women in the unplanned-pregnancy group, 8 of whom experienced seizures (61.5%). The non-compliance and subsequent occurrence of seizures may have been prevented if these women had received appropriate preconception counseling. We would like to emphasize that adjusting medications for reducing teratogenicity of fetuses during pregnancy poses a risk of inducing maternal epileptic seizures.

A decrease in the doses of AEDs during pregnancy was required only in the unplanned-pregnancy group. Pregnancy may reduce the plasma concentrations of AEDs¹⁹, and therefore, any dose adjustment that is required, usually involves increasing the concentration of AEDs as the pregnancy progresses. Since this may be counterintuitive to the natural physiology of pregnancy, the neurologists may reduce the AED dose in an unplanned pregnancy, as observed in

5 cases in this study. The occurrence of pregnancy may have been so unexpected in these cases that the doses of AEDs were decreased to reduce possibility of congenital malformation of fetuses. These changes resulted in a high rate of seizures, with 40% of these women subsequently experiencing seizures. Although the exact reasons for decreasing the dose of AEDs are unknown, we recommend a decrease in the dose before conception in cases where pregnancy is planned.

There were several limitations to this study. We focused on seizures during pregnancy, and the type of seizure and its direct impact on fetal or maternal outcomes were beyond the scope of this investigation. Nevertheless, we noted that epileptic seizures warranted termination of pregnancy in 2 cases among the planned-pregnancy group and in 5 cases in the unplanned-pregnancy group. Furthermore, cesarean delivery was performed in the unplanned-pregnancy group due to uncontrollable seizures (Table 4). The unplanned-pregnancy group had a higher rate of seizures during pregnancy and required more obstetric interventions due to epileptic seizures than the planned-pregnancy group. Thus, a planned pregnancy may result in reduced seizure activity and consequently require fewer obstetric interventions, such as termination of pregnancy or cesarean delivery. This study is retrospective in nature, and the women seeking preconceptional counseling are different from those with unplanned pregnancies.

The primary objective of a planned pregnancy in WWE is to avoid the use of AEDs, including VPA, which pose high teratogenic risks. In the present study, although VPA could be avoided in a significantly greater proportion of women in the planned-pregnancy group than in the unplanned-pregnancy group, the rate of congenital malformations in the 2 groups was similar.

This may be explained by the following 2 possibilities. First, the other AEDs are also teratogenic, and therefore, even if VPA is switched with another AED, not all congenital malformations can be prevented. A recent study on live-born infants revealed that exposure to new-generation AEDs, such as lamotrigine, oxcarbazepine, topiramate, gabapentin, and levetiracetam, during the first trimester was not associated with an increased risk of major birth defects²⁰. If older AEDs could be switched to newer AEDs before conception in a planned pregnancy, then it may be possible to decrease the risk of developing congenital malformations. Second, our hospitals are general perinatal medical centers. Many fetuses with congenital malformations diagnosed on antenatal ultrasonography are referred from nearby clinics and hospitals to our centers, and incidental detection of epilepsy in such cases may skew the results of this study. At our hospitals, the incidence of MCM is 10.7% of all deliveries, which is much higher than the incidence (1.6–2.2%)⁵⁻⁷ in the general population and also higher than the percentage of fetuses exposed to AEDs (4.2–6.7%)^{5, 6, 8-10}. Hence, this institutional bias limits our study findings on fetal congenital malformations.

Although a greater proportion of WWE in the planned pregnancy group received monotherapy of AEDs and required less VPA than the unplanned pregnancy group, possibly because of the adjustments made to AED dosage by neurologists or neurosurgeons, folate prescription levels were the same in the 2 groups. The situation on the supplementation of folic acid for women of the reproductive age in Japan may be related to these results. Folic acid intake from the Japanese diet is appropriate and neural tube defects in Japan are less frequent than that in

the other countries²¹. Therefore, the awareness of folic acid supplementation for women of reproductive age among medical doctors, even among the obstetricians, are lower in Japan than that in countries in Europe or Oceania as well as in other Asian countries, such as Korea or Taiwan, despite promotion by Japanese Ministry of Health, Labour and Welfare²². Because of these factors, neurologists or neurosurgeons may be less aware of folic acid supplementation for WWE in the planned pregnancy process, which may influence the results. Furthermore, we analyzed only WWE receiving folate prescription of 5 mg/day in the present study, and not WWE receiving over-the-counter drugs of folate supplementation (0.4 mg/day), which may also influence our results.

5) Conclusions

In WWE, planned pregnancy is associated with good seizure control during pregnancy and less fetal exposure to AEDs. In cases of unplanned pregnancy, the doses of AEDs are adjusted immediately after pregnancy is determined, which results in a higher rate of seizures during pregnancy. Although we noted that planned pregnancy may also improve maternal and neonatal peripartum outcomes, we were unable to confirm this finding in the present study.

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Disclosure of Conflicts of Interest

None of the authors has any conflict of interest to disclose.

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Table 1: Maternal characteristics

	Planned	Unplanned	P value
Number	51	81	
Age	17–42	22–38	0.012 ^a
Nullgravida	20 (39.2%)	37 (45.7%)	0.47
Nullipara	29 (56.9%)	53 (65.4%)	0.32
BMI	16.9–38.3	14.3–32.8	0.15
Japanese	49 (96.1%)	79 (97.5%)	0.64
On welfare	1 (2.0%)	4 (4.9%)	0.65

^aP < 0.05, BMI: Body mass index

Table 2: Treatment profile for epilepsy

	Planned	Unplanned	P value
AED use	39 (76.5%)	61 (75.3%)	0.88
Monotherapy ^a	31/39 (79.5%)	37/61 (60.7%)	0.049 ^b
VPA included ^a	9/39 (23.1%)	27/61 (44.3%)	0.031 ^b
FA supplementation	23 (45.1%)	30 (37.0%)	0.36

^aMothers not receiving AEDs were excluded, ^bP < 0.05, AED: antiepileptic drug, VPA: Valproic acid, FA: Folic acid

Table 3: Seizure control and AEDs during pregnancy

	Planned	Unplanned	P value
Epileptic seizure	8 (15.7%)	28 (34.6%)	0.018 ^a
AEDs after seizure			
Increased	6	20	
Stable	2	7	
Discontinued	0	1 ^b	
SUDEP	0	0	N.A
Adjusted AEDs following pregnancy diagnosis	0 (0.0%)	21 (25.9%)	< 0.001 ^a
Switched	0	5	
Decreased	0	5	
Discontinued	0	11	
AEDs discontinued by patients themselves ^c	3/39 (7.7%)	13/61 (21.3%)	0.07
Stable dose and drugs during pregnancy	39 (76.5%)	48 (59.3%)	0.042 ^a

^aP < 0.05, ^bA woman chose to discontinue AEDs against medical advice, ^cMothers not reaching AEDs were excluded, AED: Antiepileptic drugs, SUDEP: Sudden unexpected death in epilepsy

Table 4: Peripartum outcomes

	Planned	Unplanned	P value
Induced abortion	0 (0%)	4 (4.9%)	0.16
Spontaneous abortion	2 (3.9%)	5 (6.2%)	0.71
Stillbirth	0 (0%)	1 (1.2%)	> 0.99
Live birth	49 (96.1%)	71 (87.7%)	0.13
PIH ^a	2/49 (4.1%)	3/72 (4.2%)	> 0.99
NRFS ^a	7/49 (14.3%)	6/72 (8.3%)	0.3
FGR ^a	3/49 (6.1%)	4/72 (5.6%)	> 0.99
IUFD ^a	0/49 (0%)	1/72 (1.4%)	> 0.99
TOP ^b	9/49 (18.4%)	16/71 (22.5%)	0.58
Uncontrollable seizure	2	5	
Obstetric indications	5 ^c	8 ^d	
Elective	2	3	
Cesarean delivery ^b	16/49 (32.7%)	23/71 (32.4%)	0.98
Uncontrollable seizure	0	5	
Obstetric indications	12 ^e	12 ^f	
Cerebral AVM	3	3	
Moyamoya disease	0	1	
Elective	1	1	
Others	0	1	
Operative delivery ^b	3/49 (6.1%)	1/71 (1.4%)	0.30
Obstetric indications	3 ^g	1 ^h	
Normal vaginal delivery ^b	30/49 (61.2%)	47/71 (66.2%)	0.58

^aCases of abortion were excluded, ^bCases involving stillbirths and abortions were excluded, ^cFour cases with NRFS and 1 case with FGR were included, ^dFour cases with FGR, 3 cases with NRFS, and 1 case with PIH were included, ^eFive cases with NRFS, 4 cases involving breech presentations, 1 case involving a footling presentation, 1 case involving a low-lying placenta, and 1 case with prior cesarean delivery were included, ^fThree cases with NRFS, 2 cases involving breech presentations, 2 cases with prior cesarean delivery, 2 cases with prior myomectomies, 1 case of placenta previa, 1 case of obstructed labor, and 1 cases involving a twin pregnancy were included, ^gTwo cases with NRFS and 1 case of obstructed labor were included, ^hOne case with NRFS was included.

PIH: Pregnancy-induced hypertension, NRFS: Non-reassuring fetal status, FGR: Fetal growth restriction, IUFD: Intra-uterine fetal death, TOP: Termination of pregnancy

Table 5: Neonatal outcomes

	Planned	Unplanned ^a	P value
Congenital malformation ^b	4/49 (8.2%)	6/74 (8.1%)	> 0.99
Birth weight (g) ^c	1467–3718	472–3985	0.66
Apgar score (1 min) ^c	1–10	3–10	0.58
Apgar score (5 min) ^c	9–10	6–10	0.11
Withdrawal syndrome ^c	0/49 (0%)	2/73 (2.1%)	0.52
Neonatal hemorrhage ^c	0/49 (0%)	0/73 (0%)	N.A.
NICU/GCU admission ^c	8/49 (16.3%)	16/73 (21.9%)	0.45

^aFour neonatal cases involving monochorionic, diamniotic twins were included, ^bCases involving abortions were excluded, ^cCases involving stillbirths and abortions were excluded, N.A.: Not analyzed