Clinical Article

# Cervical polyps in early pregnancy are a risk factor for late abortion and spontaneous preterm birth: A retrospective cohort study

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Synopsis: Cervical polyps in early pregnancy are a risk factor for late abortion and spontaneous preterm birth.

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**Abstract**

**Objective:** The aim of this study was to determine the association between cervical polyps in early pregnancy and late abortion and spontaneous preterm birth (SPTB). We also aimed to explore the relationship between cervical polyps and cervical insufficiency in the second trimester.

**Methods:** We conducted a retrospective cohort study of 2,941 singleton pregnant women between January 2010 and December 2015. The frequency of late abortion and SPTB (before 28, 34, or 37 weeks of gestation) was compared between the two groups of 142 (4.8%) patients who had cervical polyps early in pregnancy (P group) and 2,799 who did not (non-P group). Multivariate analysis was performed to identify risk factors for late abortion and SPTB.

**Results:** The incidence of late abortion and SPTB was significantly higher in the P group than in the non-P group. Cervical polyps in early pregnancy were selected as independent risk factors for late abortion and SPTB before 28, 34, or 37 weeks of gestation. The P group had a significantly higher rate of cases requiring therapeutic cervical cerclage than the non-P group.

**Conclusion:** Cervical polyps in early pregnancy are risk factors for late abortion and SPTB. They are also associated with the occurrence of cervical insufficiency.

## Introduction

Cervical polyps are reported to occur in 2-5% of women of reproductive age [1]. Not surprisingly, they are also commonly present in women in early pregnancy and can cause repeated genital bleeding. However, there are no studies on the impact of cervical polyps on pregnancy outcomes and no compelling clinical evidence exists. Miscarriage and preterm birth in the second trimester after excision of cervical polyps early in pregnancy have been reported in some cases [2-3]. According to a cohort study on cases of polyps removed during pregnancy, the rates of late abortion, spontaneous preterm birth (SPTB) before 34 weeks of gestation, and SPTB before 37 weeks of gestation were 6.8%, 15.1%, and 20.5%, respectively, which was higher than the general SPTB rate of 5.7% among pregnant women in Japan [4]. Histopathological examination of cervical polyps resected during pregnancy showed a higher rate of miscarriage and SPTB before 37 weeks of gestation in the decidual polyp group than in the endocervical polyp group [5]. Thus, although cases of resected cervical polyps have been reported, there have been no studies on the effect of cervical polyps on pregnancy outcomes compared to the non-polyp group or on the effect of cervical polyps including non-resected cases.

We have observed many cases of late abortion and extremely preterm birth after the diagnosis of cervical polyp during early pregnancy in the obstetric practice of our high-volume perinatal centers. We also observed cases of pregnant women with cervical polyps who required therapeutic cervical cerclage due to a prolapsed fetal membrane in the second trimester. These experiences led us to speculate that cervical polyps in early pregnancy may be associated with late abortion and SPTB. Therefore, the present study aimed to determine the association between cervical polyps found in early pregnancy and subsequent late abortion and SPTB (before 28, 34, or 37 weeks of gestation). We also aimed to explore the relationship between cervical polyps and cervical insufficiency requiring therapeutic cervical cerclage in the second trimester.

## Patients and Methods

A retrospective review was conducted on 4,144 women who delivered at Sapporo City General Hospital between January 2010 and December 2015. Of these, 145 women who were referred to the hospital after the second trimester of pregnancy were excluded from this study. A further 658 women who were transported to our hospital for delivery in the late pregnancy were excluded. The

pregnancies of the remaining 3,341 women were managed from the first trimester to delivery. Women with multiple pregnancy (n=301), intrauterine fetal death (n=43), and severe fetal malformation (n=56) were excluded. The remaining 2941 women were enrolled in this study. We classified them into two groups: 142 women with cervical polyps in the first trimester (P group) and 2,799 women without cervical polyps (non-P group) (Fig. 1).

The cervix is always inspected during the first trimester of pregnancy, and a Pap tests and a chlamydia antigen tests are performed simultaneously. Therefore, the existence of cervical polyps is confirmed in all women. Pregnancy checkups in Japan are performed 4-weekly until 22 weeks of pregnancy, 2-weekly until 35 weeks, and weekly after 36 weeks. In this study, cervical polyps were defined as soft, elastic masses growing from within the cervical canal. They varied in size from the size of a rice grain to the size of a thumbnail. The diagnosis of cervical polyps was made by macroscopic examination. The need for polypectomy was determined by the respective physicians.

Obstetric background was investigated for maternal age, pregnancy history, delivery history, previous late abortion (excluding termination of pregnancy), SPTB before 34 weeks, history of conization, and bacterial vaginosis (BV).

Miscarriages at gestations more than 12 weeks but less than 22 weeks were classified as late abortions. In this study, miscarriages due to fetal death was excluded from late abortion. Termination of pregnancy less than 37 week's gestational age due to maternal complications, hypertensive disorders of pregnancy, fetal growth restriction, non-reassuring fetal status, and placenta previa were excluded from SPTB. Hypertensive disorders of pregnancy included preeclampsia and eclampsia, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Fetal growth restriction was defined as weight less than -1.5 standard deviations using the "fetal weight reference values for Japanese" [6]. Non-reassuring fetal status was defined as an "abnormal finding" on fetal cardiotocograph during pregnancy or delivery where there was no certainty that the fetus was well. Placenta previa is a condition in which the placenta covers partially or completely the internal cervical os. BV was diagnosed when the Nugent score was seven or more on vaginal secretion gram staining at the beginning of pregnancy. BV was treated with seven days of self-insertion of metronidazole vaginal tablets.

We compared the frequency of late abortion and SPTB (before 28, 34, and 37 weeks of gestation) as endpoints between the P group and non-P groups. To

investigate whether cervical polyps in early pregnancy are an independent risk factor for late abortion and SPTB (before 28, 34, and 37 weeks of gestation), we performed a univariate and a multiple logistic regression analysis with known risk factors, that is, age, multiparity, history of late abortion [7], history of preterm birth before 34 weeks of gestation [7,8], history of conization [9.10], and the presence of BV [11] as confounders.

In addition, we compared the frequency of cases of cervical insufficiency requiring therapeutic cervical cerclage in the second trimester between the two groups. Cervical insufficiency is defined as the inability of the uterine cervix to retain a pregnancy in the absence of the signs and symptoms of clinical contractions, labor, or both in the second trimester [12]. Although controversial, the diagnosis of cervical insufficiency in this study was made when the uterine os was open or the cervix measured less than 20 mm in length, without overt infection or inflammation, and in the absence of frequent uterine contractions before 28 weeks of gestation. Therapeutic cervical cerclage was actively performed in cases where uterine contractions could be controlled. To determine the risk factors for therapeutic cervical cerclage, we performed a multiple logistic regression analysis with the aforementioned risk factors as confounders.

Statistical analyses of the obstetric background and pregnancy outcomes were performed using Fishers exact test or t -test. A P-value of <0.05 was considered statistically significant. All statistical analyses were conducted using the statistical analysis software (SPSS, version.22; IBM, Tokyo, Japan).

This study was conducted with the approval of the ethical committee of Sapporo City General Hospital (No. R02-059-735). The requirement for informed consent was waived owing to the retrospective design of the study.

## Results

Table 1 shows the obstetric background of the subjects. The frequency of late abortion and SPTB before 34 weeks of gestation was significantly higher in the P than in the non-P group. On the other hand, there was no difference in the frequency of parous women, previous conization, or presence of BV.

Among 142 women with polyps, resection was performed in 36 cases (25.4%). Histopathological examination showed that, of the removed polyps, 30 (83.3%) were decidual polyps and 6 (16.7%) were endocervical polyps. The finding of inflammatory cell infiltration was observed in many of them. Of the 106 women who were conservatively managed for polyps, 22 (20.8%) were no longer visible

on vaginal examination by 12 weeks, 57 (53.8%) by 22 weeks, and the remaining 27 at delivery.

Pregnancy outcomes are shown in Table 2; gestational age and birth weight in the P and non-P groups were 37.3 ± 4.4 weeks, 2771 ± 693 grams, and 38.5 ± 2.0 weeks, 2910 ± 474 g (mean ± SD), respectively, with significantly earlier gestational age at delivery and lower birth weight in the P group. The P group had a significantly higher incidence of late abortion, and SPTB before 28, 34, and 37 weeks of gestation, all of which were significantly more common in the P than in the non-P group. Four out of five cases of late abortion in the non-P group resulted in miscarriage due to membrane rupture or fetal membrane prolapse after 20 weeks of gestation. On the contrary, in the P group, membrane rupture or genital bleeding occurred before 16 weeks without cervical enlargement or shortening of the cervix, leading to earlier miscarriage in all cases. All these late abortions were associated with pathological chorioamnionitis.

Table 3 shows the risk factors identified by a univariate analysis and a multiple logistic regression analysis for late abortion (a), SPTB before 28 weeks of gestation (b), SPTB before 34 weeks of gestation (c), or SPTB before 37 weeks of gestation (d). The independent risk factors identified by a multiple logistic

regression analysis for late abortion were history of late abortion (odds ratio [OR]: 23.8; 95% confidence interval [CI]: 4.1-137.5; p<0.001) and cervical polyp (OR: 13.0; 95%CI: 3.3-51.4; p<0.001) in the study of late abortion. History of late abortion (OR: 10.2; 95%CI: 1.0-100.1; p=0.047), history of SPTB before 34 weeks (OR: 5.2; 95%CI: 1.0-27.3; p=0.049), history of conization (OR: 26.8; 95%CI: 7.5-96.1; p<0.001), and cervical polyp (OR: 4.6; 95%CI: 1.1-18.6; p=0.034) were independent risk factors for SPTB before 28 weeks of gestation. History of late abortion (OR: 7.9; 95%CI: 1.5-41.1; p=0.014), history of SPTB before 34 weeks (OR: 6.3; 95%CI: 2.1-18.7; p=0.001), history of conization (OR: 17.8; 95%CI: 7.0-45.2; p<0.001), and cervical polyp (OR: 4.7; 95%CI: 1.9-12.0; p=0.001) were independent risk factors for SPTB before 34 weeks of gestation. History of late abortion (OR: 3.7; 95%CI: 1.2-11.5; p=0.024), history of SPTB before 34 weeks (OR: 2.5; 95%CI: 1.2-5.5; p=0.015), history of conization (OR: 7.0; 95%CI: 3.7-13.2; p<0.001), and cervical polyp (OR: 3.1; 95%CI: 1.8-5.4; p<0.001) were independent risk factors for SPTB before 37 weeks of gestation.

The incidence of cervical insufficiency requiring therapeutic cervical cerclage in the second trimester was compared between the two groups. The frequency was 5.6% in the P group compared to 0.7% in the non-P group, which was

significant (p<0.001). The independent risk factors identified by a multiple logistic regression analysis for cervical insufficiency requiring therapeutic cerclage were history of late abortion (OR: 18.6; 95%CI: 5.2-66.7; p<0.001), history of SPTB before 34 weeks of gestation (OR: 6.3; 95%CI: 2.1-19.4; p=0.001), and cervical polyp (OR: 5.7; 95%CI: 2.3-14.2; p<0.001).

## Discussion

We demonstrated for the first time in a retrospective cohort study that cervical polyps in early pregnancy are a risk factor for late abortion and SPTB.

Two complications were found in pregnant women with cervical polyps in early pregnancy that led to late abortion or SPTB: one was the onset of labor, which led to abortion or preterm birth due to infection. The other was cervical insufficiency. We hypothesize the following as mechanisms for the increased risk of preterm birth in cases of cervical polyps. Firstly, cervical polyps become the site of infection, causing ascending infection and chorioamnionitis [13], leading to the onset of labor and membrane rupture [14]. Secondly, degeneration and necrosis of cervical polyps cause inflammatory cytokines to cause cervical ripening [15], resulting in cervical insufficiency. Inflammatory cells associated with

cervical polyps produce proteases [16] which cause fragility of the fetal membranes, leading to membrane rupture. The association between cervical polyps and chorioamnionitis or cervical polyps and preterm birth has already been reported [4,5,17]. Kanayama et al. measured cervical mucus granulocyte elastase activity and cervical mucus white blood cell count in mid-pregnancy and found that they were significantly higher in the cervical polyp group, and were lower after polypectomy. Furthermore, histopathological examination of the placenta indicated an association between cervical polyps and histological chorioamnionitis [17]. Immunohistochemistry has shown the localization of elastase and granulocyte migration from the stroma to the cervical lumen [14]. These have revealed inflammation in the cervical canal due to cervical polyps. However, the details of the chemical mediators associated with cervical polyps in pregnancy have not been elucidated. Rather, we hypothesize that the cervix itself, where cervical polyps arise, may have some potential problems. The local environment of the cervix itself may be responsible for cervical maturation and failure of infection defense. From the analysis of the cases of late abortion, local inflammation associated with polyps was already induced early in pregnancy, suggesting that this may have led to early miscarriage from deciduitis or

chorioamnionitis.

In the present study, cervical polyps, history of late abortion, and SPTB before 34 weeks of gestation were risk factors for cervical insufficiency requiring therapeutic cervical cerclage. The American College of Obstetricians and Gynecologists guidelines recommend transvaginal ultrasound cervical length assessment at 16-24 weeks for pregnant women with a history of preterm birth. In addition, cervical cerclage can be recommended for singleton pregnancies with a history of preterm birth less than 34 weeks and cervical length shortening of less than 25 mm before 24 weeks [12]. In the current study, of the eight women who underwent therapeutic cervical cerclage in the P group, shortening of the cervix appeared at 17 and 18 weeks of gestation in two of the eight patients, respectively. Three patients had prolapse of the fetal membrane at around 20 weeks of gestation. In these cases, prompt therapeutic cervical cerclage resulted in continued pregnancy and a healthy baby. Therefore, we suggest that, in pregnant women with cervical polyps in early pregnancy, regardless of previous history of SPTB, cervical findings should be rigorously evaluated, and therapeutic cervical cerclage should be considered if cervical shortening is apparent and progressive.

It should be noted that in the majority of conservatively managed cases, polyps spontaneously regressed by the first half of the pregnancy and were no longer visible from the external uterine os, but it should also be noted that SPTB and cervical enlargement occurred later in the pregnancy. In other words, we would like to emphasize that cervical polyps that are no longer visible during pregnancy do not reduce the risk of SPTB and cervical insufficiency.

The limitation of this study is that we did not perform a histopathological examination for cervical polyps in non-resected cases. Since cervical polyps are infrequent but can have malignant findings [18], it is reasonable to resect them and make a histological diagnosis. Conversely, although it is difficult to completely exclude malignancy [19], the frequency of malignancy in cervical polyps in women of reproductive age is so low [20-21] that we believe that conservative management is acceptable if the cervical polyp surface is also sampled by the Pap test and is not abnormal. The relationship between polyp histological type and the occurrence of preterm birth should also be investigated in the future.

In conclusion, cervical polyps in early pregnancy are an independent risk factor for late abortion and SPTB. The risk was high at all gestations of preterm birth and comparable to that of a history of preterm birth. Cervical polyps are also

a risk factor for cervical insufficiency, as many cases of cervical insufficiency in the second trimester require therapeutic cervical cerclage. Therefore, strict cervical length surveillance with transvaginal ultrasound is necessary in pregnant women with cervical polyps in early pregnancy. It should also be recognized that these risks are still high, even if polyps are no longer visible during pregnancy.

## Author contributions

Study concept and design: EH; acquisition of data: EH, KK, KN; Analysis and interpretation of data: EH, YE; drafting of the manuscript: EY, YE; Critical revision of the manuscript for important intellectual content: EH, YE, KO. All authors have read and approved the manuscript.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

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## Figure legend

## Figure 1

Flow chart of patient selection

Table 1 Obstetric background according to the presence or absence of cervical polyp

| Characteristic | Polyp | No polyp | p-value |
|---|---|---|---|
| | (n=142) | (n=2799) | |
| Maternal age (years) | 34.7 ± 4.2 | 33.0 ± 5.1 | <0.001 |
| Multipara | 76 (53.5) | 1360 (48.6) | 0.264 |
| History of late abortion | 4 (2.8) | 20 (0.7) | 0.026 |
| History of spontaneous preterm birth before 34 week's gestational age | 12 (8.5) | 55 (2.0) | <0.001 |
| History of conization | 5 (3.5) | 54 (1.9) | 0.206 |
| Bacterial vaginosis | 20 (14.1) | 311 (11.1) | 0.276 |

Mean ± SD, number (%)

SD: standard deviation

Table 2 Pregnancy outcomes of women according to the presence or absence of cervical polyp

| Characteristics | Polyp | No polyp | p-value |
|---|---|---|---|
| | (n=142) | (n=2799) | |
| Gestational age at delivery (weeks) | 37.3 ± 4.4 | 38.5 ± 2.0 | 0.001 |
| Birth weight (g) | 2771 ± 693 | 2910 ± 474 | <0.001 |
| Late abortion | 4 (2.8) | 5 (0.2) | 0.001 |
| Spontaneous preterm birth before 28 week's gestational age | 3 (2.1) | 9 (0.3) | 0.018 |
| Spontaneous preterm birth before 34 week's gestational age | 7 (4.9) | 22 (0.8) | <0.001 |
| Spontaneous preterm birth before 37 week's gestational age | 19 (13.4) | 115 (4.1) | <0.001 |

Mean ± SD, number (%)

SD: standard deviation

Table 3 Risk factors identified by a univariate analysis and a multiple logistic regression analysis of for late abortion or spontaneous preterm birth

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| factors | Odds ratio (95% CI) | p-value | Odds ratio (95% CI) | p-value |
| (a) Late abortion | | | | |
| Age | 1.1 (0.9-1.2) | 0.475 | | |
| Multiparity | 0.3 (0.1-1.3) | 0.104 | | |
| History of late abortion | 37.8 (7.4-192.2) | <0.001 | 23.8 (4.1-137.5) | <0.001 |
| History of spontaneous preterm birth before 34 week's gestational age | 5.4 (0.7-44.0) | 0.113 | | |
| History of conization | 6.2 (0.8-50.3) | 0.088 | | |
| Bacterial vaginosis | 2.3 (0.5-10.9) | 0.310 | | |
| Cervical polyp | 16.2 (4.3-61.0) | <0.001 | 13.0 (3.3-51.4) | <0.001 |
| (b) Spontaneous preterm birth before 28 week's gestational age | | | | |
| Age | 1.0 (0.9-1.1) | 0.627 | | |
| Multiparity | 0.7 (0.2-2.1) | 0.512 | | |
| History of late abortion | 11.5 (1.4-92.7) | 0.022 | 10.2 (1.0-100.1) | 0.047 |
| History of spontaneous preterm birth before 34 week's gestational age | 8.8 (1.9-41.0) | 0.006 | 5.2 (1.0-27.3) | 0.049 |
| History of conization | 26.1 (7.6-83.4) | <0.001 | 26.8 (7.5-96.1) | <0.001 |
| Bacterial vaginosis | 0.7 (0.1-5.6) | 0.749 | | |
| Cervical polyp | 6.7 (1.8-25.0) | 0.005 | 4.6 (1.1-18.6) | 0.034 |
| (c) Spontaneous preterm birth before 34 week's gestational age | | | | |
| Age | 1.0 (0.9-1.1) | 0.598 | | |
| Multiparity | 0.7 (0.3-1.4) | 0.292 | | |
| History of late abortion | 9.7 (2.2-43.4) | 0.003 | 7.9 (1.5-41.1) | 0.014 |
| History of spontaneous preterm birth before 34 week's gestational age | 9.6 (3.5-25.9) | <0.001 | 6.3 (2.1-18.7) | 0.001 |
| History of conization | 17.5 (7.2-42.8) | <0.001 | 17.8 (7.0-45.2) | <0.001 |
| Bacterial vaginosis | 1.3 (0.4-3.7) | 0.665 | | |
| Cervical polyp | 6.5 (2.7-15.6) | <0.001 | 4.7 (1.9-12.0) | 0.001 |
| (d) Spontaneous preterm birth before 37 week's gestational age | | | | |
| Age | 1.0 (0.9-1.0) | 0.680 | | |

| | | | | |
|---|---|---|---|---|
| Multiparity | 0.7 (0.5-1.0) | 0.063 | | |
| History of late abortion | 4.3 (1.4-12.7) | 0.009 | 3.7 (1.2-11.5) | 0.024 |
| History of spontaneous preterm birth before 34 week's gestational age | 3.4 (1.7-7.0) | 0.001 | 2.5 (1.2-5.5) | 0.015 |
| History of conization | 7.2 (3.8-13.4) | <0.001 | 7.0 (3.7-13.2) | <0.001 |
| Bacterial vaginosis | 1.2 (0.7-1.9) | 0.592 | | |
| Cervical polyp | 3.6 (2.1-6.0) | <0.001 | 3.1 (1.8-5.4) | <0.001 |

CI: confidence interval

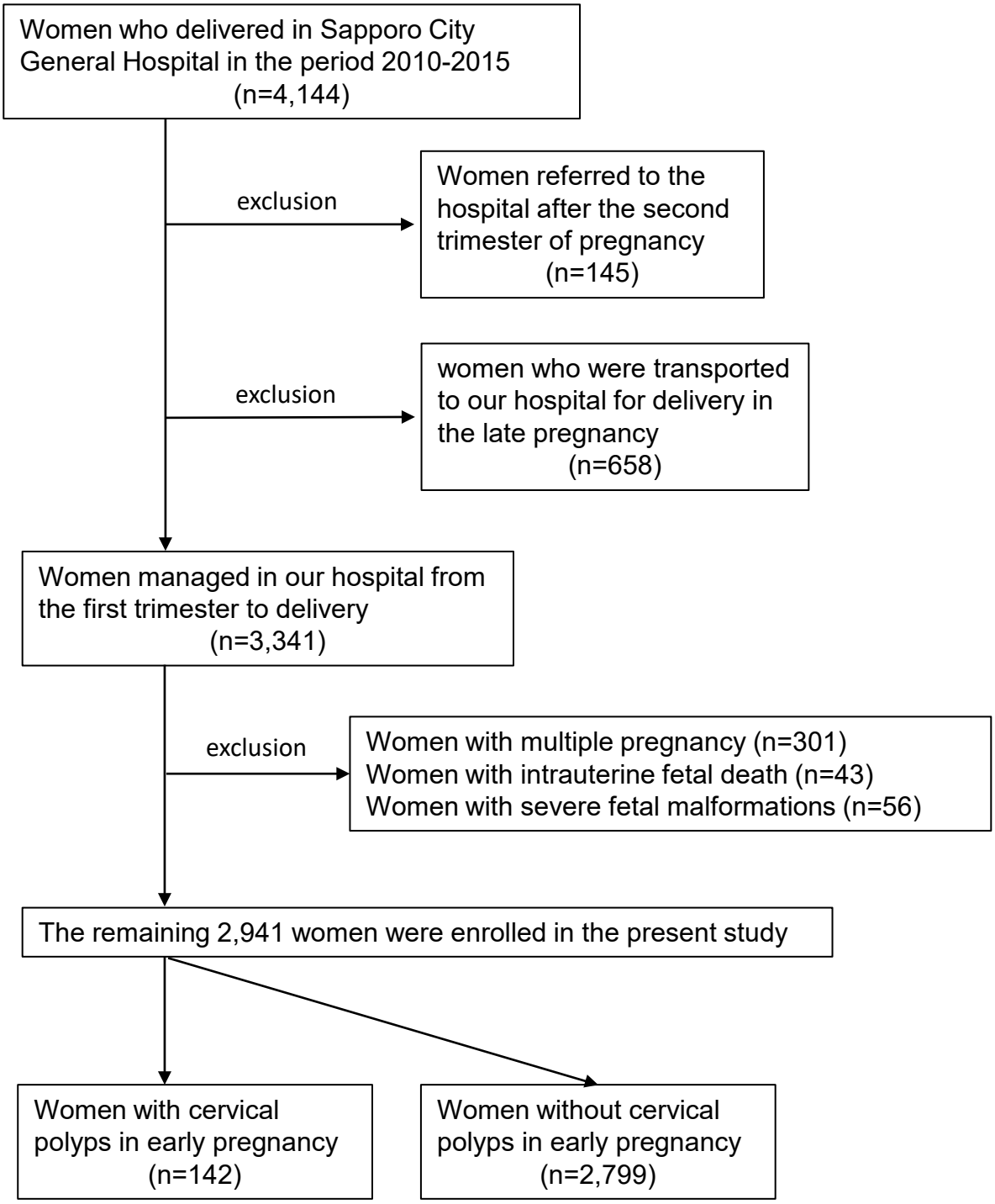
Women who delivered in Sapporo City General Hospital in the period 2010-2015 (n=4,144)
exclusion
Women referred to the hospital after the second trimester of pregnancy (n=145)
exclusion
women who were transported to our hospital for delivery in the late pregnancy (n=658)
Women managed in our hospital from the first trimester to delivery (n=3,341)
exclusion
Women with multiple pregnancy (n=301)
Women with intrauterine fetal death (n=43)
Women with severe fetal malformations (n=56)
The remaining 2,941 women were enrolled in the present study
Women with cervical polyps in early pregnancy (n=142)
Women without cervical polyps in early pregnancy (n=2,799)

Figure 1