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Evaluating Health Risks of Heavy Metals in Chinese Herbal Medicines Used by Pregnant and Postpartum Women in Kuala Lumpur, Malaysia

Normina Ahmad Bustami[1], Chung Keat Tan[1], Yu Zhao Lee[1], Rahela Zaman[1], Yu Bin Ho[2], Farahnaz Amini[1], Edmond Siah Chye Ng[1], Sharmanee Thiagarajah[1], Ahmad Zaharin Aris[3,4], Marjan Sadat[5], and Eugenie Sin Sing Tan[1*]

[1]Faculty of Medicine and Health Sciences, UCSI University, Kuala Lumpur, Malaysia
[2]Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Malaysia
[3]Department of Environment, Faculty of Forestry and Environment, Universiti Putra Malaysia, 43400 UPM, Selangor, Malaysia
[4]International Institute of Aquaculture and Aquatic Sciences, Universiti Putra Malaysia, 71050 Port Dickson, Negeri Sembilan, Malaysia
[5]Ikigai Medical Centre (BR Life Clinic), Lower Ground, 212, Downtown Dubai, Dubai Mall, Dubai, UAE

*Corresponding author: eugenietan@ucsiuniversity.edu.my; dr.eugenietan@gmail.com
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Abstract

Chinese herbal medicine (CHM) is commonly used during pregnancy and postpartum in Malaysia to promote infant health, enhance lactation, and aid maternal recovery. However, concerns persist about its safety due to the risk of heavy metal transfer from mother to foetus and infant. This study aimed to identify CHM types consumed during pregnancy and postpartum and assess their potential heavy metal contamination and associated health risks. A comparative cross-sectional study involving 113 pregnant or postpartum Chinese women (57 CHM consumers and 56 non-consumers) employed a self-administered questionnaire to gather information on socio-demographics, maternal and pregnancy characteristics, postpartum and infant characteristics, and CHM consumption patterns. The top four most consumed CHM were analyzed for heavy metals, namely arsenic (As), cadmium (Cd), lead (Pb) and chromium (Cr), using Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Health risks associated with heavy metal contamination were assessed using a method outlined by the United States Environmental Protection Agency (USEPA). Adjusted odds ratio for maternal age, personal monthly income and the place of postpartum confinement revealed that mothers who consume CHM had a statistically significant increase in odds of their infants developing neonatal jaundice (adjusted OR = 3.0, 95% CI 1.301 - 7.226). Heavy metals were detected in all four CHMs: As (188.11 ± 107.25 µg/kg), Cd (104.18 ± 83.39 µg/kg), Cr (11763.57 ± 20407.67 µg/kg), and Pb (538.24 ± 519.27 µg/kg). Cd concentration in Ba Zhen Tang exceeded the permissible limit of 0.3 mg/kg. Despite these findings, non-carcinogenic hazard health risks (HQ) and health index (HI) were below 1.0, indicating no significant non-carcinogenic health risks. Nonetheless, further studies are needed to validate these results and underscore the importance of ongoing monitoring to protect maternal and infant health.

Keywords: Heavy metals; Chinese herbal medicine; Pregnancy; Postpartum; Non-carcinogenic health risk

1. Introduction

Traditional Chinese herbal medicine (CHM) has been consumed and used for over 2,200 years, showcasing its longstanding history (Curran 2008). Given recent surge of interest in traditional and natural health remedies, the role of medicinal plants in cosmetics, food supplements and pharmaceuticals has increased (Leo *et al.* 2022; Saikia *et al.* 2006; Tan *et al.* 2021). Malaysia was reported to have a high prevalence of herbal usage of up to 70% (Siti *et al.* 2009). According to the World Health Organisation (WHO), Malaysia's traditional complementary and alternative medicine industry was valued at more than 250 million USD annually, with CHM as the preferred treatment choice (World Health Organization. Programme on Traditional 2001). Malaysian mothers frequently use herbal medicine (HM) during pregnancy and postpartum to improve babies' health, boost breastmilk production, promote slimming and uterine involution, and maintain general health (Ahmad Bustami *et al.* 2019; Ahmad Bustami, Ho, and Tan 2020; Ahmad Bustami, Ho, Tan, *et al.* 2020; Rahman *et al.* 2008; Teoh *et al.* 2013).

Heavy metals such as cadmium (Cd), arsenic (As), chromium (Cr) and lead (Pb) are naturally occurring in the earth. Still, they are ubiquitous in the environment due to anthropogenic activities as humanity boasts enormous economic development and growth in agriculture, mining and industry. These toxic elements contaminating the environment and soil will be transpired, absorbed and accumulated in plants and food-chain, including medicinal herbs (Alengebawy *et al.* 2021). Concerns regarding the safety of herbal remedies grew as several studies found heavy metal contamination in herbal plants from Brazil, Iran, Egypt, Ghana, Mali, Nigeria, South Africa (Abou-Arab and Donia 2000; Annan *et al.* 2013; Awodele *et al.* 2013; Leal *et al.* 2013; Maiga *et al.* 2005; Mulaudzi *et al.* 2017; Ungureanu *et al.* 2023). Predictably, heavy metal contamination had been detected in CHM sampled throughout China, and their wild herbal plants were contaminated in greater concentrations (Chen *et al.* 2021; Harris *et al.* 2011; Luo *et al.* 2021). The geographic location and local climate impact the dynamics of water, nutrients, carbon, and other trace elements, including heavy metals; they collect within the herbal plants, leading to inconsistent material quality and compromised medicinal benefits (Chen *et al.* 2021; Alharbi *et al.* 2024).

Consumption of contaminated medicinal plants by pregnant mothers can adversely impact foetal and infant development as heavy metals were evidenced to cross the placental barrier (Gundacker and Hengstschläger 2012; Lin *et al.* 2013; Parajuli *et al.* 2013) and transfer through breastmilk (Gundacker and Zödl 2005; Motas *et al.* 2021; Yurdakök 2015). Heavy metals disrupt physiological functions by inducing oxidative stress through the production of reactive oxygen species (ROS), causing lipid peroxidation, DNA damage, and dysfunction of enzymes (Chen *et al.* 2018). Foetal exposure to Pb has been linked to congenital heart disease (Kundak *et al.* 2017; Liu *et al.* 2018), likewise, exposure to cadmium (Cd) even at very low concentration were found significantly associated to low birth weight (Zinia *et al.* 2023). Additionally, prenatal heavy metal exposure is linked to several health conditions during later childhood, such as, intellectual deficits (Sioen *et al.* 2013), diabetes (Ludvigsson *et al.* 2019; Størdal *et al.* 2018), attention deficit hyperactivity disorder (Lee *et al.* 2018; Skogheim *et al.* 2021) and immuno-dysregulation (Kim *et al.* 2019). Besides exhibiting toxic effects on the foetus, heavy metal exposure also impacts maternal health. The As level in urine was associated with fever, nausea and diarrhoea during pregnancy, which may subsequently complicate foetus development due to poor nutritional status (Raqib *et al.* 2009). Exposure to extremely low Cd concentration can promote contractile activity triggering premature delivery (Nishijo *et al.* 2002).

Several studies in Malaysia explored the use of herbal medicines for various ailments and indications, ranging from general health maintenance to treatment of chronic diseases (Farooqui *et al.* 2016; Kew *et al.* 2015). Types of traditional herbal medicine use during the period of pregnancy and postpartum and their health risk were previously investigated with no specifics on the types of CHM

(Law and Soon 2013; Rahman *et al.* 2008; Teoh *et al.* 2013). To date, the selection of CHM used by Malaysian pregnant and postpartum mothers and its contamination by heavy metals remain untapped and scanty. Earlier our research group investigated on *Angelica sinensis* (Danggui) and found high content of heavy metals (Normina Ahmad Bustami 2020). Thus, this study is further aimed to determine the types of CHM popularly consumed during pregnancy and postpartum in Malaysian population, their potential contamination by heavy metals and their associated health risk.

2. Methodology

2.1 Study Design and Questionnaire

A comparative cross-sectional study enrolled 113 pregnant and postpartum mothers with good general health. Recruitment was conducted in Kuala Lumpur, Malaysia via convenient sampling. Mothers were grouped according to their consumption of CHMs into the 'consumer' and 'non-consumer' groups. The following inclusion criteria were applied: (1) age of 18 and above, (2) undergoing postpartum, (3) able to understand the study protocol fully, and (4) willing to give informed consent. All mothers were given a participant information sheet and thorough explanation by the investigator. A written informed consent was sought from each mother prior to their enrolment into the study.

All mothers were subjected to a self-administered questionnaire which consisted of socio-demographics (5 items), maternal and pregnancy characteristics (9 items), postpartum and infant characteristics (14 items), consumption of CHM (7 items). The questionnaires were adapted from previous studies on herbal medicine usage during pregnancy and postpartum (Chuang *et al.* 2005; Chuang *et al.* 2009; Rahman *et al.* 2008; Teoh *et al.* 2013). Data collected from the questionnaire was analysed to determine the top 4 most consumed CHM.

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Malaysia Research Ethics Committee (MREC) via approval code NMRR-15-990-25727 on 22nd Oct, 2015.

2.2 Sample Collection and Extraction

Based on the top 4 identified CHM consumed during pregnancy and postpartum, one sample for each CHM was collected from every district in Kuala Lumpur, Malaysia. A total of 44 samples were collected from 11 districts. All CHM samples were packed into sealed sample bags, marked, transported to the laboratory and stored at 4 ^{o}C. They were rinsed with tap water and then with deionised water. Subsequently, they were oven-dried at 60 ^{o}C until reaching a constant weight. Dried samples were homogenised, ground, sieved through a 0.5 mm mesh and stored in sealed bag until analysis.

Approximately, 0.5g of powdered CHM samples was added with 5 mL 65% nitric acid and 1 mL of 30% hydrogen peroxide (H2O2) in a Teflon vessel. Then, it was microwave-assisted digested following the heating program as follows: (1) 1000W at 80 ^{o}C for 5 mins, (2) 1000W at 50 ^{o}C for 5 min, (3) 1000W at 190 ^{o}C for 20 mins and (4) 0W for 30 mins (Khan *et al.* 2015). Upon cooling, the solutions were diluted to 50 ml with distilled water. The certified reference material, NIST-1547 peach leaves (Merck, Germany), was subjected to the same experimental condition as the CHM samples. The recovery values were in the range of 92 - 101% and matrix effect were in range of 1 - 1.1%, of which, both were acceptable range (Bergh *et al.* 2016; Semreen *et al.* 2019). All samples were analysed in triplicates.

2.3 Toxic Metal Analysis

Heavy metals in CHM were analysed using Inductively Coupled Mass Spectrometry (ICP-MS) (Perkin Elmer, USA). Seven-point calibration curves were constructed for all the metal ions and the calibration curve correlation coefficient was ensured to be > 0.995 before sample analysis (Chui 2007). Limit of detection (LOD) of this device for As, Cd, Pb and Cr were 0.0414, 0.0126, 0.8304 and 0.7221 μg/kg. Repeatability of the method was determined via intra-day and inter-day precision, the relative standard deviation (SD) for all repeated measurements was below 10% and considered precise (Oecd 2014). Precision, sensitivity and accuracy of the method was found to be satisfactory for all analytes (Supplementary Table S1). A laboratory reagent blank was analysed in every batch of samples to determine cross-contamination. 50 µg/kg of Rhodium was spiked to all samples and solutions as internal standard for correction of any loss during sample preparation and analysis.

2.4 Statistical Analysis

All statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, version 20 (IBM, USA). Chi-square test and Fisher's Exact test were used to analyse the association for socio-demographics, maternal, pregnancy, infant and postpartum characteristics with mother's groups. Independent t-test was used to analyse differences between mean of age and weights with mother's group. The odds ratio was calculated to assess pregnancy and birth outcomes among the mother's group, with a value >1 indicating a higher likelihood of these outcomes due to CHM consumption. The adjusted odds ratio was computed to account for potential confounders, considering sociodemographic and maternal characteristics that significantly differed between CHM consumers and non-consumers. Results considered significant if $p < 0.05$ with 95% of confidence interval.

2.5 Human Health Risk Assessments

Non-carcinogenic health risk for each heavy metal exposure was expressed using hazard quotient (HQ); defined as ratio of average daily dose (ADD) (mg/kg/day) to the oral reference dose (RfD) (mg/kg/day). RfD of As at 0.0008 mg/kg/day, Cd at 0.001 mg/kg/day, Cr at 1.5 mg/kg/day and Pb at 0.004 mg/kg/day as per the guideline from United States Environmental Protection Agency (Khan *et al.* 2008; Usepa 2005). ADD was estimated using equation (1). HQ is calculated using equation (2).

$$ADD = \frac{C \times CR \times Ef \times Ed}{BW \times AT} \quad (1)$$

Where
C = Detected concentration of metal in food (mg/kg)
CR = Consumption rate (kg/day)
Ef = Exposure frequency (days/year)
Ed = Exposure duration (years)
BW = Body weight (kg)
AT = Average exposure time (Ed x 365 days)

$$HQ = \frac{ADD}{RfD} \quad (2)$$

HQs of 4 heavy metals were summed up to obtain non-carcinogenic 'Hazard Index (HI)' for each CHM as per equation (3). HQ > 1 and HI > 1 indicate significant non-carcinogenic health risks due to heavy metals concentration (Usepa 2005).

$$HI = \sum HQ \quad (3)$$

3. Results and Discussion

3.1 Results

3.1.1 Socio-demographics and maternal characteristics

Socio-demographics and maternal characteristics of 57 CHM consumers and 56 non-consumers were summarised in Table 1. Age was significantly associated ($p < 0.01$) with CHM consumption. Mothers who consumed CHM were significantly older than non-consuming mothers. Specifically, 42.1% of CHM-consuming mothers were over the age of 35, in contrast to only 12.5% of mothers who did not consume CHM. CHM consumption was significantly associated with the mother's personal monthly income ($p < 0.05$), of which 43.9% (n = 25) of consumers had more than MYR 5000 compared to 25.0% (n = 14) of non-consumers. Also, CHM consumption was significantly associated with the mother's place of postpartum confinement ($p < 0.01$). Most mothers (92%, n = 11) who observed their 30 days postpartum in a traditional Chinese confinement home were CHM consumers, while only one mother (1.8%) did not consume CHM when residing at a confinement home.

Table 1. Socio-demographics and maternal characteristics of CHM consumers and non-consumers

Socio-demographic and maternal characteristics	Consumer (n = 57)		Non-consumer (n = 56)		p value
	n	%	n	%	
Age (years)					
Less or equal to 35	33	57.9	49	87.5	0.000[a]**
More than 35	24	42.1	7	12.5	
Occupation					
Housewife	7	12.3	7	12.5	0.154[a]
Private sector	42	73.7	33	58.9	
Government sector	8	14	16	28.6	
Level of education					
Tertiary level	45	78.9	45	80.4	0.852[a]
Secondary level or below	12	21.1	11	19.6	
Personal monthly income					
MYR5000 or less	32	56.2	42	75.0	0.035[a]*
More than MYR5000	25	43.9	14	25.0	
Household monthly income					
MYR5000 or less	5	8.8	12	21.4	0.060[a]
More than MYR5000	52	91.3	44	78.6	
Number of previous pregnancies					
One	24	42.1	33	58.9	0.201[a]
Two	21	36.8	15	26.8	
Three or more	12	21.1	8	14.3	
Number of children					
One	25	43.9	33	58.9	0.160[a]
Two	25	43.9	15	26.8	
Three or more	7	12.3	8	14.3	
History of miscarriage	5	8.8	0	0	0.057[b]
Primary care-taking time					
Daytime	1	1.8	0	0	0.552[a]
Evening or night	34	59.6	31	55.4	
Whole day	20	35.1	20	35.7	
Not the primary caretaker	2	3.5	5	8.9	
Place of postpartum confinement					
Confinement center	11	19.3	1	1.8	0.003[a]**
Home	46	80.7	55	98.2	
Breastfeeding	55	96.5	52	92.9	0.438[b]
Pre-pregnancy weight (kg), mean ± SD	53.7 ± 6.6		53.1 ± 9.3		0.673[c]
Pregnancy weight (kg), mean ± SD	68.4 ± 7.4		67.1 ± 11.1		0.487[c]
Postpartum weight (kg), mean ± SD	57.8 ± 7.4		57.6 ± 10.3		0.916[c]

[a]Chi-square test; [b]Fisher's Exact test; [c]Independent t-test; *p < 0.05; **p < 0.01

3.1.2 Pregnancy, postpartum and infant characteristics

Pregnancy, postpartum and infant characteristics were summarised in Table 2. CHM consumption was significantly associated with the method of delivery ($p < 0.05$); coincidentally, results found approximately double the proportion of mothers who had caesarean delivery to be consumers (29.8%, n = 17) than non-consumers (14.3%, n = 8). CHM consumption was significantly associated with infants' incidence of jaundice and episodes of night-time crying ($p < 0.05$); 20% more reported jaundice cases and 10% more reported night-time crying among consumers.

Three statistically significant pregnancy, infant and postpartum characteristics to CHM consumption were further subjected to odds ratio analysis (Table 3). Albeit not statistically significant, mothers consuming CHM demonstrated 2.5 times higher odds (95% CI 0.997 – 6.523) of undergoing a caesarean section delivery. Meanwhile, infants born to mothers consuming CHM had a significantly 2.2 times higher odds (95% CI 1.078 – 4.873) of developing neonatal jaundice. The odds ratio for frequent episodes of night crying was not established as there was no incident among non-CHM consumers. After adjusting for maternal age, personal monthly income and place of postpartum confinement, the odds ratio indicated that mothers consuming CHM was associated with a threefold increase in the likelihood of developing neonatal jaundice (95 CI 1.301 – 7.226), with statistical significance (Table 4).

3.1.3 Pattern and types of CHM use

CHM mothers reported their parents or parents-in-law as the main source of information regarding use of herbal medicines use during pregnancy and postpartum (n = 42, 53.8%), followed by traditional medicine practitioners (n = 19, 24.4%), articles or adverts in health magazines (n = 7, 9.0%), husbands, friends or siblings (n = 5, 6.4%) and doctor or nurse (n = 3, 3.8%). Primary purpose of CHM consumption was

Table 2. Maternal and infant characteristics during pregnancy and postpartum of CHM consumers and non-consumers

Pregnancy, infant and postpartum characteristics	Consumer (n = 57)		Non-consumer (n = 56)		p value
	n	%	n	%	
Threatened abortion	7	12.3	1	1.8	0.061[a]
Pregnancy-related illness	1	1.8	0	0	1.000[a]
Diagnosed with chronic illness	1	1.8	0	0	1.000[a]
Medication during pregnancy	1	1.8	0	0	1.000[a]
Caesarean delivery	17	29.8	8	14.3	0.047[b]*
Pre-term delivery	7	12.3	1	1.8	0.061[a]
Low birth weight	0	0	0	0	NA[#]
Low birth length	1	1.8	0	0	1.000[a]
Low head circumference	4	7.0	2	3.6	0.679[a]
Presence of jaundice	33	57.9	21	37.5	0.030[b]*
Received phototherapy[†]	21	63.6	11	52.4	0.412[b]
Frequent episodes of colic	5	8.8	1	1.8	0.206[a]
Frequent episodes of crying at night	6	10.5	0	0	0.027[a]*
Postpartum outpatient visit	2	3.5	0	0	0.496[a]
Medication during postpartum	1	1.8	0	0	1.000[a]

[†]Data from infants with presence of jaundice only; [a]Fisher's Exact test; [b]Chi-square test; [#]Not applicable; *p < 0.0

Table 3. Odds ratio and 95% confidence interval for pregnancy and birth outcomes

Pregnancy and birth outcomes	Odds ratio (consumer/ non-consumer)	95% confidence interval
Caesarean section delivery	2.550	0.997 - 6.523
Presence of neonatal jaundice	2.292	1.078 - 4.873*
Frequent episodes of crying at night	NA[#]	NA[#]

*95% CI does not include 1 [#] Not applicable

Table 4. Adjusted odds ratio with maternal age, personal monthly income and place of postpartum confinement, as well as the 95% confidence interval for the presence of jaundice

Presence of jaundice	Adjusted odds ratio (consumer/ non-consumer)	95% confidence interval
Presence of neonatal jaundice	3.067	1.301 - 7.226*

*95% CI does not include 1

improving health and energy (n = 54, 47.0%), facilitating wound healing (n = 23, 20.0%) and increasing production of breast milk (n = 18, 15.7%). CHM was usually obtained from local herbal stores (n = 39, 48.1%), parents or parents-in-law (n = 14, 17.3%) and traditional medicine practitioners (n = 11, 13.6%). Most CHM consuming mothers (n = 46, 80.7%) perceived CHM as "effective" and "brought desired effect".

The 4 most commonly consumed CHM were Bird's Nest (n = 28, 49.12%), Sheng Hua Tang (n = 28, 49.12%), Ba Zhen Tang (n = 27, 47.37%) and So Hup Pills (n = 23, 40.35%). Information on ingredients and medicinal properties of these CHM were detailed in Supplementary Table S2. Other commonly consumed CHM were Wu Jin Pills (n = 15, 26.32%), Ginseng (n = 15, 26.32%), Shi Quan Tang (n = 12, 21.05%), Si Wu Tang (n = 11, 19.30%), Du Zhong (n = 11, 19.30%), and Ning Shen Tang (n = 10, 17.54%).

3.1.4 Heavy Metal Quantification in CHM

Heavy metal quantification data was depicted in Figure 1. As, Cd and Pb were detected in every sample of all 4 types of CHM. The mean concentration of As, Cd, Cr and Pb in CHM are 188.11 ± 107.25 μg/kg, 104.18 ± 83.39 μg/kg, 11763.57 ± 20407.67 μg/kg and 538.24 ± 519.27 μg/kg respectively. The mean concentrations of each heavy metal in each specific CHM are as follows: 288.37 ± 70.33 μg/kg As, 120.38 ± 52.80 μg/kg Cd, 12768 ± 24897.85 μg/kg Cr and 470.70 ± 182.49 μg/kg Pb for Sheng Hua Tang; 139.20 ± 54.63 μg/kg As, 102.66 ± 89.35 μg/kg Cd, 7252.14 ± 7023.59 μg/kg Cr and 343.12 ± 319.80 μg/kg Pb for Ba Zhen Tang; 73.33 ± 32.87 μg/kg As, 18.52 ± 19.53 μg/kg Cd, 1128.46 ± 342.00 μg/kg Cr and 139.86 ± 67.93 μg/kg Pb for Bird's Nest; 242.95 ± 92.83 μg/kg As, 168.67 ± 69.35 μg/kg Cd, 25905.68 ± 28199.61 μg/kg Cr and 1157.67 ± 585.62 μg/kg Pb for So Hup Pills.

The lowest concentration of As and Pb were detected in So Hup Pills at 5 ± 0.4 μg/kg and 12.5 ± 5.0 μg/kg respectively. The lowest Cr level was detected in Ba Zhen Tang at 232.95 ± 45.5 μg/kg while the lowest Cd was detected in Bird's nest at 7 ± 0.3 μg/kg. The highest level of Cr and Pb were detected in So Hup Pills with the concentration of 91790.00 ± 9.90 μg/kg and 2332.50 ± 7.80 μg/kg respectively. The highest concentration of As (423.00 ± 7.10 μg/kg) was detected in Sheng Hua Tang while the highest level of Cd (366.00 ± 7.07 μg/kg) was detected in Ba Zhen Tang.

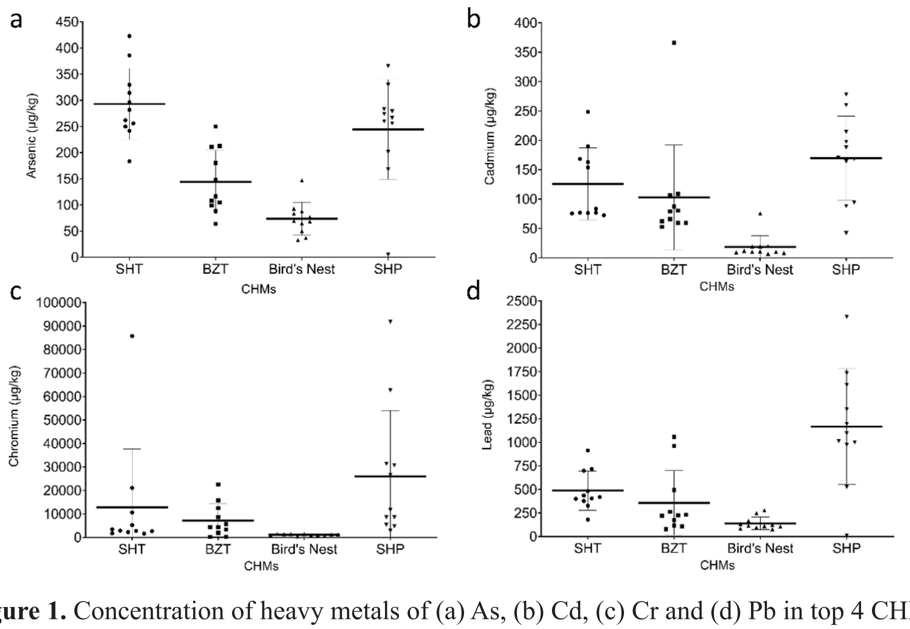

Figure 1. Concentration of heavy metals of (a) As, (b) Cd, (c) Cr and (d) Pb in top 4 CHM consumed during pregnancy and postpartum. Individual data are presented together with mean ± SD of 11 samples. CHMs: Chinese Herbal Medicines, SHT: Sheng Hua Tang, BZT: Ba Zhen Tang, SHP: So Hup Pills

3.1.5 Human Risk Assessments of Heavy Metals in CHM

Mean consumption rate (CR) were determined at 0.110 kg/day for Sheng Hua Tang, 0.102 kg/day for Ba Zhen Tang, 0.039 kg/day for Bird's nest and 0.005 kg/day for So Hup pills, while mean exposure frequency (Ef) was calculated as 4 days/year, 11 days/year, 9 days/year and 24 days/year for Sheng Hua Tang, Ba Zhen Tang, Bird's nest and So Hup Pills respectively. On the other hand, maximum CR were determined to be 0.110 kg/day for Sheng Hua Tang, 0.102 kg/day for Ba Zhen Tang, 0.070 kg/day for Bird's nest and 0.010 kg/day for So Hup pills; while EF were calculated as 14 days/year, 42 days/year, 80 days/year and 40 days/year for Sheng Hua Tang, Ba Zhen Tang, Bird's nest and So Hup Pills respectively. Average body weight (BW) of 68.4 kg was used for the calculation while average exposure time (AT) was determined as 365 days.

Hazard quotients for all metals were calculated to be less than 1 (HQ < 1) while hazard indexes were calculated to be < 1 (HI < 1) for all CHM (Table 5). The HQ for each heavy metal and their contribution to HI in all CHM were in descending order of As > Pb > Cd > Cr. HQ < 1 and HI < 1 indicated no significant non-carcinogenic health risks with As, Cd, Cr and Pb contamination in commonly consumed CHM during pregnancy and postpartum.

3.1.6 Risk Assessment for Individual Mothers

Hazard quotients were calculated according to consumption rate (CR), exposure frequency (Ef) and body weight (BW) reported by individual mothers. Hazard quotients (HQ_{mean} or HQ_{max}) were calculated by referring to the mean or highest concentration of As, Cd, Cr and Pb in CHM.

HQ_{mean}, HQ_{max} and HI_{mean} for all metals in all individual cases were calculated to be less than 1 (HQ < 1; HI_{mean} < 1). However, HI_{max} computation based on maximum detectable heavy metal levels revealed that four mothers corresponded to HI_{max} > 1 (HI_{max} 1.01 - 1.85). The mother with the highest HI of 1.85 had the lightest body weight among CHM consuming mothers. HI > 1 indicated a significant non-carcinogenic health risk with the possibility of adverse health effects from the exposure. Our findings demonstrated that HI can be more than one if the worst-case scenario of consuming the highest detected concentration of heavy metals together with a high consumption rate and a lighter body weight is considered.

3.2 Discussion

Our research investigated the various attributes and distinctions between users and non-users of CHM, focusing specifically on socio-demographic factors, pregnancy and birth outcomes, and postpartum characteristics and the associated health risk. According to the reported pattern of use for CHM, top 4 CHM were identified and analysed for heavy metal content while health risk assessments were carried out for usage of CHM during pregnancy and postpartum period. To the best of our knowledge, this is the first report associating CHM consumption and contamination to infant characteristics in Malaysian population.

Studies have shown that the pattern of use and factors influencing the consumption of herbal remedies varies across different geographical populations. For instance,

Table 5. Health risk assessments for exposure of As, Cd, Cr and Pb in CHM

CHM	HQ_{mean}				HQ_{max}				HI_{mean}	HI_{max}
	Pb	As	Cd	Cr	Pb	As	Cd	Cr		
Sheng Hua Tang	0.0021	0.0063	0.0021	0.00003	0.0215	0.0382	0.0192	0.0042	0.010	0.083
Ba Zhen Tang	0.00385	0.0078	0.0032	0.00013	0.0540	0.0607	0.0740	0.0038	0.015	0.192
Bird's Nest	0.0005	0.0013	0.0001	0.00001	0.0201	0.0529	0.0218	0.0003	0.002	0.095
So Hup Pills	0.0014	0.0014	0.0008	0.00004	0.0110	0.0088	0.0053	0.0012	0.004	0.026

in England, mothers who had given birth multiple times were more inclined to utilise herbal medicine during pregnancy (Holst et al. 2009), whereas in Australia, first-time mothers were more prone to using herbal remedies (Forster *et al.* 2006). Similarly, in Taiwan, mothers with higher levels of education showed a preference for CHM (Chuang *et al.* 2009), whereas the opposite trend was observed in Hong Kong, where there was an inverse relationship between CHM use and education levels (Ong *et al.* 2005). Previous studies on the Malaysian population demonstrated that the use of different types of traditional medicines was influenced by socio-demographic factors like ethnic group, age, education, income levels and so on (Siti *et al.* 2009; Yusoff *et al.* 2018). Our results indicated that CHM were mainly consumed by mothers of older age group of 36.3 ± 5.4 years old, with higher education and income levels. It was found that majority of Malaysian population belief that herbal products do not contain harmful chemicals and are free of side effects when compared to commercially available pharmaceutical drugs (Law and Soon 2013; Tang *et al.* 2016).

Mothers who consumed CHM showed higher incidence of jaundice in their newborn compared to non-consumers. In addition, CHM users reported higher episodes of crying at night. A study conducted locally also demonstrated a significance increase of neonatal jaundice development in infants of mothers who consumed herbal medicines during confinement (Teoh *et al.* 2013). Neonatal jaundice is generally caused by bilirubin accumulation in the blood, which can be due to failure in metabolism and excretion, oxidative stress-induced haemolysis or beta-glucuronidase activity related circumstances (Chee *et al.* 2018; Cohen et al. 2010). Heavy metals such as As, Cr, Pb, Cd induce their toxic effect through generation of oxidative stress (Flora *et al.* 2008). As heavy metals had been detected in CHM (Luo *et al.* 2021; Ting *et al.* 2013; Yap *et al.* 2018), there may be a risk of heavy metals transfer from mother to infant through umbilical cord prenatally or breastfeeding postpartum (Kim *et al.* 2015).

Jaundice among children due to hepatotoxicity had been associated with CHM ingestion but the exact cause was not clear (Zhu *et al.* 2015). Another study reported the association of musculoskeletal and connective tissues malformations in newborn with the consumption of a type of CHM, An-Tai-Yin during pregnancy (Chuang *et al.* 2006). We also found higher cases of caesarean section delivery in CHM consumers compared to their counterpart. The phenomenon was similarly observed in an early study where herbal medicine uses was associated with higher incidence of caesarean section delivery (Mabina *et al.* 1997). In fact, the use of herbal medicine during pregnancy and its potential adverse effects remains a topic of debate. While several studies have reported adverse outcomes during or after birth, many studies contradict these findings. For instance, a comprehensive systemic review carried out by Sarecka-Hujar and Szulc-Musioł (2022), of 74 online articles found associations between herbal remedies, such as, almond oil and preterm birth, raspberry leaf and cesarean delivery, licorice and preterm birth, and even maternal morbidity with African herbal medicine mwanaphepo. However, a set of 14 articles reported no adverse effects from the herbal medications they evaluated (Sarecka-Hujar and Szulc-Musiol 2022) (Zamawe *et al.* 2018). Studies on birth outcomes and neonatal effects could only be done via observational methods and are severely lacking in the current body of literatures. Our findings warrant for further exploration through different perspective including the consideration of pregnancy and postpartum use of CHM with greater number of participating mothers in different area to deduce a precise explanation for the observation.

Quality requirement from Drug Control Authority Malaysia mandated the permissible level of heavy metals concentration of Pb, As and Cd in herbal medicine to be less than 10 mg/kg, 5 mg/kg and 0.3 mg/kg respectively (National Pharmaceutical Regulatory 2021). These regulatory reference values are comparable to laws and requirements for permissible level of heavy metals in human diet from World Health Organization (WHO) and regulatory authorities of other countries. The seemingly high safety level and permissible level may give misleading proposition on the safety of consuming herbs during pregnancy since foetus has a higher toxicity risk with their relatively more sensitive and small body stature. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) from WHO had withdrawn tolerable intake for Pb and As citing no established health protective level for these metals, indicating the severe need to limit heavy metals in children's food (Wong *et al.* 2022). Pb was found to be highly neurotoxic even in low levels which could cause impaired brain development in children (Canfield *et al.* 2005). Epidemiological studies reported the manifestation of skin, neurological and gastrointestinal effects on young children exposure to As (Tsuji *et al.* 2004). Although most of our samples exhibited heavy metal levels that were well below the permissible level, it was still alarming that the Cd level in one of the samples of Ba Zhen Tang exceeded the limit of 0.3 mg/kg. Early life Cd exposure was shown to produce long-term health consequences as a result of its long half-life of 10 - 30 years in kidney (Chandravanshi *et al.* 2021). Environmental studies have also demonstrated that exposure to Cd during pregnancy and the early years of life may have an impact on the thyroid endocrine, growth hormone, and oestrogen systems (Takiguchi and Yoshihara 2006; Vahter *et al.* 2007). Throughout foetal development, Cd has the potential to impact vital organs, such as the nervous system, either directly or indirectly. Because Cd affects the metabolism of trace elements through a unique but not well-understood mechanism, its buildup in the placenta might hinder the transfer of other trace elements (such as Fe, Mn, Zn, Mo, and Cu) to the foetus (Zhou et al. 2019). During the development of foetuses, Zn and Fe are particularly important metals for the development of the brain and other systems (Chandravanshi *et al.* 2021).

Non-carcinogenic hazard index (HI) measured for all types of CHM was within the safety level. Nonetheless, our study may not reveal an accurate health risk as we did not measure and include the risk of other metals. Health risk may further escalate with increased duration of exposure from longer consumption period or number of pregnancies as heavy metals are prone to accumulate in the body (Singh *et al.* 2011). As an example, a study conducted in Romania reported a combined HQ > 1 for parsley, carrot roots, cabbage and lettuce although the individual HQ for each metal is in safe level (Harmanescu *et al.* 2011). This indicated that cumulative effects of different herb usage might pose a significant health risk if taken in the same period. Our findings emphasised the necessity for future studies on all types of toxic metal exposure in mother and child, and to focus on modifiable variable such as food intake, which may elucidate more comprehensively on maternal and infant characteristics during pregnancy and postpartum.

4. Conclusion

To summarise the findings, CHM use was favoured by older age group, higher education and income mothers. Infants born to CHM consumers had been found to have 3 times higher odds of developing jaundice compared to infants born to non-CHM consumers. The most popular CHM were Bird's Nest, Sheng Hua Tang, Ba Zhen Tang and So Hup Pills. Most of our samples exhibited heavy metal levels that were well below the government permissible level, it was still alarming that the Cd level in one of the samples of Ba Zhen Tang exceeded the limit of 0.3 mg/kg. Although no significant non-carcinogenic health risks were found, the presence of heavy metals in CHM and potential transfer from mother to foetus and infant raises concerns about the safety of consumption during pregnancy and the postpartum period. Insights into the impact of heavy metals from CHM use on the following generation may be gained by further longitudinal cohort study that allows for infant growth and development investigations across time. Our findings may serve as a key reference and safety information for CHM consumers and policymakers.

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Ethical statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Malaysia Research Ethics Committee (MREC) via approval code NMRR-15-990-25727 on 22nd Oct, 2015.

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