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# Herbal Medicine Use and Self-Reported Adverse Reactions During Pregnancy: A Nationwide Survey among Female Korean Medicine Doctors

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## Abstract

**Background**

Herbal medicine (HM) has been traditionally used to manage various pregnancy-related conditions, however, systematic safety data remain limited. This study aimed to investigate treatment patterns and self-reported adverse events (AEs) among female Korean Medicine doctors (KMDs) with personal experience of HM use during pregnancy.

**Methods**

A nationwide, web-based survey was conducted from November 2024 to August 2025 targeting female KMDs who had used HM during pregnancy within the past year. The questionnaire collected information on prescription patterns, AEs, maternal outcomes, and potential confounders. Descriptive statistics were applied, and group comparisons were performed using independent t-tests and Fisher's exact tests.

**Results**

Of 589 responses, 467 valid responses were analyzed. Among respondents, 375 (80.3%) had live births, 71 (15.2%) were currently pregnant, and 21 (4.5%) had experienced abortion. The most frequently used prescriptions were Antae-eum (35.1%), Bulsu-san (30.4%), and Dalsaeng-san (29.8%). AEs were reported by 3 participants (0.6%), accounting for 4 events in total. All events were non-serious; three involved gastrointestinal symptoms and one involved respiratory symptoms. The gastrointestinal events fully recovered, whereas the respiratory event was recovering at the time of survey. One case demonstrated a positive rechallenge with Bulsu-san.

**Conclusion**

This study documented a low self-reported AE rate (0.6%) with herbal medicine use during pregnancy among a professional cohort. Given the cross-sectional, self-reported design, however, underreporting and selection bias cannot be excluded, and these findings should be interpreted as descriptive baseline data rather than definitive safety evidence. Prospective studies incorporating formal causality assessment are warranted to establish more robust safety data.

**Clinical trial number:** not applicable


## 1. Introduction

During pregnancy, medication use requires careful consideration to ensure the health and safety of both the mother and the fetus.[1] Following the 1977 FDA guidelines that excluded women of childbearing potential from early-phase trials, substantial evidence gaps persist regarding drug safety in pregnancy and lactation. Teratogenic risks are mainly identified through case reports or small series. Voluntary reporting systems suffer from bias and incomplete follow-up, while cohort and case–control studies face major methodological, financial, and data limitations.[1–4]

Medication use during pregnancy is common and has increased over recent decades. Large population-based and multinational studies report that approximately 80% of pregnant women use at least one prescribed or over-the-counter medication, and polypharmacy affects 4.9–62.4% of pregnant women.[5, 6] These trends have been documented across diverse settings, including registry-based analyses in Scandinavia[7, 8] and self-medication studies in Brazil and Europe, [9, 10] yet systematic safety data for medications used during pregnancy remain limited.

Globally, herbal medicine (HM) use during pregnancy has been increasingly recognized as a public health concern. A systematic review examining complementary and alternative medicine (CAM) use during pregnancy reported a prevalence ranging from 5.8% to 74.2% across different populations, with HM representing one of the most commonly used modalities. [11] Among 411 systematically sampled pregnant women, 19.7% reported using HMs during their current pregnancy. [12] Unlike conventional medicines, many herbal products lack robust evidence regarding efficacy and safety, raising concerns about potential teratogenicity in this vulnerable population.

In Korea, HM has been traditionally used to manage various pregnancy-related conditions, including hyperemesis gravidarum, recurrent pregnancy loss, threatened abortion, and prevention of miscarriage.[13] Patient satisfaction with HM use was relatively high (mean score 3.44 out of 5), with 72.2% of respondents indicating willingness to use HM again in future pregnancies and 66.7% willing to recommend it to other pregnant women.[14] Despite relatively high satisfaction rates among those who have used HM during pregnancy, public perception remains cautious. A survey on public awareness of KM treatment during pregnancy found that 45.83% of respondents expressed concerns that HM use during pregnancy could potentially cause preterm birth, miscarriage, or congenital anomalies. This negative perception may be attributable, at least in part, to the lack of systematic safety data on HM use during pregnancy. [15]

A previous retrospective study examining HM use during pregnancy in Korea reported that adverse events (AEs) were mostly mild or assessed as having unclear or low causality, with all severe AEs classified as unlikely to be causally related to HM. The incidence of AEs including those with certain or unassessable causality was 1.5%, whereas the incidence based solely on events with confirmed causality was 0.3%.[13] However, these studies primarily focused on teratogenicity and patient satisfaction, while systematic AE monitoring for specific herbal prescriptions was lacking. Consequently, substantial gaps remain in safety evidence and guideline development for traditional Korean Medicine (KM) during pregnancy.

To address these limitations, the present study targeted female Korean Medicine doctors (KMDs) who had personal experience with HM use during their own pregnancies. Female KMDs are uniquely positioned for this investigation: they possess professional knowledge to accurately identify specific herbal

prescriptions, can recognize and describe AEs using appropriate medical terminology, and their dual role as both healthcare providers and patients enables more precise recall of treatment details. While this professional cohort does not represent the general pregnant population, it provides a well-defined group capable of generating high-quality descriptive data on prescription patterns and AE experiences, which may serve as a foundation for future pharmacovigilance studies targeting broader populations. Therefore, this study aimed to describe herbal medicine use patterns and self-reported AE experiences among female KMDs who used HM during pregnancy, in order to generate descriptive baseline data that may inform the design of future prospective pharmacovigilance studies on HM safety during pregnancy.

## 2. Methods

## 2.1. Study design

This was a nationwide, web-based survey designed to investigate AEs associated with herbal decoction use during pregnancy among female KMDs. Female KMDs were selected as the study population because they can accurately report both detailed prescription information and AE experiences from their own HM use during pregnancy, making them uniquely suited for investigating the safety profile of HM use during pregnancy.

## 2.2. Participants and recruitment

The study population consisted of female KMDs who had experience taking HM during pregnancy within the past year and were able to report information on prescription details, AEs, and obstetric outcomes. The survey was developed using Moaform (https://moaform.com), a web-based online survey platform. The survey link was distributed via email and text messages to all licensed KMDs registered with the Association of Korean Medicine (https://www.akom.org/english/index), which maintains up-to-date contact information for all licensed KMDs in Korea and serves as the official provider of mandatory continuing medical education.

The target sample size was calculated as 500 participants based on the following parameters: an estimated population of 7,000 female KMDs in Korea, a 95% confidence level, a proportion estimate of 0.5, and a margin of error of 4.38%, using the finite population correction formula.

## 2.3. Development of survey questionnaire

The questionnaire was a self-administered, web-based survey designed to collect information on HM use and associated AEs during pregnancy. The survey consisted of 35 questions across four sections, with conditional sub-questions based on participant responses, and required approximately 10 minutes to complete.

Section A collected treatment-related information, including HM prescriptions used during pregnancy, number of packs consumed, indications for use, timing of exposure by trimester, and concomitant treatments such as other KM therapies, conventional medications, and dietary supplements.

Section B assessed AEs, defined as any harmful and unintended reactions occurring during or after HM use. Participants reporting AEs provided details on the suspected prescription, herbal composition and dosage, timing of onset, and affected organ systems, categorized into eight systems. Additional information included prior history of similar symptoms, clinical course and outcomes, seriousness criteria, actions taken regarding HM use, re-challenge results, and treatments for AE management.

Section C collected obstetric information, including pregnancy status, delivery outcomes, high-risk pregnancy factors, and exposure to potential risk factors during pregnancy.

Section D gathered demographic and professional characteristics of respondents.

## 2.4. Data collection

Data were collected using Moaform (https://moaform.com), a web-based online survey platform. The survey was conducted from November 2024 to August 2025. All responses were downloaded from the platform, and personal identifying information was removed and anonymized before analysis by the research team.

## 2.5. Ethical considerations

This study was approved by the Institutional Review Board of the Korea Institute of Oriental Medicine (IRB No. I-2408/008-005-02). On the first page of the online survey, participants were provided with a detailed explanation of the study purpose, procedures, potential risks and benefits, and data usage. Informed consent regarding the collection and use of personal and sensitive information was obtained electronically from all participants before proceeding with the survey, in accordance with the Personal Information Protection Act of Korea. Participants who did not provide consent were unable to continue with the survey. All collected data were coded and encrypted, with access restricted to the research team.

## 2.6. Statistical analysis

Descriptive statistics were used to summarize all survey responses. Continuous variables were presented as mean ± standard deviation and compared using independent-samples t-test. Categorical variables were presented as number (percentage) and compared using Fisher's exact test. Exploratory comparisons were performed between spontaneous abortion and live birth groups, and between congenital abnormality and healthy neonate groups. Statistical significance was set at $p < 0.05$. Data were analyzed using R software (R Foundation for Statistical Computing, Vienna, Austria).

## 3. Results

## 3.1. Demographic Characteristics of Respondents

Of the 589 responses received, 122 were excluded due to incomplete responses or data inconsistencies, resulting in 467 valid responses for analysis. The mean age was 35.8 ± 4.3 years, with the majority (77.3%) aged between 30 and 39 years. Regarding clinical experience, more than half of the respondents (51.8%) had 5–9 years of experience, followed by 10–14 years (28.1%). The majority held a Bachelor's degree (62.5%). Regarding specialist certification, 31.5% were certified specialists. The most common specialties were Internal Medicine (34.0%) and Acupuncture & Moxibustion Medicine (26.5%), followed by Obstetrics and Gynecology (9.5%). (Table 1)

Table 1
Demographic characteristics of respondents (n = 467)

| Classification | N (%) or Mean ± SD |
|---|---|
| **Age (years)** | 35.8 ± 4.3 |
| < 30 | 16 (3.4) |
| 30–34 | 185 (39.6) |
| 35–39 | 176 (37.7) |
| ≥ 40 | 88 (18.8) |
| No response | 2 (0.4) |
| **Clinical experience (years)** | |
| < 5 | 54 (11.6) |
| 5–9 | 242 (51.8) |
| 10–14 | 131 (28.1) |
| 15–19 | 35 (7.5) |
| ≥ 20 | 5 (1.1) |
| **Educational degree** | |
| Bachelor's | 292 (62.5) |
| Master's | 89 (19.1) |
| Doctoral | 86 (18.4) |
| **Specialist status** | |
| General practitioner | 320 (68.5) |
| Specialist | 147 (31.5) |
| **Specialty of Korean Medicine** | |
| Internal Medicine | 50 (34.0) |
| Acupuncture & Moxibustion Medicine | 39 (26.5) |
| Obstetrics and Gynecology | 14 (9.5) |
| Ophthalmology, Otorhinolaryngology & Dermatology | 13 (8.8) |
| Rehabilitation Medicine | 12 (8.2) |
| Pediatrics | 7 (4.8) |
| Sasang Constitutional Medicine | 6 (4.1) |
| Neuropsychiatry | 6 (4.1) |

SD: standard deviation

## 3.2. Maternal Characteristics and Pregnancy Outcomes

Among the 467 respondents, 375 (80.3%) had completed pregnancy resulting in live birth, 71 (15.2%) were currently pregnant at the time of survey, and 21 (4.5%) had experienced abortion, including 17 spontaneous abortions (81.0%) and 4 induced abortions (19.0%).

Among women with live births (n = 375), 71.5% delivered vaginally and 28.5% by cesarean section. Regarding gestational age, the majority (93.9%) delivered at term, with preterm delivery occurring in 4.5%. Birth weight was normal (2.5–3.9 kg) in 95.2% of neonates. Congenital or developmental abnormalities were reported in only 3 cases (0.8%).

High-risk factors were assessed using multiple response questions. Advanced maternal age (≥ 35 years) was the most commonly reported (36.0%), followed by gestational diabetes mellitus (4.7%) and in vitro fertilization (4.7%). More than half of the respondents (51.2%) reported no high-risk factors. Coffee consumption during pregnancy was reported by 49.9% of respondents, while alcohol consumption (3.0%) and smoking (0.2%) were rare. Radiation exposure through X-ray or CT was reported by 12.0% of respondents. (Table 2)

Table 2
Maternal characteristics of respondents (n = 467)

| **Classification** | **N (%)** |
|---|---|
| ***Pregnancy status*** | |
| Live birth | 375 (80.3) |
| Mode of delivery | |
| Vaginal delivery | 268 (71.5) |
| Cesarean section | 107 (28.5) |
| Gestational age at delivery | |
| Preterm (< 37 weeks) | 17 (4.5) |
| Term (37–41 weeks) | 352 (93.9) |
| Post-term (≥ 42 weeks) | 6 (1.6) |
| Birth Weight | |
| Low BW (< 2.5kg) | 15 (4.0) |
| Normal BW (2.5-4.0kg) | 357 (95.2) |
| High BW (≥ 4.0 kg) | 3 (0.8) |
| Neonatal development status | |
| Healthy | 372 (99.2) |
| Congenital/developmental abnormality | 3 (0.8) |
| Ongoing pregnancy | 71 (15.2) |
| Abortion | 21 (4.5) |
| Spontaneous abortion | 17 (81.0) |
| Induced abortion | 4 (19.0) |
| **High-risk factors*** | |
| Advanced maternal age (≥ 35 years) | 168 (36.0) |
| In vitro fertilization | 22 (4.7) |
| Gestational hypertension | 11 (2.4) |
| Gestational diabetes mellitus | 22 (4.7) |
| None | 239 (51.2%) |
| **Lifestyle during pregnancy*** | |
| Coffee consumption | 233 (49.9) |
| Alcohol consumption | 14 (3.0) |
| Smoking | 1 (0.2) |
| None | 208 (44.5) |
| **Radiation exposure (X-ray/CT)** | |
| Yes | 56 (12.0) |
| No | 411 (88.0) |
| BW: Birth Weight | |
| *Multiple response | |

## 3.3. Herbal Prescription Patterns during Pregnancy

Among the 467 respondents, the most frequently used herbal prescription was Antae-eum (n = 164, 35.1%), followed by Bulsu-san (n = 142, 30.4%), Dalsaeng-san (n = 139, 29.8%), Dannokyong-tang (n = 75, 16.1%), Nokyongbulsu-san (n = 71, 15.2%), Gamipaljin-tang (n = 57, 12.2%), Gyullyeongbosaeng-tang (n = 47, 10.1%), and Bosaeng-tang (n = 37, 7.9%) (Supplementary Table 1).

Antae-eum (n = 164) was primarily used for threatened abortion (48.2%), vitality restoration (37.2%), and facilitation of delivery (32.9%), with a mean dosage of 50.0 ± 42.0 packs. It was most frequently used during the second trimester (43.3%), followed by the first (39.0%) and third trimesters (17.7%). Concomitant Korean Medicine treatments were reported by 27.4% of users, with acupuncture (25.0%) being the most common. Concomitant conventional medicine and supplements were used by 11.0% and 29.9%, respectively.

Bulsu-san (n = 142) was predominantly used for facilitation of delivery (95.1%), with a mean dosage of 18.5 ± 15.8 packs. Nearly all users (97.9%) took this prescription during the third trimester. Concomitant Korean Medicine treatments were reported by 19.0% of users, with acupuncture (16.2%) being the most common. Concomitant conventional medicine and supplements were used by 1.4% and 29.6%, respectively.

Dalsaeng-san (n = 139) was also primarily used for facilitation of delivery (95.7%), with a mean dosage of 32.1 ± 23.3 packs. Similarly, the majority of users took this prescription during the third trimester (95.7%). Concomitant Korean Medicine treatments were reported by 17.3% of users, with acupuncture (15.1%) being the most common. Concomitant conventional medicine and supplements were used by 4.3% and 30.2%, respectively.

Detailed characteristics of herbal medicine use are presented in Supplementary Table 2.

## 3.4. Adverse Events Associated with Herbal Medicine Use

Among 467 respondents, 4 AEs from 3 participants (0.6%) were reported during pregnancy. All cases resulted in recovery or were recovering at the time of survey.

**Case 1**

was a 35-year-old woman with advanced maternal age and radiation exposure history who experienced two separate AEs. The first event involved gastrointestinal symptoms (bloating, dyspepsia) after 15 packs of Anjeon-icheon-tang during the second trimester for threatened abortion and vaginal bleeding. No rechallenge was attempted, and the patient recovered without treatment. The second event occurred with Bulsu-san during the third trimester for facilitation of delivery, presenting as gastrointestinal symptoms (diarrhea, dyspepsia) after 3 packs. Rechallenge was positive, with symptom recurrence upon re-administration, and the patient recovered after herbal medicine treatment. This case resulted in a healthy term delivery via vaginal birth with normal birth weight.

**Case 2**

was a 34-year-old pregnant woman who developed respiratory symptoms (allergic rhinitis, conjunctivitis) after 60 packs of Hwanggeum-tang during the second trimester for vitality restoration. No rechallenge was attempted, and the patient was recovering with herbal medicine treatment at the time of survey.

**Case 3**

was a 28-year-old pregnant woman who experienced gastrointestinal discomfort after 120 packs of Antae-eum during the second trimester. No rechallenge was attempted, and the patient recovered without treatment.

All reported AEs primarily involved gastrointestinal (75%) or respiratory (25%) symptoms. No serious AEs, congenital abnormalities, or pregnancy losses attributable to herbal medicine use were reported. (Table 3)

Table 3
Adverse events during pregnancy

| Maternal Characteristics | | | | | | | Concomitant treatment | Herbal Medicine | | | Adverse |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Case No | Pregnant status | Age | Gestational age (weeks) | Mode of delivery | Birth weight (kg)/ Neonatal development status | Risk factor | | Herbal medicine | Period of use | Purpose of use | Adverse Reactio |
| 1–1 | Postpartum | 35 | 40 | Vaginal delivery | Healthy /Normal BW | Advanced maternal age, X-ray/CT exposure | Vitamins, Folic acid, Iron | AIT* | Second trimester | Threatened abortion, Vaginal bleeding | GI (bloa dyspep disorde |
| 1–2 | | | | | | | | BSS# | Third trimester | Facilitation of delivery | GI (diar dyspep disorde |
| 2 | Pregnant | 34 | - | - | - | Coffee consumption | Vitamins, Folic acid | HGT† | Second trimester | Vitality restoration | Respira (allergic rhinitis, conjunc |
| 3 | Pregnant | 28 | - | - | - | Coffee consumption | none | ATE | Second trimester | Vitality restoration, Facilitation of delivery | GI (abd discom |

*Abbreviations:* AE, adverse event; AIT, Anjeon-icheon-tang (Andian Ertian Tang, □□□□□); ATE, Antae-eum (An Tai Yin, □□□); BSS, Bulsu-san (Fo Shou San, □□□); BW, birth weight; CT, computed tomography; HGT, Hwanggeum-tang (Huang Qin Tang, □□□); GI, gastrointestinal

*AIT: Ginseng Radix 12g, Rehmanniae Radix Preparata 12g, Atractylodis Rhizoma 12g, Dioscoreae Rhizoma 8g, Corni Fructus 8g, Eucommiae Cortex 6g, Dolichoris Semen 4g, Lycii Fructus 4g, Glycyrrhizae Radix et Rhizoma 4g (per day)

#BSS: Angelicae Gigantis Radix 24g. Cnidii Rhizoma 16g, Cervi Parvum Cornu 6g (per day)

†HGT: Scutellariae Radix 18g, Pinelliae Tuber 18g, Paeoniae Radix 18g, Zizyphi Fructus 18g, Glycyrrhizae Radix et Rhizoma 12g, Zingiberis Rhizoma Recens 9g (per day)

## 3.5. Comparison of Herbal Prescription Patterns and Lifestyle Factors between Spontaneous Abortion and Live Birth Groups

To explore potential associations between herbal medicine use and pregnancy outcomes, we compared prescription patterns between women who experienced spontaneous abortion (n = 17) and those with live births (n = 375).

Antae-eum was significantly more frequently used in the spontaneous abortion group compared to the live birth group (82.4% vs 35.7%, $p < 0.001$). In contrast, Dalsaeng-san (0.0% vs 35.5%, $p = 0.001$) and Bulsu-san (5.9% vs 34.7%, $p = 0.015$) were significantly more frequently used in the live birth group. No significant differences were observed for other prescriptions.

However, the spontaneous abortion group demonstrated significantly higher prevalence of known risk factors for pregnancy loss. The mean age was significantly higher in the spontaneous abortion group (39.1 ± 5.3 vs 36.1 ± 4.3 years, $p = 0.006$), and advanced maternal age was more prevalent (70.6% vs 35.7%, $p = 0.008$). Notably, smoking was significantly associated with spontaneous abortion (5.9% vs 0.0%, $p = 0.043$), and alcohol consumption showed a trend toward higher frequency in the spontaneous abortion group (11.8% vs 2.7%, $p = 0.090$), although this did not reach statistical significance.

These findings suggest that the higher frequency of Antae-eum use in the spontaneous abortion group likely reflects confounding by indication rather than a causal relationship, as Antae-eum is traditionally prescribed for threatened abortion. Women at higher risk of pregnancy loss—characterized by advanced maternal age, smoking, and alcohol consumption—were more likely to receive this prescription. Conversely, Dalsaeng-san and Bulsu-san are indicated for facilitation of delivery in the third trimester; women who experienced early pregnancy loss would not have had the opportunity to receive these prescriptions. (Table 4)

Table 4
Herbal prescription patterns and risk factors between spontaneous abortion and live birth

| | Spontaneous Abortion (n = 17) | | Live Birth (n = 375) | | P-value† |
|---|---|---|---|---|---|
| | N (%) | | N (%) | | |
| ***Herbal Prescription*** | | | | | |
| Antae-eum | 14 | (82.4) | 134 | (35.7) | < 0.001* |
| Bosaeng-tang | 1 | (5.9) | 27 | (7.2) | 1.000 |
| Gyullyeongbosaeng-tang | 0 | (0.0) | 33 | (8.8) | 0.381 |
| Geumgwedanggui-san | 0 | (0.0) | 23 | (6.1) | 0.612 |
| Gamipaljin-tang | 2 | (11.8) | 48 | (12.8) | 1.000 |
| Gungguigyoae-tang | 2 | (11.8) | 20 | (5.3) | 0.246 |
| Gyoaesamul-tang | 1 | (5.9) | 18 | (4.8) | 0.578 |
| Dalsaeng-san | 0 | (0.0) | 133 | (35.5) | 0.001* |
| Gunggui-tang | 0 | (0.0) | 25 | (6.7) | 0.615 |
| Bulsu-san | 1 | (5.9) | 130 | (34.7) | 0.015* |
| Dannokyong-tang | 1 | (5.9) | 71 | (18.9) | 0.332 |
| Nokyongbulsu-san | 0 | (0.0) | 68 | (18.1) | 0.052 |
| Dangguijakyak-san | 1 | (5.9) | 15 | (4.0) | 0.515 |
| Custom prescription | 0 | (0.0) | 19 | (5.1) | 1.000 |
| Others | 0 | (0.0) | 48 | (12.8) | 0.245 |
| **Risk factors** | | | | | |
| Age | 39.1 ± 5.3 | | 36.1 ± 4.3 | | 0.006* |
| Advanced maternal age (≥ 35) | 12 | (70.6) | 134 | (35.7) | 0.008* |
| In vitro fertilization | 2 | (11.8) | 17 | (4.5) | 0.196 |
| Gestational hypertension | 0 | (0.0) | 10 | (2.7) | 1.000 |
| Gestational diabetes mellitus | 0 | (0.0) | 18 | (4.8) | 1.000 |
| Coffee consumption | 9 | (52.9) | 178 | (47.5) | 0.805 |
| Alcohol consumption | 2 | (11.8) | 10 | (2.7) | 0.090 |
| Smoking | 1 | (5.9) | 0 | (0.0) | 0.043* |
| Radiation exposure (X-ray/CT) | 0 | (0.0) | 50 | (13.3) | 0.145 |

†Continuous variables compared by independent t-test; categorical variables compared by Fisher's exact

## 3.6. Comparison of Herbal Prescription Patterns and Lifestyle Factors between Congenital/developmental abnormality and Healthy Neonate Groups

Among 375 live births, 3 cases (0.8%) reported congenital or developmental abnormalities. In all three cases, herbal medicine use occurred during the second or third trimester, after the critical period of organogenesis (first trimester). No statistically significant differences were observed in prescription patterns between the congenital abnormality and healthy neonate groups.

Regarding lifestyle factors, all three cases reported coffee consumption, while none reported alcohol use or smoking. One case reported radiation exposure (X-ray/CT). No statistically significant differences were observed in lifestyle factors between groups (all $p > 0.05$).

## 4. Discussion

This study described herbal medicine (HM) use patterns and self-reported AEs among female Korean Medicine doctors (KMDs) who had personally used HM during their own pregnancies within the past year. Among 467 valid responses, 3 participants (0.6%) self-reported AEs, all of which were non-serious and primarily involved gastrointestinal or respiratory symptoms. No serious AEs, congenital abnormalities, or pregnancy losses were reported as attributable to HM use. These findings should be interpreted as descriptive baseline data; the low self-reported AE rate may substantially underestimate the true incidence,

given the potential for reporting bias, recall bias, and selection bias inherent to the cross-sectional, self-reported design. Furthermore, the small number of AEs (n = 4) precludes any statistically meaningful subgroup analysis or formal causality assessment, limiting the pharmacovigilance utility of these findings.

## 4.1. Low adverse event rate and comparison with existing evidence

The AE rate of 0.6% observed in the present study is notably low compared with previously reported rates. A Korean medicine literature review synthesizing 52 studies reported that the AE incidence of Korean herbal medicine use during pregnancy was 1.5% when including events with certain or unassessable causality, and 0.3% when restricted to events with confirmed causality; all severe AEs were assessed as unlikely to be causally related to herbal medicine.[13] The somewhat lower rate in our study may be attributable to the characteristics of our study population; female KMDs, as healthcare professionals, are likely to select prescriptions more judiciously and manage dosing more appropriately than the general population.

At the broader international level, the safety of herbal medicine use during pregnancy remains a subject of ongoing investigation. The largest-scale systematic review and meta-analysis to date, synthesizing evidence from 111 studies including RCTs and observational studies, indicated that no significant increase in adverse offspring outcomes was observed with herbal use at the overall level, although isolated safety signals for specific herbal products were identified. [16] Similarly, it has been noted that while harms have been reported with herbal product use during pregnancy, the overall benefit-to-harm balance remains uncertain due to methodological limitations in the existing literature.[17] It has further been emphasized that although herbal products are frequently perceived as natural and harmless, they contain active substances that can potentially affect fetal development, underscoring the importance of safety monitoring. [18] In a retrospective cohort study, adverse reactions were reported in 5.8% of women who used herbal products during pregnancy, with gastrointestinal symptoms being the most commonly observed; importantly, no significant differences in neonatal outcomes including gestational age, Apgar score, and congenital malformations were observed between herbal users and non-users. [19]

## 4.2. Characteristics of reported adverse events

All AEs reported in this study were non-serious and self-limiting. Gastrointestinal symptoms, including bloating, dyspepsia, and diarrhea, accounted for 75% of reported events, while respiratory symptoms (allergic rhinitis, conjunctivitis) comprised the remaining 25%. These findings are consistent with prior literature indicating that gastrointestinal discomfort is among the most commonly reported adverse effects associated with herbal medicine use during pregnancy.[16, 19]

Notably, one case demonstrated a positive rechallenge with Bulsu-san, providing stronger evidence for a causal relationship between this prescription and gastrointestinal symptoms. Despite the positive rechallenge, the AE remained non-serious and resolved following herbal medicine treatment. This finding highlights the importance of systematic rechallenge documentation in pharmacovigilance and suggests that even well-established prescriptions may cause mild adverse reactions in individual patients.

## 4.3. Prescription patterns and confounding by indication

The three most frequently used prescriptions in this study were Antae-eum (35.1%), Bulsu-san (30.4%), and Dalsaeng-san (29.8%), reflecting the traditional use of Korean herbal medicine in pregnancy management. Antae-eum was primarily prescribed for threatened abortion, while Bulsu-san and Dalsaeng-san were predominantly used for facilitation of delivery during the third trimester.

Our comparison between the spontaneous abortion and live birth groups revealed a significantly higher frequency of Antae-eum use in the spontaneous abortion group (82.4% vs 35.7%, $p < 0.001$). However, this finding is best understood as confounding by indication, as Antae-eum is traditionally prescribed specifically for threatened abortion. It has been noted in the context of conventional medication studies that observational analyses linking medication use and health outcomes are frequently subject to indication bias, wherein the underlying condition prompting prescription—rather than the medication itself—may account for the observed association.[8] This principle applies directly to our findings: the spontaneous abortion group was also characterized by significantly higher maternal age (39.1 ± 5.3 vs 36.1 ± 4.3 years, $p = 0.006$), higher prevalence of advanced maternal age (70.6% vs 35.7%, $p = 0.008$), and higher rates of smoking (5.9% vs 0.0%, $p = 0.043$)—all established risk factors for pregnancy loss. This pattern is consistent with evidence from a large-scale meta-analysis showing that observational studies adjusted for confounding did not demonstrate significant associations between prenatal herbal medicine use and major adverse offspring outcomes including miscarriage.[16]

Conversely, the significantly higher use of Bulsu-san and Dalsaeng-san in the live birth group reflects the fact that these prescriptions are indicated for third-trimester delivery facilitation; women who experienced early pregnancy loss would not have had the clinical indication to receive these prescriptions. A systematic review of herbal medicines for induction of labour reported that herbal medicines were effective for labour induction but concluded that safety evidence remained inconclusive due to the lack of high-quality data.[20]

## 4.4. Pregnancy outcomes and congenital abnormalities

Among the 375 live births, 95.2% were delivered at term, 71.5% were vaginal deliveries, and 95.2% had normal birth weight, suggesting generally favorable pregnancy outcomes in this cohort. Congenital or developmental abnormalities were reported in only 3 cases (0.8%); however, given the absence of clinical verification and a standardized case definition, direct comparison with population-based prevalence estimates was not performed. In all three cases, HM exposure occurred during the second or third trimester, after the critical period of organogenesis, suggesting a low likelihood of teratogenic association. A large-scale meta-analysis reported that prenatal herbal medicine use was associated with a lower risk of birth defects in RCTs (RR = 0.46, 95% CI: 0.22–0.94), primarily among women undergoing assisted reproduction, while observational studies did not show significant associations with congenital abnormalities after adjusting for confounders.[16] Consistent with these findings, a retrospective cohort study similarly found no significant differences in congenital malformation rates between herbal medicine users and non-users.[19]

## 4.5. The role of healthcare provider-patient communication

The unique study design employing female KMDs as both practitioners and patients offers distinct advantages for safety surveillance. A systematic review and meta-analysis encompassing 111 studies across 51 countries reported that the pooled prevalence of HM use during pregnancy was 34.4% globally, yet only 27.9% of HM users disclosed their use to healthcare providers.[21] Non-disclosure was primarily attributed to the perception that HM is harmless (53.6%) and to healthcare providers not inquiring about HM use (39.4%), with 91.7% of women reporting that they had never been asked about HM use during antenatal care.[21] This substantial disclosure gap has important implications for pharmacovigilance, as underreporting of herbal medicine use limits the ability to monitor AEs in routine clinical settings.

In the present study, the respondents' professional background as KMDs substantially mitigated this disclosure gap. Unlike general pregnant populations who may not recognize or accurately describe HM-related AEs, female KMDs possess the clinical knowledge to identify specific prescriptions, recognize AE patterns, and report outcomes using appropriate medical terminology. This capacity for accurate reporting is a key methodological strength of the present study.

## 4.6. Strengths and limitations

This study has several strengths. First, surveying female KMDs who used HM during their own pregnancies ensures high accuracy in prescription identification and AE recognition, as these respondents possess both clinical knowledge and personal experience. Second, the nationwide scope and relatively large sample size for a professional subgroup (n = 467) strengthen the internal validity of the findings; however, generalizability to the broader pregnant population remains limited given the restriction to healthcare professionals and the potential for self-selection bias. Third, the comprehensive questionnaire design captured detailed information on prescriptions, timing, dosage, concomitant treatments, and obstetric outcomes, enabling multifaceted analysis.

However, several limitations should be acknowledged. First, as a cross-sectional survey relying on self-reported data, the study is subject to recall bias and reporting bias. Participants who experienced AEs may have been less likely to respond to the survey, and the professional background of KMDs may have led to under-attribution of mild symptoms as AEs; both mechanisms would result in underestimation of the true AE rate. Second, the study population is limited to healthcare professionals, and the findings are not directly generalizable to the general pregnant population, who may use HM without professional guidance and under substantially different clinical circumstances. The restriction to a professional subgroup also introduces selection bias, as KMDs are likely to use HM more judiciously and at more appropriate dosages than the general population, further limiting the external validity of the observed AE rate. Third, the very low number of AEs (n = 4) precludes any statistically meaningful subgroup analysis and renders the observed rate of 0.6% statistically unstable; the true population AE rate may differ substantially from this estimate. Fourth, formal causality assessment using standardized pharmacovigilance tools, such as the WHO-UMC system or the Naranjo algorithm, was not applied to the reported AEs, as the survey design did not capture sufficient clinical detail for systematic causality evaluation. This represents a fundamental limitation of the pharmacovigilance utility of the AE data collected. Fifth, the cross-sectional design precludes establishment of temporal causality between HM use and pregnancy outcomes. Sixth, while the survey collected information on concomitant medications and supplements, potential interactions between HM and concurrent treatments were not systematically evaluated.

## 4.7. Implications and future directions

The present study provides descriptive baseline data on HM use patterns and self-reported AEs among a professional cohort, contributing a foundation upon which more rigorous pharmacovigilance studies can be built. However, several fundamental limitations constrain the interpretability of these findings. The cross-sectional, self-reported design is susceptible to reporting bias and selection bias, the restriction to a professional subgroup limits generalizability to the general pregnant population, and the rarity of reported AEs (n = 4) renders any formal safety conclusion statistically unsupported. Accordingly, these findings should not be interpreted as evidence of an acceptable safety profile, but rather as preliminary descriptive data that highlight the need for more systematic investigation. The benefit-to-harm balance of herbal products during pregnancy remains to be established through higher-quality evidence. [17] Continuous safety monitoring remains essential, as herbal products contain pharmacologically active substances that may pose risks during pregnancy. [18]

Future studies should prioritize prospective cohort designs with pre-specified pharmacovigilance protocols, including formal causality assessment using standardized tools such as the WHO-UMC system, to enable more rigorous AE evaluation. Multi-center registry-based studies with larger sample sizes would provide the statistical power necessary for meaningful subgroup analyses. Critically, extending the study population beyond healthcare professionals to include general pregnant women who use HM would substantially improve generalizability and policy relevance. The present findings, while limited to a professional cohort, underscore the importance of systematic HM use documentation in clinical settings as a foundation for such future research. Development of evidence-based clinical guidelines for HM use during pregnancy, informed by prospective safety data, remains an important and as yet unmet goal for the field.

## Declarations

**Author contributions**

Conceptualization: Mi Ju Son

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**Ethical statement**

This research was reviewed and approved by the Institutional Review Board of the Korea Institute of Oriental Medicine (I-2408/008-005-02).

**Data availability**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.FrequencyofHerbalPrescriptionsUsedDuringPregnancy.xlsx
- SupplementaryTable2.CharacteristicsofHerbalMedicinePrescriptionUse.xlsx
- SupplementaryQuestionnaireEN.xlsx