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Association between intake of soy isoflavones and blood pressure among urban and rural Malaysian adults

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ABSTRACT

Introduction: Intake of soy isoflavones has been shown to be beneficial in reducing blood pressure, a known cardiovascular risk factor. This study investigated the association between intake of soy isoflavones and blood pressure among multi-ethnic Malaysian adults. **Methods:** A total of 230 non-institutionalised Malaysians aged 18-81 years were recruited through multi-stage random sampling from urban and rural areas in four conveniently selected states. Participants were interviewed on socio-demographics, medical history, smoking status, and physical activity. Measurements of height, weight, waist circumference (WC), and blood pressure (BP) were taken. Information on usual intake of soy foods was obtained using a validated semi-quantitative food frequency questionnaire. **Results:** The mean intake of soy protein of both urban (3.40g/day) and rural participants (3.01g/day) were lower than the USFDA recommended intake level of soy protein (25.00g/day). Urban participants had significantly higher intake of isoflavones (9.35±11.31mg/day) compared to the rural participants (7.88±14.30mg/day). Mean BP levels were significantly lower among urban (136/81mmHg) than rural adults (142/83mmHg). After adjusting for age, gender, educational level, household income, smoking status, physical activity, BMI and WC, soy protein intake was significantly associated with both SBP (R^2=0.205, β=-0.136) and DBP (R^2=0.110, β=-0.104), whilst soy isoflavones intake was significantly associated with SBP (β=-0.131). Intake of 1 mg of isoflavone is estimated to lower SBP by 7.97 mmHg. **Conclusion:** Higher consumption of isoflavones among the urban participants showed an association with lower levels of SBP. Use of biological markers for estimating isoflavones levels is recommended to investigate its protective effects on blood pressure.

Keywords: Soy protein, soy isoflavones, adults, urban, systolic blood pressure

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INTRODUCTION

Cardiovascular disease (CVD) has been the leading cause of death in Malaysia since the 1980's (Noor Hassim *et al.*, 2016). Amiri *et al.* (2014) has reported that obesity, hypertension and hypercholesterolaemia were the most predominant CVD risk factors in Malaysia, induced by unhealthy lifestyle and predominantly made up of low-income Malaysians. According to the Fifth National Health and Morbidity Survey of Malaysia (2015), obesity, hypercholesterolaemia and hypertension accounted for 51.2%, 47.7%, and 30.3% respectively among Malaysians.

Urbanisation, characterised with rapid economic development, fosters adverse effects concerning population health status, which is further influenced by a sedentary lifestyle that further magnifies the risk of developing CVD (Amiri *et al.*, 2014). However, several Malaysian studies reported a higher prevalence of CVD risk factors among populations in rural areas (Ching *et al.*, 2018; Noor Hassim *et al.*, 2016) due to older age, lower educational status, higher prevalence of smokers, obesity, hypertension, diabetes, unhealthy diet and more likely, depression (Noor Hassim *et al.*, 2016).

Among the many risk factors of CVD, diet plays an important role in its development and prognosis (Amiri *et al.,* 2014). The Dietary Approaches to Stop Hypertension (DASH) demonstrated the impact of dietary composition in combating the incidence of CVD, of which intermediate sodium level could lower mean systolic blood pressure (SBP) compared to the usual control diet (Blumenthal *et al.,* 2010). Besides this, several foods and food groups have been reported for their potential cardioprotective effects. These include long-chain n-3 fatty acids, dietary fibre, phytochemicals and vegetable proteins, especially soy (Alissa & Ferns 2014). Soy-based foods have attracted scientific attention since 1999, when the United States Food and Drug Administration (FDA) approved the health claim that 25 g of soy protein daily, along with a diet low in saturated fat, may reduce the risk of CVD (USFDA, 2018). Further, soy isoflavones in soy protein have been reported to have similar efficacy and health benefits towards prevention of CVD by reducing blood pressure among selected populations (Beavers *et al.,* 2012).

There are a number of large prospective cohort studies among Asian populations, investigating whether habitual soy food or isoflavones consumption is related to the incidence of CVD. Cumulative evidence from randomised clinical trials (RCT) included in meta-analysis as reported by Beavers *et al.* (2012), indicated that exposure to soy isoflavones can modestly, but significantly, improve endothelial function as measured by flow-mediated dilation. The Shanghai Women's Health Study reported an inverse relationship between soy food intake and the risk of coronary heart disease (CHD) (Zhang *et al.*, 2012).

By contrast, no significant associations were found between long-term soy food, soy protein, and soy isoflavones consumption on CHD, stroke, and total CVD-related mortality in the Singapore Chinese Health Study (Talaei *et al.,* 2014). It was postulated that low consumption of soy food in Western cohorts made it difficult to determine longitudinal associations between intake of isoflavones and CVD incidence or mortality (Zamora-Ros *et al.*, 2012). These inconsistent findings call for further investigations on the association of isoflavones consumption and the risks of CVD among multi-ethnic Malaysian adults residing in urban and rural areas. It is hypothesised that CVD risk was higher in rural communities associated with lower isoflavones consumption.

MATERIALS AND METHODS

Recruitment of subjects

This cross-sectional study was part of the Malaysian population survey (Malaysian Community Salt Survey – MyCoSS). A sub-study to obtain data on isoflavones intake was conducted in four states of Malaysia namely, Kelantan, Terengganu, Pahang, and Johor that fell within the data collection period from October to December 2017. Informed consent was obtained from each participant, and ethical approval was obtained from the Universiti Kebangsaan Malaysia Medical Research and Ethics Committee (UKMMREC) (UKM1.21.3/244/NN-2017-142) and the Medical Research and Ethics Committee (MREC) of the Ministry of Health Malaysia (NMRR-17-3354-37402).

A total of 230 eligible participants were randomly selected from urban and rural areas or recognised as strata and achieved 100% response rate. The selection was provided by the Department of Statistics (DOS), Malaysia. The urban areas were development areas with a population of at least 10,000 and 60% of the population aged 15 years and above engaged in non-agricultural activities, while the remaining areas were classified as rural areas (DOS, 2015). The process of selecting a participant was cascading from a primary sampling unit (PSU), which is the cluster of enumeration blocks (EBs) to living quarters (LQs) to eligible persons and finally to sample the individual. When there was more than one eligible adult living in the same LQ, only one subject was selected using a Kish Table. Inclusion criteria were: Malaysian citizens aged 18-81 years old, non-institutionalised living status, and able to understand, communicate and speak well in Malay or English. Those who were pregnant and had been on isoflavone supplements for the past three months were excluded from this study.

Participants were interviewed to collect background data on:

1) socio-demographics: age, gender, ethnic, occupational, educational level and household income
2) medical history: diabetes mellitus (DM), hypertension, hypercholesterolaemia, heart diseases, stroke and kidney diseases
3) smoking status: categorised as never, current (smoked regularly in the last 12 months), and ex-smoker (stopped smoking more than 12 months ago)
4) dietary intake based on a semi-quantitative food frequency questionnaire (SFFQ) on isoflavones consumption

Habitual physical activity status was also obtained using a short form International Physical Activity Questionnaire (IPAQ) in a week was converted into metabolic equivalent task minutes per week (MET-minutes/week) and categorised as low (<600 MET-min/week), moderate (>600 MET-min/week) and high (>3000 MET-min/week).

Anthropometric measurements including height and weight were also taken and body mass index (BMI) was calculated and categorised based on World Health Organization (WHO) (1998) guidelines. Weight was measured using a validated and calibrated digital weighing scale (TANITA HD-319) and height using stadiometer SECA 213. Waist circumference (WC) was measured using SECA measuring tape and referred to WHO stepwise approach (WHO, 2008). Systolic (SBP) and diastolic blood pressures (DBP) were measured using a digital OMRON HBP-1300 and categorised as normal (systolic BP ≤130 mmHg/diastolic BP ≤80 mmHg) and hypertension (systolic BP >130 mmHg/ Diastolic BP >80 mmHg) (AHA, 2018).

Dietary intake of soy protein, isoflavones, daidzein and genistein

The usual intake of soy isoflavones, daidzein, and genistein of the participants were based on nine items in a semi-quantitative food frequency questionnaire (SFFQ) for soy products. The SFFQ was validated by Haron (2009) based on a soy SFFQ to estimate the intake of isoflavones among US adults (Frankenfeld *et al.*, 2002). The SFFQ was modified to take into account local soy products commonly consumed by Malaysians (Tee *et al.*, 1997). Unfried *tofu*, fried *tofu*, soft *tofu*, egg *tofu*, *fucok* (*tofu* skin), tempeh, boxed soy bean drink, homemade soy bean drink and *tofu fah* was selected to be included in the SFFQ. The serving size was based on soy products of the Malaysian Food Composition Table (Tee et al, 1999). Frequency of consumption and portion size (small, medium, large) consumed during the previous one month were asked of the participants and rated using a four-point scale, ranging from never, to how many times in a day, week or month. The isoflavone intake was determined by referring to analytical values outlined by Haron (2009) and computed using the following equation:

$$\frac{\text{Participant's portion size}}{\text{Reference portion}} \times \text{frequency} \times \text{isoflavones content (mg) of the food item}$$

Estimation of soy protein (g) intake was also derived from the Singapore Food Composition Database and the United States Department of Agriculture (USDA) Nutrient Data Laboratory. Data were entered into a nutrition database (Nutritionist Pro™ Version 3.1.10, Axxya System, Texas, USA) for analysis.

Statistical analysis

The data were analysed using Statistical Package for Social Sciences (SPSS) version 23.0. Descriptive statistics were used to determine the association between socio-demographics data, anthropometric measurements, and BP with soy phytochemicals intake, based on strata. Since the intakes of soy protein, isoflavones, daidzein, and genistein were not normally distributed, all of the contributions from soy components were transformed using $\log^{10}$. Chi-square contingencies test was used to determine the difference between categorical data.

The Simple Linear Regression (SLR) was used to determine the association between continuous data of soy proteins, isoflavones, daidzein and genistein intakes with SBP and DBP. Multiple linear regression (MLR) was performed to determine the predictors by controlling for other covariates.

RESULTS

Participants living in rural areas had significantly lower educational levels and household incomes compared to urban residents. The prevalence of smoking, DM, hypertension, and hypercholesterolaemia were not statistically significant between the urban and rural subjects. The physical activity level was significantly higher among the rural respondents (Table 1).

There was no significant difference in mean body mass index (BMI) between men and women from urban and rural areas. However, the percentage of obesity among urban men was higher (66.7%) than their rural counterparts (33.3%). High mean values of waist circumferences (88.01 ± 13.39 cm) and SBP (141.56 ± 19.50 mmHg) were more prevalent among rural women (68.6%) as compared to urban women. A higher prevalence of rural women (68.6%) had abdominal obesity compared to urban women.

Table 1. Socio-demographics, medical history, smoking status, physical activity, anthropometric measurements and blood pressure according to urban and rural participants

Parameter	*N*	*Urban (N=94)*	*Rural (N=136)*	*p-value*
Gender				0.058
Men	102	48 (47.1%)	54 (52.9%)	
Women	128	46 (35.9%)	82 (64.1%)	
Age				0.901
18 – 39	60	26 (43.3%)	34 (56.7%)	
40 – 64	122	49 (40.2%)	73 (59.8%)	
> 64	48	19 (39.6%)	29 (60.4%)	
Age (*M*±*SD*)	230	50.68±14.23	50.76±15.34	0.969
Occupation				0.364
Unemployed	89	34 (38.2%)	55 (61.8%)	
Public/private sector	55	27 (49.1%)	28 (50.9%)	
Self-employed	86	33 (38.4%)	53 (61.6%)	
Ethnic				0.050
Malay	189	72 (38.1%)	117 (61.9%)	
Chinese	35	18 (51.4%)	17 (48.6%)	
Indian	6	4 (66.7%)	2 (33.3%)	
Educational level				0.020*
Did not go to school	25	6 (24.0%)	19 (76.0%)	
Primary/secondary school	157	63 (40.1%)	94 (59.9%)	
Tertiary education	48	25 (52.1%)	23 (47.9%)	
Household income				0.011*
<500	18	4 (22.2%)	14 (77.8%)	
500-2500	131	47 (35.9%)	84 (64.1%)	
>2500	81	43 (53.1%)	38 (46.9%)	
Household income (*M*±*SD*)	230	3793.09±4417.85	2206.54±195.63	0.000**
Medical history				
Heart diseases	13	7 (53.8%)	6 (46.2%)	0.243
Stroke	2	0 (0.00%)	2 (100%)	0.349
Diabetes mellitus	32	12 (37.5%)	20 (62.5%)	0.415
Hypertension	55	25 (45.5%)	30 (54.5%)	0.262
Hypercholesterolaemia	60	26 (43.3%)	34 (56.7%)	0.381
Kidney diseases	6	4 (66.7%)	2 (33.3%)	0.188
Smoking status				
Former	78	36 (46.2%)	42 (53.8%)	0.243
Current	51	20 (39.2%)	31 (60.8%)	0.785

Physical activity				0.238
Category 1 - Low physical activity level	54	19 (35.2%)	35 (64.8%)	
Category 2 - Moderate physical activity level	95	45 (47.4%)	50 (52.6%)	
Category 3 - High physical activity level	81	30 (37.0%)	51 (63.0%)	
Physical activity (*M*±*SD*) (MET-min/week)	230	2588.14±2875.25	3872.47±5475.02	0.038*
Body mass index (%)				
Men				0.322
Underweight (< 18.5)	2	1 (50.0%)	1 (50.0%)	
Normal (18.5 to 24.9)	47	20 (42.6%)	27 (57.4%)	
Overweight (25 to 29.9)	35	15 (42.9%)	20 (57.1%)	
Obese (> 30)	18	12 (66.7%)	6 (33.3%)	
Women				0.176
Underweight (< 18.5)	5	1 (20.0%)	4 (80.0%)	
Normal (18.5 to 24.9)	43	21 (48.8%)	22 (51.2%)	
Overweight (25 to 29.9)	45	13 (28.9%)	32 (71.1%)	
Obese (> 30)	35	11 (31.4%)	24 (68.6%)	
BMI (*M*±*SD*) (kg/m^2)				
Men	102	26.18±4.82	24.61±3.69	0.066
Women	128	26.27±5.39	27.70±5.86	0.175
Waist circumference (%)				0.030*
Low risk (men WC≤93.9 cm; women WC≤79.9cm)	114	50 (43.9%)	64 (56.1%)	
Increased risk (men WC 94.0 to 101.9cm; women, WC 80.0 to 87.9cm)	46	11 (23.9%)	35 (76.1%)	
High risk (men WC≥102.0cm; women, WC≥88.0cm)	70	33 (47.1%)	37 (52.9%)	
Waist circumference (*M* ±*SD*) (cm)				
Men	102	91.10 ± 10.87	88.48 ± 8.41	0.173
Women	128	86.01 ± 12.86	88.01 ± 13.39	0.414
Blood pressure (%) (mmHg)				0.495
Normal (Systolic BP ≤130 / diastolic BP ≤80)	131	57 (43.5%)	74 (56.5%)	
Hypertension (Systolic BP >130 / Diastolic BP >80)	99	37 (37.4%)	62 (62.6%)	
Blood pressure (*M* ± *SD*) (mmHg)				
Systolic		136.05 ± 19.50	141.56 ± 19.50	0.049**
Diastolic		81.52 ± 12.82	83.13 ± 13.12	0.357

*Significant difference at $p<0.05$ using chi-square contingencies test
**Significant difference at $p<0.05$ using independent samples t-test

Table 2. Mean intakes of soy protein, isoflavones, daidzein, and genistein

Parameter	N	Soy protein (g/day)		Isoflavones (mg/day)		Daidzein (mg/day)		Genistein (mg/day)	
		M±SD	p-value	M±SD	p-value	M±SD	p-value	M±SD	p-value
Strata									
Urban	94	3.40±3.85	0.014*	9.35±11.31	0.017*	6.47±8.00	0.027*	2.91±4.24	0.002*
Rural	136	3.01±5.27		7.88±14.30		5.91±10.41		1.96±4.77	
Gender									
Men	102	3.31±5.25	0.525	10.0±15.73	0.132	6.89±10.29	0.114	3.10±6.24	0.317
Women	128	3.06±4.30		7.28±10.58		5.54±8.79		1.75±2.44	
Ethnic									
Malay	189	2.84±4.73	0.007*	7.36±12.97	0.000*	5.36±9.21	0.000*	2.01±4.65	0.000*
Non-Malay	41	4.72±4.49		13.67±12.93		9.74±10.00		3.90±3.89	
Age									
18 – 39	60	3.16±3.77	0.553	10.05±14.77	0.088	7.27±10.16	0.078	2.76±5.82	0.565
40 – 64	122	2.95±4.55		7.33±11.08		5.44±8.79		1.91±3.23	
> 64	48	3.73±6.13		9.46±15.68		6.52±10.34		2.96±5.62	
BMI									
Underweight	7	1.63±1.12	0.394	2.13±2.11	0.159	1.88±2.16	0.276	0.48±0.49	0.063
Normal	90	3.14±4.30		7.89±10.87		6.10±8.76		1.78±2.83	
Overweight	80	3.55±5.00		9.81±14.16		6.70±9.58		3.11±5.42	
Obese	53	2.85±5.32		8.33±15.68		5.91±11.04		2.42±5.65	
WC									
Low risk	114	2.80±3.82	0.130	7.75±12.56	0.281	5.59±8.91	0.405	2.17±4.68	0.146
Increased risk	46	3.57±4.56		9.49±12.59		6.92±9.21		2.57±4.24	
High risk	70	3.51±6.03		9.02±14.52		6.53±10.60		2.49±4.66	
BP									
Normal	131	3.17±4.09	0.341	8.50±12.31	0.397	6.00±8.45	0.603	2.50±4.71	0.293
Hypertension	99	3.17±5.50		8.46±14.26		6.32±10.74		2.15±4.40	

*Significant difference at $p<0.05$ using Mann Whitney test

Table 3. Relationship between phytoestrogens intake and blood pressure of urban and rural participants

Phytochemicals	*Systolic blood pressure*					*Diastolic blood pressure*				
	SLR		*MLR*†			*SLR*		*MLR*†		
	β (95% CI)	*p-value*	*Adjusted* β (95% CI)	R^2	*p-value*	β (95% CI)	*p-value*	*Adjusted* β (95% CI)	R^2	*p-value*
Soy protein	-0.124 (-9.09, 0.20)	0.061	-0.162 (-10.37, -1.27)	0.205	0.012*	-0.202 (-7.20, -1.62)	0.002*	-0.201 (-7.31, -1.45)	0.110	0.004*
Isoflavones	-0.144 (-10.76, -0.57)	0.030*	-0.131 (-10.25, -0.10)	0.197	0.046*	-0.100 (-5.51, 0.73)	0.132	-0.112 (-5.99, 0.60)	0.086	0.108
Daidzein	0.119 (-0.25, 6.12)	0.071	0.103 (-0.48, 5.57)	0.192	0.099	0.078 (-0.78, 3.12)	0.237	0.066 (-0.98, 2.96)	0.079	0.321
Genistein	0.101 (-0.52, 4.24)	0.125	0.089 (-0.61, 3.87)	0.189	0.152	0.073 (-0.64, 2.26)	0.272	0.057 (-0.81, 2.09)	0.078	0.386

†The model was adjusted for age, gender, ethnic, educational level, household income, smoking status, physical activity, BMI and waist circumference
*Significance at *p*-value<0.05

Table 4. Relationship between isoflavones intake by quartiles and CVD risk parameters of urban and rural participants

CVD risk parameters		*Quartile range for isoflavones intake (mg/day)*				*p-value*
		Q1 = 0.74	*Q2 = 2.37*	*Q3 = 5.72*	*Q4 = 25.29*	
BMI						
M±SD		26.26±5.40	26.82±5.41	26.52±5.55	25.87±4.51	0.803
Obese (>30 kg/m^2), *n* (%)	53	14 (26.4)	14(26.4)	15(28.3)	10(18.7)	
WC						
M±SD		87.48±13.53	89.47±12.85	87.97±11.54	88.58±10.51	0.824
High risk (men WC≥102.0 cm; women WC≥88.0 cm), *n* (%)	70	18 (25.7)	19 (27.1)	14(20.0)	19 (27.1)	
SBP						
M±SD		145.75±25.94	138.77±18.95	135.93±19.18	136.74±19.59	0.038*
% High blood pressure (SBP ≥ 130 mmHg), *n* (%)	146	39 (26.7)	38 (26.0)	37 (25.3)	32 (21.9)	
DBP						
M±SD		84.38±13.72	82.76±11.86	82.09±13.64	80.62±12.72	0.236
% High blood pressure (DBP ≥ 80 mmHg), *n* (%)	140	38 (27.1)	37 (26.4)	33 (23.6)	32 (22.9)	

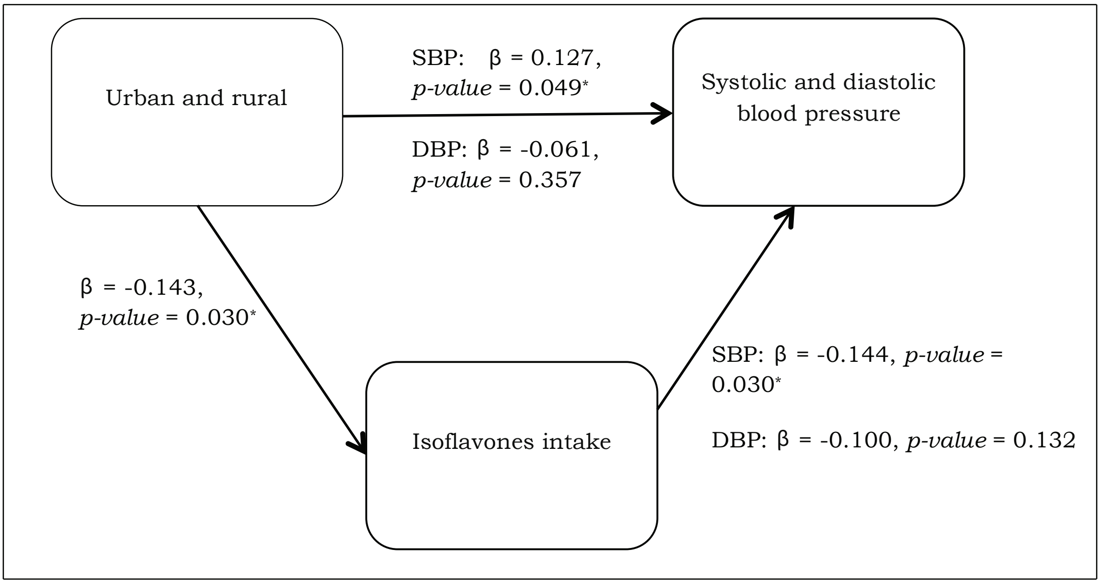
**p*<0.05, indicates significant difference between isoflavones intake and CVD risk parameters using ANOVA test.

Mean intake of soy protein, isoflavones, daidzein and genistein were significantly different (p<0.05) between subjects from urban and rural areas. Urban respondents had higher intakes of these isoflavones (9.35 ±11.31mg/day) compared to the rural respondents (7.88±14.30mg/day) (p<0.05). Soy foods were popular among non-Malays with higher mean intake of isoflavones (13.67 ± 12.93 mg/day) compared to Malays (7.36 ±12.97mg/day) (p<0.05) (Table 2).

There was a significant association between soy protein intake of all participants with DBP (R^2=0.015, β=-0.202) and between intake of isoflavones with SBP (R^2=0.021, β=-0.144) (Table 3). After adjusting for age, gender, education level, smoking status, physical inactivity, BMI and WC, intake of soy protein was significantly associated with both SBP (R^2 =0.205, β=-0.162) and DBP (R^2=110, β=0.104). Intake of soy isoflavones remained significantly associated with SBP (R^2=0.197, β=-0.131) after adjusting for those covariates. The higher the intake of isoflavones, the lower the SBP with 1 mg of isoflavones associated with a lower level of SBP by 7.97 mmHg. Daidzein and genistein intakes showed no significant association with all the CVD risk parameters being investigated in this study.

Intakes of isoflavones at higher quartiles (Q3 and Q4) were associated with lower mean values of the studied CVD risk parameters (Table 4). However, only SBP level showed a significant difference across the quartiles.

The mediation analysis (Figure 1) shows a significant) effect of urban/rural strata effect on blood pressure changes in response to soy isoflavones consumption. After controlling for isoflavone intakes as a covariate, urban and rural strata no longer showed a significant difference on SBP level. This finding indicates that the intake of isoflavones could lower the SBP of the participants.



*p<0.05, indicated there is significant difference between isoflavones intake with the parameter using SLR test

Figure 1. Mediation analysis of strata, isoflavones intakes, and blood pressure.

DISCUSSION

The findings of this study revealed that adults in rural areas had a higher risk of CVD compared to the urban as indicated by high SBP and abdominal obesity. This could be due to rural participants being older with lower educational levels, lower household income, and higher prevalence of smokers, as also reported in other study (Noor Hassim *et al.*, 2016). Low socioeconomic status in the rural area, as assessed by occupation, education and income level was closely related to poor diet quality (Psaltopoulou *et al.*, 2017) and sedentary lifestyles (Amiri *et al.*, 2014), thus leading to higher risk of CVD events.

The high number of smokers among rural participants has led to increased risk of CVD and other non-communicable diseases. Their low educational level has increased the prevalence of hypertension and smoking (Psaltopoulou *et al.,* 2017) due to a lack of knowledge on the adverse effects of tobacco. Besides, low awareness and knowledge on the risks of CVD among rural populations has further attenuated the desire for a healthy lifestyle and regular health monitoring (Aminde *et al.*, 2017). The lack of sensibility in living a healthy lifestyle has led to poor dietary intake, inadequate physical activities and delay in seeking health or medical treatment especially among rural population (Aminde *et al.*, 2017).

Estimation of intake of isoflavones

The mean of soy protein intake among adults in the urban and rural areas observed in this study was 3.40g/day and 3.01g/day, respectively. These intake levels were much lower compared to the 25.00g/day intake of soy protein suggested by the United States Food and Drug Administration (USFDA) (1999) and the Ministry of Health Malaysia (2011). The intake of soy isoflavones among urban respondents (9.35±11.31mg/day) was higher compared to that in the rural area (7.88±14.30 mg/day). This may be attributed to media exposure about soybean nutrition and its benefits among urban residents (Sadeghian *et al.,* 2014). Urban Malaysian adults showed high acceptability towards soybean products due to its nutritive value (Murad *et al.*, 2014).

The intake of isoflavones in this study was much lower compared to the level reported by another Asian study (Wada *et al.,* 2013), but higher than that reported in a Western population of 0.50 - 0.80mg/day (Zamora-Ros *et al.*, 2012). Most of the Asian studies from Japan and China reported high intake of soy isoflavones as soy foods have been part of their diets culturally (Yamori *et al.*, 2017; Wada *et al.,* 2013). There are also differences in isoflavones content in soybeans, depending on both genetic and environmental factors including climate, the location of the plantation, planting date, crop year and storage conditions (Teekachunhatean, Hanprasertpong & Teekachunhatean, 2017).

In this study, Chinese and Indians had a higher intake of soy isoflavones, particularly from *tofu*, compared to Malay respondents. Shurtleff & Aoyagi (2013) reported that most Chinese and Indian consumed soy food in their daily diet. Indian vegetarians tend to consume high amount of soy products as their source of protein (Shurtleff & Aoyagi, 2013).

Association between intake of isoflavones and and blood pressure

This study found that soy protein and soy isoflavones intake had a significant association with blood pressures (BP). Soy protein intake showed a significant association with DBP, while soy isoflavones intake showed a significant association with SBP. It is known that blood pressure, especially SBP, is important as an independent risk factor for coronary events, stroke, heart failure, and chronic kidney disease (Richardson *et al.,* 2016).

After adjusting for the covariates including age, gender, ethnic, educational level, household income, smoking status, physical activity, WC, and BMI, mean SBP was significantly lower among those who consumed higher quintiles of soy isoflavones, indicating a potentially cardioprotective effect due to soy intake. A meta-analysis of 11 trials by Liu *et al.* (2012) reported that isoflavones intake of 65–153mg/d demonstrated a significant, larger effect on lowering SBP among hypertensives (5.9mmHg).

Factors including racial differences influence the capacity of intestinal flora to convert the isoflavones glycosides, daidzein to its metabolites (Taku *et al.,* 2010). These metabolites have been reported to play a crucial role in the clinical efficacy of soy isoflavones in relations to cardiovascular health (Taku *et al.* 2010). The BP-lowering effect of isoflavones may also be attributed to the activation of endothelial nitric oxide synthase (eNOS) and stimulation of nitric oxide (NO) production (Richardson *et al.,* 2016). A study has suggested that isoflavones attenuate blood pressure elevation through acceleration of NO production and inhibition of inflammation (Yu *et al.* 2016). An increased in soy consumption has been associated with higher plasma concentrations of NO due to its direct non-genomic effects on eNOS activity in human aortic endothelial cells. (Si *et al.,* 2012).

Limitations of study

This study estimated the isoflavones intake using subjective dietary assessments which do not estimate normal eating intakes. Sodium intake, which is a major contributor to high blood pressure, was not included in this study. The CVD risk parameters included in this study were limited to anthropometric and blood pressure measurements. Hence, additional clinical data are suggested for future studies to determine the effect of different levels of isoflavones intake on the risk of cardiovascular diseases and health, preferably through a longitudinal study design.

CONCLUSION

Mean SBP was higher among rural participants and this was found associated with lower intake of soy isoflavones. The use of biological markers for estimating intake levels of isoflavones is suggested through a prospective study design or clinical trials to investigate the protective effects of isoflavones on blood pressure and other CVD risks.

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Authors' contributions

NFMR, conducted the study, data analysis and interpretation, prepared the draft of the manuscript and reviewed the manuscript; SS, principal investigator, conceptualized and designed the study, led the data collection, advised on the data analysis and interpretation, assisting in drafting of the manuscript and reviewed the manuscript; HH, led the data collection, advised on the data analysis and interpretation and reviewed the manuscript; RA, led the data collection, advised on the data analysis and interpretation and reviewed the manuscript; FO, led the data collection, advised on the data analysis and interpretation and reviewed the manuscript.

Conflict of interest

The authors report no conflict of interest to disclose in this work.

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