Pregnancy outcomes and fertility after ligation of uterine artery only and hypogastric artery only in postpartum hemorrhage

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Abstract

Objective: To determine and compare pregnancy outcomes after bilateral uterine artery ligation (BUAL) or bilateral hypogastric artery ligation (BHAL) for postpartum hemorrhage (PPH).

Material and Methods: This retrospective cross-sectional study was conducted from January 2010 to June 2018 at a tertiary referral hospital. Patients who had undergone arterial ligation for PPH were included in the study. Patients who had undergone BUAL and BHAL were compared with a control group in terms of fertility and pregnancy outcomes.

Results: A total of 156 patients were included, of whom 47 underwent BUAl, 59 underwent BHAL and 50 were in the control group. There was no significant difference between the groups in subsequent pregnancies in terms of the incidence of miscarriage, fetal growth restriction, preeclampsia, primary cesarean deliveries, and infertility ($p>0.05$). There was a significant difference between all groups in gestational age at birth and birthweight. Preterm birth was observed in 32.2% of patients in the BHAL group, and this rate was significantly higher than in the BUAL (12.8%) and control (6%) groups ($p=0.001$).

Conclusion: PPH is a life-threatening obstetric problem. The effects of interventions performed to reduce pelvic blood flow in patients may lead to persistent problems, such as preterm birth and low birth weight in the next pregnancy. However, these interventions do not appear to affect the risk of miscarriage. In subsequent pregnancies of patients who received BHAL, special attention should be paid to preterm birth. (J Turk Ger Gynecol Assoc. 2024; 25: 132-7)

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Introduction

Postpartum hemorrhage (PPH) remains a major cause of maternal morbidity and mortality throughout the world, including in industrialized countries. Severe PPH of more than 1000 mL occurs in about 1% of births (1). The cause of around 90% of all cases is uterine atony. In patients who do not respond to drug treatment and intrauterine balloon tamponade, surgical vascular ligations, such as bilateral uterine artery ligation (BUAL), gradual uterine devascularization, and/or bilateral hypogastric artery ligation (BHAL), and uterine

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compression sutures are effective alternatives to hysterectomy (2). Theoretically, all of these procedures, except hysterectomy, offer the advantage of preserving fertility.

The hypogastric artery (internal iliac artery) is a branch of the common iliac artery and is the main blood supply to the pelvic structures. There are a large number of small vessels, collateral circulation, and variations in the pelvic vasculature (3,4). The role of BHAL in controlling severe pelvic bleeding was described by Kelly (5) in 1893 during a Wertheim operation. This procedure has become a life-saving procedure for the control of PPH in subsequent years. In massive pelvic bleeding, bilateral ligation of the hypogastric artery reduces pelvic arterial blood flow by 49% and pulse pressure by 85% (6). After bilateral ligation of the hypogastric artery, blood supply to the pelvis is maintained without necrosis by the collateral circulation, consisting of profundal femoral artery, superior gluteal artery, obturator artery, and ovarian artery. It has been shown that in patients who have undergone postpartum BHAL, the collateral circulation generally functions well and the complication rate is significantly lower than in oncologic patients. The relatively young age of the patients and the low rate of atherosclerotic vascular disease explain this difference (7). However, there are studies showing that uterine and ovarian blood flow decreases in the early postoperative period (8,9). It is unclear how this situation affects subsequent fertility and pregnancy.

BUAL is a relatively safe, simple and fast surgical procedure compared to BHAL. The surgical success rate is over 90%. ACOG endorsed its use in postpartum haemorrhage in 2006 (10). Recanalization of uterine arteries has been demonstrated radiologically after uterine artery embolization for uterine fibroids in the sixth month after surgery (11). However, uterine artery flow patterns have been shown to change significantly in patients who have undergone BUAL (12). Studies investigating the effects of uterine artery occlusion on subsequent fertility and pregnancy outcomes have provided limited data, and most of them relate to uterine artery embolization for the treatment of fibroids (13-15).

Although there are published case series investigating pregnancies after BHAL and BUAL, we found no study comparing fertility and pregnancy outcomes after BHAL and BUAL. The aim of the present study was to determine and compare fertility and pregnancy outcomes after BHAL and BUAL for postpartum haemorrhage.

Material and Methods

This retrospective, cross-sectional study was performed in a tertiary center. Ethical approval was obtained from the University of Health Sciences Turkey, Etlik Zübeyde Hanım Woman's Health Training and Research Hospital Local Ethics Committee (approval number: 04, date: 16.03.2022).

Sociodemographic and clinical data were obtained from the medical records of the participants. The following data were collected: age, parity, previous miscarriage, smoking, assisted reproduction, previous cesarean delivery, indication for vascular ligation, fertility status, and feto-maternal outcomes such as preterm birth, fetal growth restriction (FGR), preeclampsia, low birth weight, and presence of fetal anomaly in the subsequent pregnancy.

Based on the surgical approach, the groups were defined as group 1 (BUAL), group 2 (BHAL), and group 3 (controls). Then, these data were compared among the three groups. All patients received fundal massage, bimanual compression, standard administration of oxytocin (40 IU in 500 mL intravenously) and methyl ergonovine maleate (0.20-0.40 mg, intramuscularly) before the surgical procedure. For severe PPH that did not respond to these measures, BHAL or BUAL was administered. Administration of BHAL or BUAL depended on the surgeon's judgment and experience. The control group consisted of patients with PPH who responded to standard medical therapy. Only patients who underwent cesarean section were included in the study. Patients younger than 18 years and patients with other causes of PPH, such as coagulation disorders or retained placenta, were excluded. The study did not include patients who had been treated with balloon tamponade, B-lynch suture, or other hemostatic sutures or who had undergone hysterectomy. In addition, patients with gestational diabetes, preeclampsia, hypertension, and other chronic conditions were excluded from the study because they are at risk for adverse obstetric events such as intrauterine growth retardation and preterm delivery.

Statistical analysis

All statistical analyzes were performed using the RStudio integrated development environment for statistical computing (Affero General Public License v3; released 2011. RStudio for Linux, version v2021.09.4+403.pro3 Ghost Orchid; September 19, 2022; developed by Posit, PBC.). Variables were examined using visual (histogram, probability plots) and analytic methods (Kolmogrov-Simirnov/Shapiro-Wilk test) to determine whether or not they were normally distributed. Descriptive analyzes were performed using means and standard deviations for normally distributed variables. The One-Way method ANOVA was used to compare these parameters between groups. Levenes test was used to assess homogeneity of variance. Descriptive analyzes using medians and quartiles (Q1-Q3) were performed for numerical data that were not normally distributed. Kruskal-Wallis tests were performed to compare these parameters between groups.

The Mann-Whitney U test was performed to test the significance of pairwise differences, using the Bonferroni

correction to adjust for multiple comparisons. Descriptive analyzes were performed for categorical variables using frequency and percentage. Relationships between categorical variables were analyzed using the chi-square test or Fisher's exact test (when the assumptions of the chi-square test did not apply because of low expected cell counts). An overall 5% type 1 error level was used to infer statistical significance. A p-value of less than 0.05 was considered to show a statistically significant result.

Results

Between January 2010 and June 2018, 162 patients were analyzed who underwent 77 (47.5%) BHAL and 85 (52.5%) BUAL due to PPH. Patients' records for five years postpartum were reviewed and their birth histories were evaluated. Of these initial 162, 26 patients from the BUAL group and 22 patients from the BHAL group used a contraceptive method and did not want another pregnancy. Three patients from the BUAL group and two patients from the BHAL group became menopausal. One patient from the BUAL group and two patients from the BHAL group had infertility from unknown causes. In total, 47 patients who received BHAL and 59 patients who received BUAL became pregnant again after delivery and 106 patients who became pregnant after these procedures and a control group of 50 women who had not undergone any of these procedures in their previous pregnancy were included for analysis. The demographic and clinical characteristics of the patients are shown in Table 1. There were no differences between groups in age, parity, smoking status, and use of assisted reproductive techniques in current pregnancies.

The BUAL group and the BHAL group had significantly more previous miscarriages than the control group (63.8%, 69.5%, and 42%, respectively; p=0.010). In addition, the BUAL group and the BHAL group were significantly more likely to have a previous cesarean delivery than the control group (36.2%, 39%, and 10%, respectively; p=0.001). The most common indication for arterial ligation in both groups was uterine atony (66% in the BHAL group and 45.8% in the BUAL group). In addition, a significantly higher spectrum of placenta accreta was observed in the BHAL group than in the BUAL group (p=0.037).

The subsequent pregnancy outcomes of the patients are shown in Table 2. There was no significant difference between groups in the incidence of miscarriage, FGR, preeclampsia, primary cesarean deliveries, and fetal anomalies in subsequent pregnancies. While the median gestational age at delivery was 39 weeks in the control group, it was 38 in the BUAL group and 37 weeks in the BHAL group. There was a significant difference between all groups in gestational age at delivery and birth weight. Preterm birth was observed in 32.2% of patients in the BHAL group, and this rate was significantly higher than in the BUAL (12.8%) and control (6%) groups (p=0.001). The percentage of low birth weight children was 42.4% in BHAL group and was significantly more likely than in BUAL group (21.3%) and control group (10%) (p=0.001).

Table 1. Sociodemographic and clinical characteristics

	BUAL, (n=47)	**BHAL, (n=59)**	**Control, (n=50)**	**p**
Age (years)	**30 (26-34)**	**30 (26-34)**	**28 (26-31.25)**	**0.363**
Parity (n, %)				
1	17 (36.2%)	18 (30.5%)	14 (28%)	0.556
2	19 (40.4%)	23 (39%)	26 (52%)	
≥3	11 (23.4%)	18 (30.5%)	10 (20%)	
Previous miscarriage (n, %)				
No	17 (36.2%)	18 (30.5%)	29 (58%)	**0.010***
Yes	30 (63.8%)	41 (69.5%)	21 (42%)	
Smoking (n, %)	9 (19.1%)	15 (25.4%)	6 (12%)	0.208
ART (n, %)	0	3 (5.1%)	2 (4%)	0.311
PCD (n, %)	17 (36.2%)	23 (39%)	5 (10%)	**0.002****
Indication for vessel ligation (n, %)				
Uterine atony	31 (66%)	27 (45.8%)	N/A	0.06
PAS	7 (14.9%)	24 (40.7%)	N/A	**0.007**
EUI/UL	5 (10.6%)	4 (6.8 %)	N/A	0.506
PH	4 (8.5%)	4 (6.8%)	N/A	>0.05

P<0.05 means there is significantly statistical difference between groups. Data are given as median (Q1-Q3) or n (%). *: The difference between the BHAL vs. controls is significant, **: The difference between the BUAL vs. controls and BHAL vs. controls is significant, BUAL: Bilateral uterine artery ligation, BHAL: Bilateral hypogastric ligation, ART: Assisted reproductive technology, PCD: Previous cesarean section, PAS: Placenta accreata spectrum, EUI/UL: Extended uterine incision/uterine laceration, PH: Pelvic hematoma

Table 3 shows the fertility results. Although one patient from the BUAL group and two patients from the BHAL group stopped using a contraceptive method within 5 years of their procedures, they did not become pregnant again. There was no significant difference between the groups in terms of infertility ($p>0.05$).

Discussion

PPH is an important cause of morbidity and mortality that seriously threatens maternal health. The main cause is uterine atony, but the number of placental invasion disorders is steadily increasing. Postpartum atony is considered an emergency, and if bleeding persists despite initial measures, surgical intervention is initiated (16).

The hypogastric artery, which plays an important role in blood supply to the pelvis, and its branch, the uterine artery, are both subject to ligation for the treatment of PPH (17). In theory, these treatments reduce uterine blood flow, control bleeding, and prevent hysterectomy. However, the effects of these devascularization treatments on subsequent pregnancies are not clearly known. The literature contains information on arterial ligation, which is used to reduce blood flow, particularly in the treatment of uterine fibroids. Torre et al. (18) found no loss of ovarian function in any of the patients. In the present study, no significant difference in infertility was found between groups undergoing arterial ligation. Pregnancy did not occur in two patients with BHAL and one patient with BUAL, although they tried to become pregnant for at least five years after the procedures. However, these patients did not want to receive infertility treatment during this time.

Karlsen et al. (19), in a meta-analysis of 988 patients from 17 studies, found that the miscarriage rate in pregnancies after uterine artery embolization for fibroid treatment was 34%. In the present study the miscarriage rate in patients who underwent arterial ligation was 14.9% in the BUAL group and 13.6% in the BHAL group. Chen et al. (20) studied the subsequent pregnancies of 423 women who had undergone uterine artery ligation, and 7 of 17 (24%) pregnancies ended in miscarriage. These authors suggested that this procedure should be avoided in patients who wish to become pregnant again in the future (20). In the present study, a total of 106 patients were treated with BHAL or BUAL, and miscarriage occurred in 15 pregnant women (14%). No significant difference was found between the patients who received BHAL and BUAL and the control group in terms of miscarriage rate. According to a systematic review, the risk of miscarriage is 15.3% (95% confidence interval: 12.5-18.7) of all recognized pregnancies (21). Considering the similar result in our study, it appears that BHAL and BUAL do not cause a risk of miscarriage that is different from the general risk in society. Although the number of abortions in previous pregnancies was significantly higher in the BHAL and BUAL groups compared with the control group, the number of abortions in postoperative pregnancies showed no difference. In light of this information, we believe that contrary to the studies in the literature, it is not necessary to avoid the BHAL and BUAL procedures to avoid miscarriage in subsequent pregnancies. This suggests that the possible reduction of blood flow in the uterus may not responsible for miscarriages in early pregnancy, but may come into play in late pregnancy.

Table 2. Subsequent pregnancy outcomes

	BUAL, (n=47)	BHAL, (n=59)	Control, (n=50)	p
Miscarriage (n, %)	7 (14.9%)	8 (13.6%)	4 (8%)	0.537
Gestational age at delivery (weeks)	38 (37-39)	37 (35-37)	39 (38.25- 40)	**<0.001***
Preterm birth (<37 weeks) (n, %)	6 (12.8%)	19 (32.2 %)	3 (6%)	**0.001****
Fetal growth restriction (n, %)	5 (10.6%)	8 (13.6%)	4 (8%)	0.648
Preeclampsia (n, %)	2 (4.3%)	2 (3.4%)	3 (6%)	0.803
Postpartum hemorrhage (n, %)	1 (2.1%)	6 (10.2%)	0	**0.019*****
Birthweight (g)	3100 (2900-3330)	2600 (2220-3100)	3365 (3105-3600)	**<0.001***
Low birthweight infant (<2500 g) (n, %)	10 (21.3%)	25 (42.4%)	5 (10%)	**0.001****
Fetal anomaly (n, %)	1 (2.1%)	2 (3.4%)	0	0.585

Data are given as median (Q1-Q3) or n (%). *: The difference between all groups are significant, **: The difference between the BUAL vs. BHAL and BHAL vs. controls is significant, ***: The difference between the BHAL vs. controls is significant, BUAL: Bilateral uterine artery ligation, BHAL: Bilateral hypogastric ligation

Table 3. Infertility outcome

	BUAL, (n=48)	BHAL, (n=61)	p
Infertility (n, %)	1 (2%)	2 (3%)	>0.05

BUAL: Bilateral uterine artery ligation, BHAL: Bilateral hypogastric ligation

It is known that the blood flow to the uterus gradually increases during pregnancy and the fetus benefits from this flow through the placenta. There is little information in the literature on the outcome of pregnancy after surgery that reduces blood supply to the pelvis in humans. Although Morikawa and Takamizawa (22) reported a fetus with low gestational age in their case report of bilateral UAL, Mengert et al. (23) reported a term and uneventful pregnancy after uterine artery ligation in their series of three cases. In addition, in animal studies in which uterine artery ligation was performed during pregnancy, fetuses have been shown to miscarry, and preterm labor, intrauterine growth restriction, and neural development abnormalities occur. This study highlighted that uterine artery ligation causes placental insufficiency and leads to developmental delay in fetuses (24). We hypothesized that placental insufficiency may also occur in pregnancies after arterial ligation. However, in our study, there was no significant difference between the groups in terms of FGR. Therefore, it may be that the collateral circulation also prevents placental insufficiency in subsequent pregnancies. In addition, there was no difference between groups in terms of rates of preeclampsia in our study. As there was no significant difference between groups in rates of FGR, abortion, and preeclampsia suggests that the BHAL and BUAL procedures do not pose a problem in either overall uterine perfusion or microvascular function. Chang et al. (25) found that uterine artery occlusion for the treatment of fibroids increased the risk of preterm delivery, miscarriage, and FGR due to decreased uterine and placental perfusion as a result of decreased blood flow to the myometrium and endometrium. In the present study, we found that of these risks, only the incidence of preterm birth, which also affects birth weight, was increased but only in the BHAL group. This suggests that ligation of the hypogastric artery may affect gestational week in subsequent pregnancies. This may be due to more proximal obliteration of the vascular tree, which may be anastomosed and suggests that proximal artery occlusion contributes to preterm labor by preventing healthy function of the existing anastomoses. We suggest that the physiology of preterm birth is not fully understood and that possible local inflammatory reactions after ligation may increase the risk of preterm birth.

We hypothesize that the reason why atony indication was more frequent in the BUAL group was because of easier technical applicability. However, there was no difference between the BUAL and BHAL groups. The fact that the placenta accreta spectrum produces more indications for BHAL may support the idea that this is due to surgeon preference. It is known that women with a history of previous atony are at higher risk for PPH in their next pregnancies (26). Consistent with the literature, we found that there was a higher PPH rate in the BHAL group compared with the BUAL group in subsequent pregnancies. We suggest that, in view of these data, surgeons prefer BHAL for the control of severe bleeding and that more PPH may be observed in the patients' next pregnancies because there is a higher predisposition to PPH in pregnancies in which BHAL was used. None of the women in the control group had PPH in a subsequent pregnancy.

For indications requiring arterial ligation, the patient's desire to become pregnant again should be clearly understood and she should be informed about possible complications of subsequent pregnancies. In addition, in this context, the patients' informed consent should be obtained before the procedure. Arterial ligation should be performed taking into account the possibility of preterm labor in subsequent pregnancy.

More comprehensive studies are needed. To this end, investigators should be supported and a surgical procedure should be established to address subsequent pregnancies with regard to the management of PPH. Thus, it can be ensured that legal responsibilities are clearly laid out.

Study limitations

Our study was a retrospective study and it can not clearly reveal the difference in the weeks of birth between the groups and the indication of delivery. When current patient data are categorized by birth indications, there is not enough patient data to reliably understand the effect of homogeneous distribution and the results of subsequent pregnancies. The number of patients was too small to draw conclusions about infertility after these procedures. However, to the best of our knowledge, this study is the most comprehensive study in the literature investigating pregnancy outcomes following arterial ligation for PPH and this is also the strength of our study.

Conclusion

PPH is one of the peripartum causes of maternal mortality. In cases where medical treatment is inadequate, arterial ligation is performed to reduce blood supply to the pelvis through surgery. However, the results of the present study suggest that later pregnancies of patients who have undergone arterial ligation should be carefully monitored for preterm labor.

Ethics Committee Approval: *Ethical approval was obtained from the University of Health Sciences Turkey, Etlik Zübeyde Hanım Woman's Health Training and Research Hospital Local Ethics Committee (approval number: 04, date: 16.03.2022).*

Informed Consent: *Retrospective study.*

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