ORIGINAL ARTICLE

Heavy Metals in Danggui (*Angelica sinensis*) Consumed by Postpartum Mothers and Its Health Risk

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ABSTRACT

Introduction: Consumption of Chinese Herbal Medicine (CHMs) have escalated globally. They are preferred treatment for minor diseases or disorders. In Malaysia, CHMs are common home remedies during pregnancy and postpartum. *Angelica sinensis* (Danggui) is a staple CHMs during postpartum for purpose of nourishing blood and resolving stasis. Concerns are raised over possible heavy metals toxicity. Objective: This study aims to (i) determine Danggui consumption among postpartum mothers, (ii) quantify its heavy metals level, namely Lead (Pb), Cadmium (Cd), Arsenic (As) and Chromium (Cr) and (iii) determine health risks of Danggui consumption among mothers. **Methods:** A cross-sectional study involving 112 postpartum mothers was carried out in Kuala Lumpur. Danggui samples were collected from nine districts in Kuala Lumpur (Segambut, Seputeh, Cheras, Kepong, Bandar Tun Razak, Titiwangsa, Setiawangsa, Batu and Lembah Pantai). Heavy metals were extracted using microwave digester and analysed using Inductively coupled plasma mass spectrometry (ICPMS). Hazard Quotient (HQ) was used to determine non-carcinogenic health risks for herbal medicine consumption. **Results:** Danggui was consumed by 19.6% of mothers (n=22). Among them, incidence of jaundice was 63.6% and need for phototherapy was 40.9%. Heavy metals contaminations were found in the decreasing order of Cr > As > Pb > Cd with median (interquartile) of 3996.3 (2805.6) µg/kg, 128.3 (56.7), 98.6 (99.1) and 37.0 (35.0) respectively. No non-carcinogenic health risks were found for all four metals. **Conclusion:** Alarming concentrations of heavy metals were quantified in Danggui warranting for further investigation to safeguard health of postpartum mothers.

Keywords: *Angelica sinensis* (Danggui), Pregnant and postpartum mothers, Heavy metals exposure, Non-carcinogenic health risk, Chinese herbal medicines

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INTRODUCTION

Consumption of herbal medicines have been used globally with the World Health Organisation (WHO) predicting that 80% of the world populations consuming herbal remedies (1). Chinese herbal medicines (CHMs) has often been considered as the first choice of treatment of minor diseases and disorders (2).

In Malaysia, CHMs are consumed for many decades and is rampantly use of during the pregnancy and postpartum period. One of the indications for use of CHMs is to improve pregnancy outcomes for women who had episodes of miscarriages in their previous pregnancies (3). It was also believed that CHMs could maintain hormonal balance, provide healing to the uterus after pregnancy as well ensure that the walls of the abdomen is restored to their original tone and strength. In addition, CHMs were believed to provide nutrients and increased milk production (4).

Angelica sinensis, also known as Danggui, is one of the many types of CHMs which had been used for tonifying, replenishing and invigorating blood. Danggui was also used to reduce pain, lubricate intestines and treat ailments related to menses such as irregular menses and amenorrhoea (5). Most commonly consumed CHMs among pregnant and postpartum women in China is Danggui with 28.8% during pregnancy and 26.8% during first six months postpartum (6).

As one of the most commonly used herbs in traditional medicine, the frequent usage of Danggui had triggered the interest of researchers to conduct various studies on usage of Danggui as well as its safety. One of such studies indicated that Danggui may pose a risk for females with hormone-sensitive conditions (7). In addition, CHMs

had also been reported to cause adverse effects such as hepatoxicity, fetal distress, low birth weight birth defects as well as carcinogenicity (8). Another concern is contamination of toxic heavy metals. A group of researchers in their study of women in Taiwan reported that CHMs consumption during pregnancy and lactation resulted in higher lead concentrations in breast milk (9).

Being one of the commonly used herbs during pregnancy and postpartum, this study aims to determine Danggui consumption among mothers; quantify its heavy metals level namely lead (Pb), Cadmium (Cd), Arsenic (As) and Chromium (Cr); as well as determine health risks of its consumption among mothers.

MATERIALS AND METHODS

Study design

A cross-sectional study was carried out in Kuala Lumpur, Malaysia among Chinese mothers. Participants were required to complete a set of questionnaires which included information on socio-demographic, maternal, pregnancy, postpartum and infant characteristic, as well as frequency and usage of herbal medicine during pregnancy and postpartum period. All questionnaires answered were reviewed and analyzed. All participants were given information sheet which included information on purpose and benefits of participating in the research and were required to sign the informed consent before participating in the study. This study was granted ethical approval by Malaysian Research Ethics Committee (MREC) [Ref: NMRR-15-990-25727(IIR)].

Danggui which was one of the most commonly consumed CHMs during pregnancy and postpartum period (6) were collected from nine districts in Kuala Lumpur (Segambut, Seputeh, Cheras, Kepong, Bandar Tun Razak, Titiwangsa, Setiawangsa, Batu and Lembah Pantai).

Microwave digestion

A total of 0.5 gram of powdered herbs sample were digested with 5 mL of nitric acid and 1 mL of hydrogen peroxide. The samples were radiated in microwave digester for 15 minutes (10). Upon cooling, the solutions were diluted to 50 ml with 1% nitric acid.

Sample extraction analysis

Lead (Pb), cadmium (Cd), chromium (Cr) and arsenic (As) were the heavy metals analysed in this study. Quantification of heavy metals was done using Inductively coupled plasma mass spectrometry (ICPMS). Validation of method was carried out via quantification of certified reference material (NIST 1547). Each batch of sample analysis was also injected with method blank throughout the entire sample preparation and analytical process (11).

Quantitative Health Risk Assessments

Non-carcinogenic health risk was expressed using hazard quotient (HQ). HQ is defined as ratio of chronic chemical daily intake (mg/kg/day) to the reference dose (RfD) (mg/kg/day) (12) and calculated according to Eq. 1. HQ greater than 1 (HQ > 1) indicates presence of non-carcinogenic health risk.

$$HQ = ADD/RfD \quad \text{Eq. 1}$$

in which ADD is average daily exposure to heavy metals (mg/kg/day) and RfD is reference dose for heavy metals (mg/kg/day) (13).

ADD was estimated according to Eq. 2.

$$ADD = C \times CR \times EF \times ED / BW \times AT \quad \text{Eq. 2}$$

whereby C denotes concentration of heavy metals in food (mg/kg), CR denotes consumption rate (kg/day), EF refers to exposure frequency (days/year), ED denotes exposure duration (years), BW denotes to average body weight of the receptor over the exposure period (kg) and AT refers to averaging time (days) (13).

Sum of HQs of different metals calculates the Hazard Index (HI) to estimate the risk of mix metal contaminates (13) as shown in Eq. 3.

$$HI = \Sigma HQ \quad \text{Eq. 3}$$

Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) software. Data analysis includes descriptive analysis and Chi-square cross tabulation test. Each participant was identified via a code upon database entry. In view of the study question, all data were organized to analyze the characteristics of all participants. Significance level at 0.05 was used for all statistical measures.

RESULTS

Danggui consumption among mothers

Among 112 of the participants, 50.9% (n=57) consumed herbal medicines during pregnancy or postpartum while 49.1% (n=55) of participants were non-consumers. Danggui was found to be consumed by 19.6% of participants (n=22). Out of the 22 participants who consumed Danggui, 95.5% (n=21) consumed the herb during confinement, followed by 31.8% (n=7) during third trimester of pregnancy, 27.3% (n=6) during second trimester of pregnancy and 22.7% (n=5) during first trimester of pregnancy.

The participants reported the main purpose of Danggui consumption was to improve health and energy (100%,

Table I: Purpose of Danggui consumption among mothers

	Number of participants consuming Danggui	
	n	%
Improve health and energy	22	100
Facilitate wound healing	11	50
Increase breast milk production	5	22.7
Facilitate labour	2	9.1

n=22), facilitate wound healing (50%, n=11), and increase breast milk production (22.7%, n=5). Table I shows the purpose of Danggui consumption among the mothers. 77.3% of the participants stated parents or in-laws as their main influence to consume Danggui (n=17), followed by traditional medical practitioner (31.8%, n=7) and themselves (31.8%, n=7). Influence of herbal medicines consumption to mothers is further shown in Table II. The mothers' main source of herbs are local herbal stores (77.3%, n=17) and traditional medical practitioner (31.8%, n=7). Danggui consumers obtained information on herbal medicines from parents or in-laws (68.2%, n=15), traditional medical practitioner (31.8%, n=7) and articles or adverts in health magazines (13.6%, n=3). Table III outlines the source of information reported by participants in this study.

Table II: Influence on herbs consumption among Danggui consumers

	Number of participants consuming Danggui	
	n	%
Parents or in-laws	17	77.3
Traditional medical practitioner	7	31.8
Self-influence	7	31.8
Husband, friends, siblings	3	13.6

Table III: Source of information on herbal medicines among Danggui consumers

	Number of participants consuming Danggui	
	n	%
Parents or in-laws	15	68.2
Traditional medical practitioner	7	31.8
Articles and adverts in health magazines	3	13.6
Doctor or nurse	2	9.1
Husband, friends, siblings	2	9.1

63.6% of Danggui consumers in this study reported presence of neonatal jaundice in their offsprings (n=14) with 40.9% required phototherapy (n=9). Significant difference was found on presence of neonatal jaundice among infants of Danggui consumers compared to non-consumers ($p<0.05$) whereby 38.2% (n=21) of participants who did not consume herbs during pregnancy and postpartum reported incidence of neonatal jaundice (Table IV). 81.8% of the infants

Table IV: Presence of jaundice in newborns

	Number of participants consuming Danggui	Number of participants not consuming Danggui	p value
Presence of neonatal jaundice			0.043
Yes	14	21	
No	8	34	

were born full term (n=18) while 18.2% were born prematurely (n=4). Among mothers who delivered their babies full term, only 5.6% (n=1) reported low birth length while all of them reported normal birth weight for their newborns (n=18).

Heavy metals concentration and health risk assessment

Heavy metals contaminations were found in the decreasing order of chromium > arsenic > lead > cadmium with median (interquartile) of 3996.3 (2805.6) µg/kg, 128.3 (56.7), 98.6 (99.1) and 37.0 (35.0) respectively.

Non-carcinogenic health risks due to heavy metals exposure were calculated using Hazard Quotient (HQ). Average daily exposure (ADD) was compared to reference dose (RfD) of lead at 0.004 mg/kg/day (14-18), cadmium at 0.001 mg/kg/day (19), chromium at 1.5 mg/kg/day (19) and arsenic at 0.0008 mg/kg/day (19). Referring to the median concentration of chromium (3996.3 ug/kg), lead (98.6 ug/kg), arsenic (128.3 ug/kg) and cadmium (37.0 ug/kg), hazard quotient for all metals were calculated as 0.00002, 0.0002, 0.0010 and 0.0002 respectively. These results indicated no non-carcinogenic health risks with lead, arsenic, cadmium and chromium contamination in Danggui (HQ < 1). Table V outlines heavy metals concentration and hazard quotient for Danggui.

Table V: Heavy metals concentration and hazard quotient for Danggui

	Heavy metals concentration in Danggui			
	Chromium (Cr)	Lead (Pb)	Arsenic (As)	Cadmium (Cd)
Median (interquartile), ug/kg	3996.3 (2805.6)	98.6 (99.1)	128.3 (56.7)	37.0 (35.0)
Hazard Quotient	0.00002	0.0002	0.0010	0.0002

DISCUSSION

Danggui consumption among mothers

A cross sectional survey which was conducted in China reported Danggui being a popular herbal medicine consumed during pregnancy and postpartum with 28.8% and 26.8% respectively (6). This study found that Danggui was consumed by 19.6% of the participants, in which some of the participants consumed the

herb during both pregnancy and postpartum period. Consumption during pregnancy period, which was reported to be as early as first trimester in this study raises concern over possible congenital malformation events. Recent systematic review reported that mothers who consumed An-Tai-Yin containing A. sinensis during the first trimester of their pregnancy gave rise to increased incidence of musculoskeletal and connective tissue congenital malformations (AOR 1.61, 95% CI 1.10–2.36), as well as eye congenital malformations (AOR 7.30, 95% CI 1.47–36.18) among their children (20). This warrants for further exploration of herbal medicines usage and safety precautions during this critical period.

The participants reported the main purpose of Danggui consumption was to improve health and energy, facilitate wound healing, and increase breast milk production. This result is similar to previous studies which reported increase breast milk production, improvement of health and energy of mothers and to facilitate labour as the main reasons for herbs consumption during pregnancy and postpartum (21, 22).

Most of the mothers in this study stated parents or in-laws as their main influence to consume Danggui. This is similar to previous study by Tang et al. in China who reported that mothers were advised to consume CHMs by their mother or mother-in-law (6).

Significant difference was found on presence of neonatal jaundice among infants of Danggui consumers compared to non-consumers ($p<0.05$) in this study in which 63.6% of Danggui consumers in this study reported presence of neonatal jaundice in their offspring compared to 38.2% among non-consumers. This is consistent with the findings by Teoh et al. who reported significance neonatal jaundice development among infants of mothers who consumed herbs during confinement period compared to non-consumers (22). Both these results raise the need for possible intervention from related parties to ensure safety of both mothers and infants.

Heavy metals contamination and health risk assessment

Heavy metals contamination had been found in not only herbs but vegetables including leafy and root vegetables as well as tea leaves (17, 23-25). Additional consumption of herbs on top of daily vegetables may lead to heavy metals accumulation and raises the total amount of heavy metals intake in daily life.

This study found no non-carcinogenic health risks for Danggui consumption. Other studies in the region had reported mixed findings on non-carcinogenic health risks with herbs, tea leaves or vegetables consumption (17, 24). Some researchers found significant combined health risks in heavily contaminated areas compared to other investigated areas (17). This further emphasize the possible health risks with cumulative effects of different herbal medicines usage.

CONCLUSION

Toxic metals namely, Arsenic, Cadmium, Chromium and Lead were quantified in Danggui which were consumed by 19.6% of mothers participating in this study during both pregnancy and postpartum period. Heavy metals contaminations were found in the decreasing order of chromium > arsenic > lead > cadmium with median (interquartile) of 3996.3 (2805.6) μg/kg, 128.3 (56.7), 98.6 (99.1) and 37.0 (35.0) respectively. Although no significant non-carcinogenic health risks were found, presence of heavy metals and potential transfer from mother to fetus and infant raises concerns on safety of consumption during pregnancy and postpartum period.

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