

Association of dietary inflammatory potential (DIP) and endothelial function biomarkers among female nurses of Isfahan hospitals

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Abstract

Background Dietary inflammatory index (DIP) is a new dietary index designed to evaluate individuals' diets. In addition, adhesion molecules are important biomarkers for assessing endothelium inflammation that they related to atherosclerosis and cardiovascular disease. Also, there is no study for assessing the association between adhesion molecules and DIP until now as well as other studies that assessed the relationship between dietary inflammatory index or DIP have controversy. **Aim of the Work** The purpose of this cross-sectional study was to determine the correlation between DII and endothelial markers such as E-selectin, intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (sVCAM-1) among female nurses from Isfahan. In this study, dietary inflammatory potential (DIP) was used instead of DII. **Patients and Methods** This study was performed on 420 healthy nurses. The nurses were selected by random cluster sampling method from private and public Isfahan hospitals. A validated food frequency questionnaire (FFQ) was applied to assess the dietary inflammatory potential. A fasting blood sample was collected for measuring the plasma levels of the endothelial markers and other variables. **Results** After adjusting different potential confounders, no statistical association was found between DIP and sICAM-1, E-selectin and sVCAM-1 in model I ($P=0.57$, 0.98 and 0.45), model II ($P=0.57$, 0.98 and 0.45) and model III ($P=0.67$, 0.92 and 0.50) in comparison to the crude group ($P=0.35$, 0.83 and 0.49 , respectively). **Conclusion** The results revealed that the plasma levels of endothelial markers including E-selectin, sICAM-1, and sVCAM-1 were not significantly associated with DIP in female nurses.

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Patients and Methods

This study was performed on 420 healthy nurses. The nurses were selected by random cluster sampling method from private and public Isfahan hospitals. A validated food frequency questionnaire (FFQ) was applied to assess the dietary inflammatory potential. A fasting blood sample was collected for measuring the plasma levels of the endothelial markers and other variables.

Results

After adjusting different potential confounders, no statistical association was found between DIP and sICAM-1, E-selectin and sVCAM-1 in model I ($P=0.57, 0.98$ and 0.45), model II ($P=0.57, 0.98$ and 0.45) and model III ($P=0.67, 0.92$ and 0.50) in comparison to the crude group ($P=0.35, 0.83$ and 0.49 , respectively).

Conclusion

The results revealed that the plasma levels of endothelial markers including E-selectin, sICAM-1, and sVCAM-1 were not significantly associated with DIP in female nurses.

Keywords : Dietary inflammatory potential, sICAM-1, endothelial markers, sVCAM-1, E –selectin

What's known?

This is a novel study in women for evaluating the association between the dietary inflammatory index and sICAM-1, sVCAM-1, and E-selectin.

One previous study that assessed the relationship between DII and adhesion molecules including ICAM-1 VCAM-1 in adolescent. They found a positive association between DII and sVCAM-1, however, similarly to our finding, they did not represent any association between DII and sICAM-1 concentrations. Moreover, some recent studies evaluated the correlation between DII and cardiovascular diseases. However, they did not find any association between DII and cardiovascular ischemic diseases, myocardial infarction in women inversely men. Although, some studies found a positive relationship between DII and carotid plaque severity, diabetic mellitus, high blood pressure, cholesterol and obesity.

What's new?

Furthermore, current study confirmed the result of Shivappa et al about ICAM-1. But, opposite to their findings, we did not observe any correlation between DII and sVCAM-1. Whereas, these two studies did not perform on the same age and sex groups.

There is no study assessing the association between DII and E-selectin.

Introduction

Atherosclerosis is a continuing inflammatory state of the vessels [1]. The progression of atherosclerosis leads to myocardial infarction and sudden death [2]. It is believed that atherosclerosis is an inflammatory condition that is largely responsible for cardiovascular disease (CVD) mortality [3, 4]. Endothelial dysfunction contributes to the pathogenesis of vascular disease and plays an important role in CVD as well [5, 6]. Endothelial dysfunction is characterized by impaired activity of endothelial derived relaxant factors and increased activity of vasoconstrictor factors. However, cell adhesion molecules (CAM) including E-selectin, intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (sVCAM-1) accelerate atherosclerosis [4, 7-9].

Adhesion molecules are normally expressed by the endothelium. They also play a role in leukocyte rolling, firm adhesion, and transmigration. Furthermore, they are associated with a variety of pathophysiological processes and inflammatory disorders. Atherosclerotic lesions and fatty streaks increase the expression of sICAM-1, sVCAM-1, and P- and E-selectin on the human endothelial cells [10, 11]. E-selectin plays an important role in acute inflammation [12-14]. Moreover, sICAM-1 and sVCAM-1 are involved in chronic inflammation [15, 16]. Leukocyte adhesion is an important component of some vascular diseases and atherogenesis. Leukocyte recruitment occurs in a multistep process and selectin, which is expressed on the activated

endothelial cells, is involved in the initial rolling process of leukocytes [12, 17]. The leukocyte surface has sites for selectin ligand [18]. $\beta 1$ and $\beta 2$ integrin are expressed on leukocytes and act as binding sites for sVCAM-1 or sICAM-1. Furthermore, selectin plays a role in the initial rolling process of leukocytes whereas sICAM-1 and sVCAM-1 mediate leukocyte arresting and firm adhesion [12, 18-20].

Dietary inflammatory potential (DIP) is a new dietary index designed to evaluate the individual's diets. DIP is a tool to assess the potential inflammatory and anti-inflammatory properties of a diet based on food elements. In this index, values of +1, 0, and -1 indicate pro-inflammation, indifferent and anti-inflammation reactions, respectively [21]. Actually, DIP is a resource to assess pro-inflammatory effects of food ingredients based on anti-inflammatory functions [21, 22]. DIP has been linked to a variety of systemic biomarkers such as interleukin 6 (IL-6), tumor necrosis factor alpha (TNF- α), C-reactive protein (CRP) and several metabolic diseases such as CVD, cancers, and diabetes. Many studies have found that DIP is associated with the risk of metabolic syndrome and cardiovascular diseases [23-28].

Many studies have reported a positive association between DIP and CVDs [29, 30]. Due to the increase in the global risk of CVDs and related diseases in the world, it is important to find healthy dietary patterns with low inflammatory scores to tackle inflammation and CVDs. The purpose of this study was to determine the association between DIP and endothelial markers such as sICAM, sVCAM, and E-selectin in female nurses working in Isfahan hospitals.

2. Materials and methods

2.1. Participants

Four hundred and eighty healthy female nurses aged >30 years participated in this cross-sectional study. The participants were selected randomly from seven public and private hospitals in Isfahan, Iran. The female nurses with a history of diabetes, malignancy, infections, and CVDs were excluded. Furthermore, the subjects who did not complete the FFQ questionnaire were also excluded from the study. Finally, 420 nurses were enrolled in the study. The participants fill in a consent form based on ... university of medical sciences ethics rules for participating on this study.

The study protocol was approved by university of medical sciences (IR.TUMS.VCR.REC.1399.584).

2.2. Blood sampling

Blood samples were collected from the participants after 12 hours of fasting to measure the levels of endothelial markers, lipid profile, and fasting blood glucose. Then, the sample were centrifuged for 30-45 minute and frozen at 70°C. The levels of sVCAM-1, sICAM-1, and E-selectin were measured using commercial ELISA kits (Biosource International and Bender MED Systems) according to the manufacturer's instructions. ELISA kits were also used to measure low-density lipoprotein (LDL) and high-density lipoprotein (HDL).

2.3. Dietary inflammatory score

The method developed by Shivappa *et al* was applied to calculate the DIP scores of the diets. The Food Frequency Questionnaire (FFQ) was used to determine the dietary intake [21]. In the Iranian dietary pattern, 29 out of 45 items of DII are very common, including Macronutrients (energy, carbohydrates, fat, protein, fiber), Fat (cholesterol, saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA)), Water-soluble vitamins (pyridoxine, folic acid, niacin, thiamin, ascorbic acid and riboflavin). Fat-soluble vitamins (A,D and E), Minerals (iron, magnesium, zinc, and selenium), as well as caffeine, β -carotene, onion, garlic, pepper, and black tea [31]. Other DIP items that were uncommon in the Iranian dietary regimen were omitted from the list of FFQ.

The intake of the above dietary items was adjusted according to the daily energy intake [32]. A z-score was generated for all of the 29 items of the FFQ list for each participant. For each subject, the "standard global mean" was subtracted from the mean consumed food and divided by "global standard deviation". The global means and standard deviations were obtained by the method developed by Shivappa *et al* [21]. To decrease the skewness of the variables, the variables were converted to a centered percentile score. This

score was then extended by the impact for every item [21]. The DIP scores of all foods were summed to calculate the overall score. More positive values indicated a higher inflammatory dietary potential.

2.4. Assessment of other variables

A computerized scale was used for weight measurement (to the nearest 0.1 kg). The subjects were asked to wear light clothing with no shoes. The height was also measured on the same visit day. Finally, weight (kg) and height (m) were used to calculate the body mass index (BMI) according to the following formula: weight (kg)/ height (m)².

The International Physical Questionnaire was used to evaluate daily physical activity [33, 34] as MET-hour per week. The factors such as education level, family size, and economic status were inquired from all the participants to determine their socioeconomic status. Moreover, covariate data including age, marital status, menopause situation, past medical history, smoking or medication/supplementation history were self-reported by all the participants.

2.5. Statistical analysis

The final analysis was performed on 420 individuals. Energy adjustment of the variables was carried out using the residual method. After completing the FFQ, the data were entered into an Excel datasheet and daily dietary intakes were compared using the IBM SPSS version 26 (IBM SPSS Statistics for Win, Armonk, NY) and Nutritionist IV (N4) software. Since there were three DIP groups (tertiles), one-way ANOVA was used for continuous variables including age, body mass index (BMI), weight, waist circumference, physical activity, and systolic and diastolic blood pressure, and Pearson's chi-square test was applied to categorical variables such as oral contraceptive (OCP) use, current corticosteroid use, menopause, marital status, overweight/obesity and socioeconomic status. Similarities between the energy intakes of the participants were adjusted by linear regression. Finally, the associations between DIP and E-selectin, ICAM, and VCAM in three tertiles was analyzed using ANCOVA.

3. Results

The mean±SD age of the participants was 34.44±7.27, 34.59±6.8 and 36.47±7.4 years in the 1st, 2nd, and 3rd tertile, respectively. The demographic characteristics of the subjects are presented in Table 1.

The distribution of the DIP score between tertiles is shown in Table 2. Large differences in DIP scores were observed for fat (P-value:0.04), riboflavin (P-value<0.001), folic acid (P-value<0.001), cobalamin (P-value=0.005), ascorbic acid (P-value<0.001), vitamin A (P-value<0.001), beta carotene (P-value<0.001), zinc (P-value<0.001), tea (P-value=0.002), magnesium (P-value<0.001), onion (P-value<0.001), fiber (P-value<0.001), caffeine (P-value=0.03), SAFA (P-value=0.02), and cholesterol (P-value<0.01) between the tertiles.

The mean±SD plasma levels of endothelial markers in different tertiles are shown in Table 3. There was no significant association between DIP and E-selectin in the crude model (P-value= 0.35) compared to model I (P-value= 0.57), model II (P-value= 0.57) and model III (P-value= 0.67) after adjusting for potential confounders (Figure 1).

The results showed no significant association between DIP and the plasma level of sICAM-1 in the crude model (P-value: 0.83) compared to model I (P-value: 0.98), model II (P-value: 0.98) and model III (P-value: 0.92) after adjusting for potential confounders (Figure 2).

In addition, no significant association was found between DIP and the plasma level of sVCAM-1 in the crude model compared to model I (P-value: 0.49), model II (P-value: 0.45) and model III (P-value: 0.50) after adjusting for potential confounders (Figure 3).

4. Discussion

No association was observed between dietary inflammatory potential (DIP) and endothelial biomarkers including E-selectin, sVCAM-1 and sICAM-1 in the participants. This dissociation remained significant

after adjusting for possible confounders. This is the first study of the association between adhesion molecules and DIP. Other studies assessed the correlation between DIP and cardiovascular disease.

Adhesion of circulating molecules, including E-selectin, sICAM-1 and sVCAM-1, plays an essential role in endothelial dysfunction and atherosclerosis [14, 35-39]. Furthermore, reactive oxygen species (ROS) activate endothelial markers by inducing E-selectin, sICAM-1 and sVCAM-1. It has been reported that sICAM-1 plays an important role as a predictor of CVD [40]. Moreover, the sVCAM-1 expression represents the inflammatory conditions of the vascular walls and predicts fatal coronary artery disease in the future [39, 41]. Plasma levels of endothelial markers such as sE-selectin and sICAM-1 correlate with prognosis [11]. Many studies have assessed the correlation of DIP with CVD.

The results of the present study are consistent with a study by Imran khan *et al* who carried out a cohort study on 1111 subjects to evaluate the relationship between DIP and cardiovascular disease (CVD). The results showed no a significant correlation between DIP and CVD in females while a significant relationship was found in male subjects [42]. Similarly, Gabriela Pocovi-Gerardino *et al* conducted a cross-sectional study on 105 women with a mean age of 45.4 years old and found no significant correlation between the DIP score and CVD markers [43]. A study of 585 women aged 50-55 years old by Linda E. T. Vissers *et al* failed to show any correlation between DIP and CVD, ischemic heart disease, and myocardial infarction (MI) [44]. Furthermore, a prospective case-control study of 100000 participants showed no significant relationship between DII and MI [45].

By contrast, Bondonno *et al* reported that a high DIP score was associated with atherosclerotic vascular disease in women aged over 70 although they did not find any association between DIP and carotid plaque severity [46]. Moreover, Stefanos Tyrovolas *et al* carried out a dose-dependent study to assess the correlation between DIP and CVD risk factors. They found a significant correlation between DIP and CVD risk factors such as diabetes mellitus, obesity, hypertension, and hypercholesterolemia. In addition, the participants with a high DIP score in the 3rd and 4th quartile had at least one CVD risk factor in comparison to the participants in the 1st quartile [47].

It was difficult to sort out consistent results with our findings because many studies were carried out on subjects with unhealthy conditions. Moreover, there were differences between the studies in terms of the sample size. The geographic dietary pattern may also affect the results. Furthermore, many studies did not measure the plasma levels of sICAM-1, sVCAM-1 and E-selectin directly. Therefore, more studies are required to assess the correlation between endothelial markers and the DIP score.

This study had some limitations. For example, it had a cross-sectional design and therefore no conclusions can be made regarding causality. Moreover, there were some unknown confounders including shift time, bias in reporting food items, and difference in the dietary pattern between nurses in private and public hospitals, which could affect the results. Studies with larger sample sizes are required to obtain concrete results.

Conclusion

In summary, the findings suggest that the plasma levels of endothelial markers including E-selectin, ICAM-1 and sVCAM-1 have no significant correlation with dietary inflammatory potential in females.

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Conflict of interest:

The authors have no conflict of interest to declare.

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Table 1 characteristics of individuals by tertiles of dietary inflammatory potential (means+SD)

P-value ^a	P-value ^a	Tertiles of energy by DIP	Tertiles of energy by DIP	Tertiles of energy by DIP	Variables
		T3=129	T2=134	T1=133	
0.04	0.04	34.44±7.27	34.59±6.8	36.47±7.4	Age(years)
0.49	0.49	63.2±10.32	69.2±82.7	63.0±8.7	Weight(kg)
0.85	0.85	23.97±3.65	24.0±3.80	24.2±3.37	BMI(kg/m ²) ^b
0.89	0.89	81.04±10.82	80.51±9.83	81.02±9.91	WC(CM)
0.05	0.05	95±101	78±77	60±79	PA(MET-h/wk)
0.24	0.24	107±1.24	109±1.20	108±1.04	SBP ¹ (mmHg)
0.08	0.08	68±0.97	70±1.05	71±0.88	DBP(mmHg)
0.84	0.84	5.9	7.4	5.9	Current OCP use (%)
0.67	0.67	0.7	2.2	1.5	Current corticosteroid use(%)
0.30	0.30	4.4	4.4	8.1	Menopausal (%)

P-value ^a	P-value ^a	Tertiles of energy by DIP	Tertiles of energy by DIP	Tertiles of energy by DIP	Variables
0.87	0.87	73.9	73.5	71.3	Married (%)
0.55	0.55	43	36.9	37.7	Overweight or obese (%)
0.34	0.34	22.3 48.9 28.7	34.7 40 25.3	24.4 44.4 31.1	SES (%) ^c High Medium Low
BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, OCP: oral contraceptives	BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, OCP: oral contraceptives	BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, OCP: oral contraceptives	BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, OCP: oral contraceptives	BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, OCP: oral contraceptives	BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, OCP: oral contraceptives

1. achieved from chi-square for categorical variables and analysis of variance for continues variables.
2. High SES; socioeconomic status was defined based on income, educational level, family size, renting the house, being owner of the house or house area, being owner of the car and number of the cars and kind of the car(s), number of bedrooms and determination of who was in charge of the family.
3. Body mass index [?]²⁵

Table 2. dietary inflammatory potential intake of participants after adjusted energy (mean±SD)

	Tertile of energy –energy adjusted DIP	Tertile of energy –energy adjusted DIP	Tertile of energy –energy adjusted DIP
Nutrients	T1(n=136)	T2(n=137)	T2(n=137)
Protein	124±98	135±139	102±99
Fat	103±17	117±88	102±21
Carbohydrate	338±59	321±61	335±71
Thiamin	3±2	5±25	2±2
Riboflavin	1.8±0.51	1.6±0.39	1.4±0.47
Niacin	18.9±3	18.8±3	18.4±5
Pyridoxine	2.2±0.6	2.6±8	1.6±0.6
Folic acid	410±121	304±41	226±54
Cobalamin	4.7±2	5±2	4±2
Ascorbic acid	281±111	181±50	126±40
Vitamin A	1928±939	1276±302	887±335
Vitamin E	64±16	69±19	65±21
Beta carotene	1527±897	904±291	582±311
Vitamin D	1.4±1.5	2.2±11	0.9±1.3
Selenium	0.04±0.16	0.48±5	-0.01±0.17
Zinc	10±4	10±6	8±4
Iron	22±6	25±49	20±8
Tea	356±263	324±316	242±220
Magnesium	326±59	267±35	216±46
Onion	54±34	40±27	29±19
Garlic	1.9±0.17	1.9±0.25	2±0.002
Fiber	10±3	7±2	5±1

	Tertile of energy –energy adjusted DIP	Tertile of energy –energy adjusted DIP	Tertile of energy –energy adjusted DIP
Caffeine	82±57	83±127	59±50
Pepper	10±7.3	10±8.7	8±8.5
SAFA	25±8	27±14	23±9
PUFA	40±9	46±44	39±11
MUFA	32±8	47±146	30±9
CHOL	234±85	263±93	232±99

SAFA; saturated fatty acid, PUFA; poly unsaturated fatty acid, MUFA; monounsaturated fatty acid. CHOL; cholesterol.

Table 3. Index of endothelial functions across tertile categories of dietary inflammatory potential

Tertile of energy- adjusted DIP

	T1(n=133)	T2(n=136)	T3(n=135)	P for trend ^e
E-selectin (ng/L)	E-selectin (ng/L)	E-selectin (ng/L)	E-selectin (ng/L)	E-selectin (ng/L)
Crude	81.6±4.5	85.5±4.5	93.7±4.5	0.35
Model I ^b	80±5.6	88±5.3	80±6.0	0.57
Model II ^c	79±5.6	88±5.3	81±6.1	0.57
Model III ^d	79±5.7	88±5.8	82±6.7	0.67
sICAM-1 (mg/L)	sICAM-1 (mg/L)	sICAM-1 (mg/L)	sICAM-1 (mg/L)	sICAM-1 (mg/L)
Crude	221±6.68	211±6.63	213±6.65	0.83
Model I	215±10.9	225±10.2	215±11.7	0.98
Model II	215±10.9	225±10.4	215±10.8	0.98
Model III	214±9.5	213±9.6	212±11.1	0.92
sVCAM-1 (mg/L)	sVCAM-1 (mg/L)	sVCAM-1 (mg/L)	sVCAM-1 (mg/L)	sVCAM-1 (mg/L)
Crude	503±11.76	482±11.63	509±11.67	0.49
Model I	479±23.2	496±21.8	515±25.3	0.45
Model II	478±23.1	490±22.0	516±25.2	0.45
Model III	477±24.3	492±24.8	502±28.9	0.50

1. Values are mean±SE in the tables and were compute by the use of ANCOVA.
2. Model I: adjusted for physical activity (MET-h/wk), marital status (categorical), socioeconomic status (categorical). energy intake, age, current corticoid steroids use (yes or no), menopausal status (yes or no), current OCP use (yes or no), systolic blood pressure, diastolic blood pressure.
3. Model II: Further adjusted for body mass index.
4. Model III: more adjusted for lipid profiles and blood sugar.
5. *p* -Value was calculated from linear regression of adhesion molecules (E-selectin, sICAM-1 and sVCAM-1) on a categorical variable of dietary in index intake.

Figure 1. The E-selectin plasma concentration in tertiles (mean±SEM)

Figure 2. The ICAM-1 plasma concentration in tertiles (mean±SEM)

Figure 3. The sVCAM-1 plasma concentration in tertiles (mean±SEM)

Figure 1

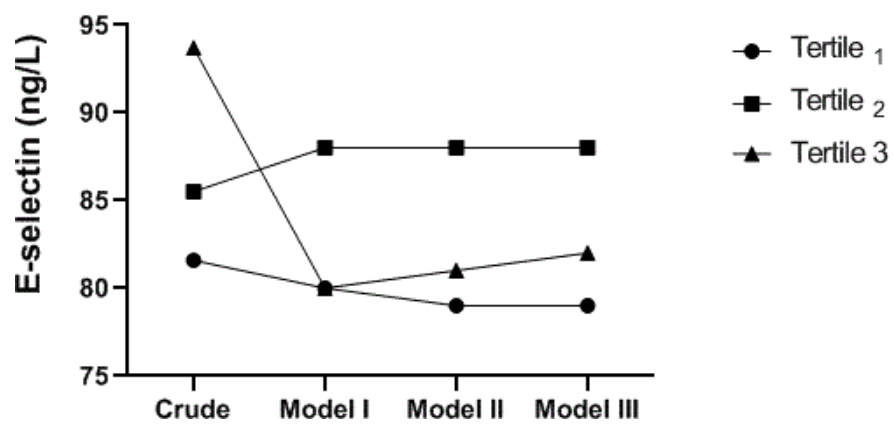


Figure 2

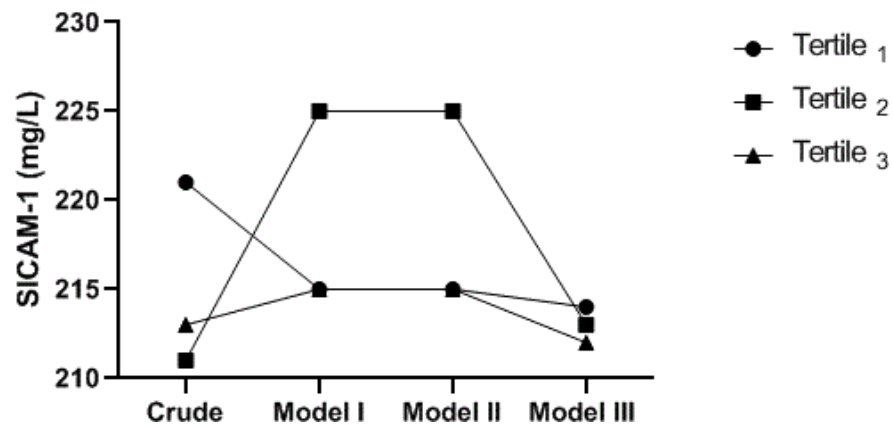


Figure 3

