SciMedCentral
Journal of Endocrinology, Diabetes & Obesity

Research Article

A Dietary Pattern Characterized by a High Consumption of Vegetables and Fruits is related to lower Concentrations of Serum Bilirubin in Japanese women

Akie Hirata[1]*, Keizo Ohnaka[2], Maya Tanaka[1], Zhenjie Wang[1], Makiko Morita[1], Kengo Toyomura[1], Suminori Kono[1] and Ryoichi Takayanagi[3]

[1]*Department of Preventive Medicine, Kyushu University, Japan*
[2]*Department of Geriatric Medicine, Kyushu University, Japan*
[3]*Department of Medicine and Bioregulatory Science, Kyushu University, Japan*

***Corresponding author**
Akie Hirata, Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University, Maidashi 3-1-1, Higashi-ku, Fukuoka 812-8582, Japan; Tel: +81-92-642-6913; Fax: +81-92-642-6911; E-mail: hirata-a@phealth.med.kyushu-u.ac.jp

Submitted: 20 December 2013
Accepted: 18 January 2014
Published: 20 January 2014
ISSN: 2333-6692

Keywords
- Bilirubin
- Dietary pattern
- Oxidative stress
- Fruit
- Vegetable

Abstract

Background: Bilirubin is a potent anti-oxidant, and has been shown to be inversely related to diabetes mellitus, cardiovascular diseases, and stroke. Few studies have reported the relation of specific foods to serum bilirubin, but none has examined the association between dietary patterns and bilirubin. We investigated the relation between dietary patterns and serum bilirubin in Japanese men and women.

Methods: The study subjects were men and women aged 49 to 76 years who participated in the baseline survey of a cohort study of lifestyle-related diseases between February 2004 and August 2007. The dietary patterns were derived from principal component analysis of the intakes of 31 foods and food groups ascertained by the food-frequency questionnaire. Analysis of covariance was used to estimate geometric means of serum bilirubin according to quintiles of the dietary pattern scores with adjustment for potential confounding factors.

Results: Only one dietary pattern was distinguishable, and the dietary pattern was characterized by high intakes of vegetables and fruit. The dietary pattern was not related to serum bilirubin concentrations in men, and showed an inverse association with bilirubin in women (trend $P = 0.04$).

Conclusions: A dietary pattern represented by high intakes of vegetables and fruit was inversely associated with serum bilirubin in women, but not in men.

INTRODUCTION

Bilirubin is an end product of heme catabolism and is a potent endogenous anti-oxidant at low concentrations [1-3]. Bilirubin scavenges reactive oxygen species (ROS) in vitro and reduces oxidant-mediated cellular damage in vivo [1]. Bilirubin also has an inhibitory effect on the production of ROS by inhibiting the activity of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, an important source of ROS production [1]. Anti-oxidative and anti-inflammatory effects of bilirubin have drawn much interest in the occurrence of diseases related to oxidative stress. Mildly elevated levels of serum bilirubin have consistently been shown to be associated with lower risks of cardiovascular diseases in many prospective studies, as reviewed elsewhere [2,3]. A limited evidence also suggests protective associations of serum bilirubin with diabetes mellitus and stroke [4]. Furthermore, a large prospective study reported that serum bilirubin was associated with a significant decrease in total mortality [5]. Thus factors associated with serum bilirubin are also of interest. Several studies reported that serum bilirubin concentrations were correlated inversely with body mass index (BMI) and smoking [5-7] Studies on dietary factors and serum bilirubin are very few [8-10]. In these studies, citrus fruits and cruciferous vegetables were reported to be associated with lower bilirubin concentrations in subjects with a low-activity genotype of uridine 5'-diphosphate (UDP)-glucuronosyltransferases (UGT) 1A1 [8-10]. To our knowledge, none has addressed the association between dietary patterns and bilirubin. The dietary pattern analysis has been recognized as a useful tool in nutritional epidemiology. Foods and nutrients are consumed in combination and may interact with each other [11]. The analysis of dietary pattern is more efficient than that of single nutrients or specific foods in the research on diet and diseases [11-13]. The aim of the present study was to investigate the relation between dietary patterns and serum concentrations of bilirubin in Japanese adults.

MATERIALS AND METHODS

Study subjects

The study subjects were participants in the baseline survey of the Kyushu University Fukuoka Cohort Study, living in the East Ward of Fukuoka City, aged 49 to 76 years. The study was approved by the Ethics Committee of the Kyushu University Faculty of Medical Sciences. The subjects aged 50 to 74 years were invited by mail to participate in the study, and were informed of details of the baseline and follow-up surveys. Between February 2004 and August 2007, a total of 12948 persons (5817 men and 7131 women) participated in the survey. The participation rate was 24%. All subjects gave written informed consent before participating in the study. Stored serum for the measurement of bilirubin was available for 12942 participants.

In the present study, we excluded the subjects who were under medical care for coronary artery disease, arteriosclerosis obliterance, stroke, cancer, chronic liver disease, chronic renal failure, or diabetes mellitus under medication; those with a prior history of myocardial infarction, coronary angioplasty, or stroke; those with abnormal laboratory tests: serum creatinine > 3.0 mg/dL, glycated hemoglobin (HbA_{1c}) > 6.5%, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >120 U/L, C-reactive protein (CRP) > 10 mg/L, bilirubin > 3.0 mg/dL; and those whose information on covariates was missing. A total of 2605 subjects with these exclusion criteria were excluded. We further excluded 208 subjects who were in the top 1% or bottom 1% of total energy intake. A total of 10129 subjects (4167 men and 5962 women) remained in the analysis.

Baseline survey

Details of the baseline survey were described previously [14]. Each participant completed a self-administered questionnaire and underwent blood pressure measurement, anthropometric measurements (height in cm and body weight in kg), and venous blood drawing. The questionnaire inquired about the smoking habits and alcohol intake, physical activity, dietary intake, diseases under current or previous treatment, use of drugs, and others.

Past smokers were distinguished from lifelong non-smokers, and the average number of cigarettes smoked per day and years of smoking were ascertained. Past alcohol drinkers were distinguished from lifelong non-drinkers. Current alcohol drinkers reported frequencies and amounts of intake of 5 different alcoholic beverages on average in the past year. The total ethanol intake per day was estimated on the basis of beverage-specific ethanol concentrations. Questions on physical activity ascertained the amount of time for three types of leisure-time physical activities (light, moderate, and heavy) over the previous year. The intensity of each physical activity was determined in terms of metabolic equivalent (MET) value [15] and expressed as a sum of MET multiplied by time in hours spent in the activity (MET-hr). BMI was calculated as weight (kg) divided by squared height (m^2).

In the dietary assessment, we used a validated 47-item food-frequency questionnaire developed by Tokudome et al. [16,17], with slight modification; replacing a single question on alcohol intake with questions on 5 alcohol beverages (sake, shochu, beer, whiskey/brandy, and wine) and adding questions on 6 non-alcohol beverages (green tea, black tea, oolong tea, coffee, vegetable juice, and fruit juice). We used a total of 31 foods and food groups, excluding the alcohol items for the dietary pattern analysis. Details of the dietary assessment were described elsewhere [14]. Average intakes over the previous year of each food item were ascertained. For most items, the participants reported consumption frequency by choosing 1 of 8 options (almost null, 1–3 times/mo, 1–2 times/wk, 3–4 times/wk, 5–6 times/wk, 1 time/d, 2 times/d, or ≥3 times/d). The consumption frequencies and amounts were ascertained regarding 3 items of staple foods (rice, bread, and noodles) eaten at breakfast, lunch, and supper; 6 frequency options (almost null, 1–3 times/mo, 1–2 times/wk, 3–4 times/wk, 5–6 times/wk, or daily) were given for the staple foods. The size of bowl and number of bowls were ascertained for rice consumption. Number of slices/pieces and bowls per meal were also ascertained for bread and noodle consumption respectively. The reported frequency of consuming each food other than staple foods was converted to a frequency of consumption per week; the following values were assigned: almost null, 0; 1–3 times/mo, 0.5; 1–2 times/wk, 1.5; 3–4 times/wk, 3.5; 5–6 times/wk, 5.5; 1 time/d, 6.5; 2 times/d, 10.5; and ≥ 3 times/d, 17.5 times/wk. Regarding the staple foods, values of weekly frequency (0–6.5) were assigned. The portion size of each food item other than staple foods was in accordance with the amount used by Tokudome et al. [18] or typical serving size. Total dietary energy intake and nutrient intake were estimated with reference to the Food Composition Tables in Japan [19-23].

Laboratory measurements

Bilirubin concentrations were measured using serum stored at −80°C, and were assayed by absorptiometric assay with chemical oxidation by vanadic acid [24] HbA_{1c} and serum concentrations of high-sensitivity CRP were measured at the baseline survey. HbA_{1c} was assayed by using a latex agglutination turbidimetry, and CRP was assayed by using a latex-enhanced immunonephelometric assay on a Behring Nephelometer II analyzer (Dade Behring, Marburg, Germany). HbA1c, CRP, and bilirubin were measured at an external laboratory (SRL, Hachiohji, Japan).

Recorded information was referred to regarding eight items of serum biochemistry including AST, ALT, and creatinine if these measurements had been done in the past year. When recorded information was not available, 5 mL of venous blood was taken for the measurements, and serum samples were shipped to an external laboratory (SRL, Hachiohji, Japan).

Statistical analyses

Several food items were aggregated into food groups on the basis of similar nutrient characteristics or hypothesized biological effects (**Appendix**). Individual food items, constituting distinct items on their own, were remained as such without aggregation. Intakes (grams) of these foods and food groups were adjusted to the energy of 2000 kcal/d by using the regression residual method. Then we performed principal component analysis based on the energy-adjusted intakes of 31 foods and food groups to derive dietary patterns in men and women combined, because the identified dietary patterns were qualitatively similar between men and women in sex-specific analyses. We determined dietary patterns with eigenvalues, the scree test, and the interpretability of the factor. The factor score for a specified dietary pattern was calculated for each participant by summing intakes of foods and food groups weighted by their factor loadings. We arbitrarily used quintiles of the factor score as cutoffs.

The distribution of bilirubin values was skewed to the right side, and we used the natural logarithm of the values. Analysis of covariance was used to calculate adjusted geometric means and 95% confidence intervals (CI) of serum bilirubin according to quintile categories of the dietary pattern score. Because there were distinctive differences in some covariates between men and women, we always performed the sex-specific analysis regarding the association between dietary patterns and bilirubin. The selected confounding variables were BMI, smoking (never, past, and current smoking with a consumption of < 20 or ≥ 20 cigarettes/day), alcohol intake (never, past, and current drinking with an intake of < 30, 30 to 59 or ≥ 60 mL of alcohol/day in men and < 10, 10 to 19 or ≥ 20 mL of alcohol/day in women), and physical activity (sex-specific quartiles of MET-hr/week for leisure time activity). The trend of the association was assessed by using multiple linear regression analysis, with ordinal values assigned to the quintile categories of each dietary pattern. Two-sided P values < 0.05 were regarded as significant. All analyses were performed by using Statistical Analysis System (SAS) version 9.2 (SAS Institute, Cary, NC).

RESULTS

Characteristics of the study subjects were shown for men and women separately in (Table 1). Women were less likely to be smokers and alcohol drinkers. Men had higher total energy intakes. Serum concentrations of high-sensitivity CRP were lower in women, while median of serum bilirubin concentrations did not differ by sex.

In the principal component analysis, only one dietary pattern was distinguishable with an eigenvalue of 4.5. There were 8 other components showing an eigenvalue > 1.0. The eigenvalue of the second component decreased by 2.2, but the subsequent changes in the eigenvalues of the 8 components were very small with a range of 0.02 to 0.67. The dietary pattern was named as vegetable and fruit dietary pattern because of the highest loadings for vegetables and fruit (Table 2), and the dietary pattern accounted for 14.5% of the variance in food and food group intakes.

The characteristics of the subjects according to quintiles of the vegetable and fruit dietary pattern score were shown in (Table 3). In brief, both men and women with a higher score of the dietary pattern were less likely to be smokers and alcohol drinkers and were more likely to be older and physically active in leisure time. BMI was not associated with the dietary pattern. As for nutrient intakes, subjects with higher scores of the vegetable and fruit dietary pattern had higher intakes of anti-oxidative vitamins.

Geometric means of serum bilirubin concentrations according to quintile categories of the vegetable and fruit dietary pattern

Table 1: Characteristics of the study subjects by sex*

Variable	Men (*n* = 4167)	Women (*n* = 5962)
Age (years), mean (SD)	62.3 (6.8)	61.8 (6.7)
Current smoking (%)	31.3	6.0
Current alcohol use (%)†	73.4	27.3
Body mass index (kg/m^2), mean (SD)	23.5 (2.7)	22.5 (3.1)
Leisure time activity (MET-hr/wk)	5 (2-6)	5 (1-14)
Total energy intake (kcal/d), mean (SD)	1594 (348)	1376 (273)
Serum bilirubin (mg/dL)	0.5 (0.3-0.7)	0.5 (0.4-0.6)
Serum aspartate aminotransferase (U/L)	22 (19-27)	21 (19-25)
Serum alanine aminotransferase (U/L)	21 (16-28)	17 (14-22)
Serum C-reactive protein (mg/L)	0.48 (0.26-1.01)	0.37 (0.20-0.76)
Glycated hemoglobin (%)	5.0 (4.8-5.3)	5.1 (4.8-5.3)

*Variables are median (interquartile range) unless otherwise specified.
†Consumed once per week or more frequently in the past year.

Table 2: Factor loadings for the vegetable and fruit dietary pattern in men and women combined (*n* = 10129).

Food and food group*	Factor loading
Green-yellow vegetables	0.76
Other vegetables	0.73
Mushrooms	0.67
Potatoes	0.62
Fruit	0.61
Seaweed	0.54
Soy foods	0.49
Yogurt	0.46
Japanese-style sweets	0.44
Black tea	0.36
Fish products	0.32
Fish and other marine foods	0.30
Nuts	0.29
Fish	0.28
Oils	0.28
Green tea	0.27
Western-style sweets	0.27
Red meat	0.23
Poultry	0.23
Milk	0.23
Processed meat	0.22
Fish roe	0.22
Bread	0.20
Vegetable juice	0.19
Fruit juice	0.19
Egg	0.18
Liver	0.13
Oolong tea	0.06
Noodles	0.05
Coffee	0.05
Rice	-0.32

*Component foods are listed in **Appendix**.

Table 3: Characteristics and nutrient intakes of subjects according to quintiles of the vegetable and fruit dietary pattern score.

	Quintile of vegetable and fruit dietary pattern score					
Variable	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Trend *P****
Men						
n	1641	1090	730	470	230	
Age (*y*), mean	60.9	61.7	63.8	64.8	65.8	<.0001
Current smoking (%)	41.0	29.3	24.6	21.7	14.0	<.0001
Current alcohol use (%)	80.9	74.0	68.8	63.2	54.2	<.0001
Body mass index (kg/m^2), mean	23.5	23.5	23.5	23.5	23.7	0.72
High physical activity (%) †	40.7	50.3	55.6	60.7	57.6	<.0001
Total energy (kcal/d), mean	1572	1557	1620	1647	1727	<.0001
Nutrient intake, geometric mean ‡						
Carbohydrates (g/d)	255	255	254	256	249	0.23
Protein (g/d)	53	62	67	71	77	<.0001
Total fat (g/d)	35	44	50	53	59	<.0001
α-carotene (µg/d)	113	212	280	355	430	<.0001
β-carotene (µg/d)	1416	2512	3284	4083	5033	<.0001
α-tocopherol (mg/d)	5	7	8	9	11	<.0001
Vitamin C (mg/d)	74	112	139	165	196	<.0001
Women						
n	384	936	1296	1556	1790	
Age (*y*), mean	60.2	60.9	61.3	61.9	63.0	<.0001
Current smoking (%)	22.7	8.3	5.8	4.6	2.8	<.0001
Current alcohol use (%)	38.5	33.6	29.5	25.6	21.9	<.0001
Body mass index (kg/m^2), mean	22.7	22.5	22.5	22.4	22.6	0.97
High physical activity (%) †	30.7	38.6	46.2	47.5	54.2	<.0001
Total energy (kcal/d), mean	1279	1280	1307	1373	1499	<.0001
Nutrient intake, geometric mean ‡						
Carbohydrates (g/d)	275	274	269	267	260	<.0001
Protein (g/d)	57	64	68	77	77	<.0001
Total fat (g/d)	41	47	51	54	59	<.0001
α-carotene (µg/d)	150	247	311	392	507	<.0001
β-carotene (µg/d)	1734	2611	3301	4174	5396	<.0001
α-tocopherol (mg/d)	6	7	8	9	11	<.0001
Vitamin C (mg/d)	97	127	152	179	219	<.0001

* Based on linear regression analysis for continuous variables and the Mantel-Haenszel chi-square test for categorical variables, with ordinal scores assigned to the quintile categories.
† MET-hr/week above the sex specific-median.
‡ Nutrient intakes were energy-adjusted to 2000 kcal/day.
Abbreviations: Q: Quintile; **MET:** Metabolic equivalent.

score are shown in (Table 4). The vegetable and fruit dietary pattern was not related to serum bilirubin concentrations in men in either age-adjusted or multivariate-adjusted analyses (P for trend = 0.63, 0.64, respectively). In women, while the dietary pattern was unrelated to bilirubin in the age-adjusted analysis (P for trend = 0.63), the multivariate-adjusted geometric mean was statistically significantly lower with higher scores of the dietary pattern (P for trend = 0.04).

DISCUSSION

This was the first study that examined the association between dietary patterns and serum bilirubin. In the present study population of middle-aged Japanese men and women, only one dietary pattern, characterized by high intakes of vegetables and fruit, was recognizable. This dietary pattern showed an inverse relation to serum bilirubin concentrations in women, but not in men.

Table 4: Geometric means and 95% confidence intervals (CI) of serum bilirubin concentrations (mg/dL) according to quintile categories of the vegetable and fruit dietary pattern score in men and women (*n* = 10129)*.

	Quintile of vegetable and fruit dietary pattern score					
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**Trend *P*†**
Men						
n	1641	1090	730	470	236	
Age-adjusted	0.55 (0.54-0.56)	0.55 (0.53-0.56)	0.54 (0.53-0.56)	0.55 (0.53-0.57)	0.54 (0.51-0.56)	0.63
Multivariate-adjusted‡	0.55 (0.54-0.56)	0.54 (0.53-0.56)	0.54 (0.53-0.56)	0.55 (0.53-0.57)	0.54 (0.51-0.56)	0.64
Women						
n	384	936	1296	1556	1790	
Age-adjusted	0.46 (0.45-0.48)	0.47 (0.46-0.48)	0.47 (0.46-0.48)	0.47 (0.46-0.48)	0.47 (0.46-0.47)	0.63
Multivariate-adjusted‡	0.48 (0.46-0.50)	0.47 (0.46-0.49)	0.47 (0.46-0.48)	0.47 (0.46-0.48)	0.46 (0.45-0.47)	0.04

* Geometric means were obtained from analysis of covariance.

† Based on multiple linear regression analysis, with ordinal values of 0-4 assigned to quintile categories of the dietary pattern.

‡ Adjusted for age (years), body mass index (< 20.0, 20.0 to 22.4, 22.5 to 24.9, 25.0 to 27.4, ≥ 27.5 kg/m^2), smoking (life-long nonsmoker, past smoker, or current smoker with a consumption of < 20 or ≥ 20 cigarettes/day), alcohol consumption (life-long nondrinker, past drinker, and current drinking with a intake of < 30, 30 to 59, or ≥ 60 mL of alcohol/day for men, < 10, 10 to 19, or ≥ 20 mL of alcohol/day for women), leisure-time physical activities (sex-specific quartiles of MET-hr/week).

Abbreviations: CI: confidence interval; **Q:** Quintile; **MET:** Metabolic equivalent.

A limited number of studies have investigated the influence of dietary factors on serum concentrations of bilirubin. Because specific phytochemicals are known to induce UGT1A1, an enzyme glucuronidating bilirubin, the associations between specific vegetables and fruit and serum bilirubin have been examined with reference to *UGT1A1* genotypes [8-10]. One study reported that intakes of cruciferous vegetables were associated with lower bilirubin concentrations in men and women combined who had a low-activity genotype of *UGT1A1*, i.e., homozygosis of *UGT1A1**28 polymorphism [8]. Another study showed lower bilirubin concentrations in relation to the consumption of citrus fruit in women, but not in men, who were homozygous for *UGT1A1**28 [9]. In a feeding trial [10], as compared with a diet without either vegetables or fruit, a diet with crucifers, soy, and citrus resulted in a decrease in serum bilirubin concentrations in women as a whole, but not in men, although the decrease was confined to women with the low-activity genotype of *UGT1A1*. The present findings are partly compatible with these previous observations although the *UGT1A1* genotypes were not considered. Phytochemicals activate aryl hydrocarbon receptor (AhR) [25-27], a positive regulator of *UGT1A1* transcription [28]. Estrogen receptor α (ERα) was shown to increase the activity of AhR-dependent transcription [29]. Ligand-binded AhR can serve as a positive transcriptional co-regulator of ERα [30]. The activation of the transcriptional function of both AhR and ERα may result in lower bilirubin concentrations exclusively in women.

Several intervention trials addressed the effects of the intake of vegetables and fruit on oxidative stress markers or antioxidant biomarkers other than bilirubin, reporting inconsistent results. Increased consumption of vegetables and fruit was shown to lower lipid peroxidation [31, 32] and to increase plasma glutathione, an endogenous antioxidant [33]. Adherence to a Mediterranean diet resulted in an increase of plasma total antioxidant capacity in a 2-month intervention trial [34]. However, other trials failed to show such an effect of supplementation of fruit/vegetable concentrate on biomarkers of antioxidant or oxidative stress [35,36].

In the present study, the vegetable and fruit dietary pattern was associated with higher intake of dietary antioxidants such as α-carotene, β-carotene, α-tocopherol, and vitamin C. Many studies reported the beneficial effects of vegetables and fruit on the plasma/serum concentrations of diet-derived antioxidants, such as β-carotene and vitamin C [32, 34-36], but the effects of such dietary antioxidants on the activity of endogenous antioxidants like glutathione is controversial [33, 35-37]. One intervention study reported that daily intake of 600 g fruit and vegetables increased the activity of erythrocyte glutathione peroxidase [33] and another intervention study showed that high intake of black currant and apple juices increased the activity of glutathione peroxidase in plasma [37]. On the other hand, intakes of fruit and vegetables showed no effect on glutathione in other studies [35,36] although serum concentrations of vitamin C and carotenoids were increased.

Advantages in the present study were the large size of the study population, sex-specific analysis, consideration of potential confounders, and uniform measurement of serum bilirubin. We should note several limitations, however. The low participation rate (24%) was a concern. Selection bias would be possible if participation had been influenced by both serum bilirubin and dietary pattern. Another problem was subjectivity in determining and labeling the dietary pattern. The genotypes of UGT1A1 were not analyzed in the present study. Future studies on the possible interaction between UGT1A1 genotype and dietary pattern on serum bilirubin would be warranted.

CONCLUSION

In a large Japanese community-based cross-sectional study, the vegetable and fruit dietary pattern was not related to serum bilirubin concentrations in men, and showed an inverse association with bilirubin in women.

ACKNOWLEDGEMENTS

This study was supported by a Grant-in-Aid for Scientific Research (B) (24390166) from the Japan Society of the Promotion of Science, Japan. The authors are grateful to the East Division of the Fukuoka City Medical Association for cordial support.

REFERENCES

1. Vítek L, Schwertner HA. The heme catabolic pathway and its protective effects on oxidative stress-mediated diseases. Adv Clin Chem. 2007; 43: 1-57.
2. Ohnaka K, Kono S. Bilirubin, cardiovascular diseases and cancer: epidemiological perspectives. Expert Rev Endocrinol Metab. 2010; 5: 891-904.
3. Abraham NG, Kappas A. Pharmacological and clinical aspects of heme oxygenase. Pharmacol Rev. 2008; 60: 79-127.
4. Vítek L. The role of bilirubin in diabetes, metabolic syndrome, and cardiovascular diseases. Front Pharmacol. 2012; 3: 55.
5. Horsfall LJ, Rait G, Walters K, Swallow DM, Pereira SP, Nazareth I, et al. Serum bilirubin and risk of respiratory disease and death. JAMA. 2011; 305: 691-697.
6. Van Hoydonck PG, Temme EH, Schouten EG. Serum bilirubin concentration in a Belgian population: the association with smoking status and type of cigarettes. Int J Epidemiol. 2001; 30: 1465-1472.
7. Madhavan M, Wattigney WA, Srinivasan SR, Berenson GS. Serum bilirubin distribution and its relation to cardiovascular risk in children and young adults. Atherosclerosis. 1997; 131: 107-113.
8. Peterson S, Bigler J, Horner NK, Potter JD, Lampe JW. Cruciferae interact with the UGT1A1*28 polymorphism to determine serum bilirubin levels in humans. J Nutr. 2005; 135: 1051-1055.
9. Saracino MR, Bigler J, Schwarz Y, Chang JL, Li S, Li L, et al. Citrus fruit intake is associated with lower serum bilirubin concentration among women with the UGT1A1*28 polymorphism. J Nutr. 2009; 139: 555-560.
10. Chang JL, Bigler J, Schwarz Y, Li SS, Li L, King IB, et al. UGT1A1 polymorphism is associated with serum bilirubin concentrations in a randomized, controlled, fruit and vegetable feeding trial. J Nutr. 2007; 137: 890-897.
11. Jacobs DR Jr, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. Am J Clin Nutr. 2003; 78(suppl): 508S-513S.
12. Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? Am J Clin Nutr. 2001; 73: 1-2.
13. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002; 13: 3-9.
14. Nanri A, Yoshida D, Yamaji T, Mizoue T, Takayanagi R, Kono S, et al. Dietary patterns and C-reactive protein in Japanese men and women. Am J Clin Nutr. 2008; 87: 1488-1496.
15. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc. 1993; 25: 71-80.
16. Tokudome S, Goto C, Imaeda N, Tokudome Y, Ikeda M, Maki S, et al. Development of a data-based short food frequency questionnaire for assessing nutrient intake by middle-aged Japanese. Asian Pac J Cancer Prev,. 2004; 5: 40-43.
17. Tokudome Y, Goto C, Imaeda N, Hasegawa T, Kato R, Hirose K, et al. Relative validity of a short food frequency questionnaire for assessing nutrient intake versus three-day weighed diet records in middle-aged Japanese. J Epidemiol. 2005; 15: 135-145.
18. Tokudome S, Ikeda M, Tokudome Y, Imaeda N, Kitagawa I, Fujiwara N. Development of data-based semi-quantitative food frequency questionnaire for dietary studies in middle-aged Japanese. Jpn J Clin Oncol. 1998; 28: 679-687.
19. Science and Technology Agency, Japan. Standard Tables of Food Composition in Japan. The Fourth Edition. Ministry of Finance, Tokyo, 1982 (in Japanese)
20. Science and Technology Agency, Japan. Fatty acids, Cholesterol, Vitamin E Composition Table of Japanese Foods. Ishiyaku shuppan, Inc, Tokyo, 1989 (in Japanese)
21. Science and Technology Agency, Japan. Standard Tables of Food Composition in Japan. The Fifth Edition. Ministry of Finance, 1993, Tokyo (in Japanese)
22. Science and Technology Agency, Japan. Follow-up of Standard Tables of Food Composition in Japan. Ishiyaku Shuppan, Inc, Tokyo, 1992 (in Japanese)
23. Imaeda N, Tokudome Y, Fujiwara N, Nagaya T, Kamae M, Tsunekawa S, et al. Data checking and standardization in a weighted food dietary record survey. Jpn J Nutr. 2000; 58:67-76.
24. Tokuda K, Tanimot K. A new method of measuring bilirubin in serum by vanadic acid (in Japanese). Rinsho Kagaku. 1993; 22: 116-122.
25. Amakura Y, Tsutsumi T, Nakamura M, Kitagawa H, Fujino J, Sasaki K, et al. Activation of the aryl hydrocarbon receptor by some vegetable constituents determined using in vitro reporter gene assay. Biol Pharm Bull. 2003; 26: 532-539.
26. Ciolino HP, Daschner PJ, Yeh GC. Dietary flavonols quercetin and kaempferol are ligands of the aryl hydrocarbon receptor that affect CYP1A1 transcription differentially. Biochem J. 1999; 340 : 715-722.
27. Pohl C, Will F, Dietrich H, Schrenk D. Cytochrome P450 1A1 expression and activity in Caco-2 cells: modulation by apple juice extract and certain apple polyphenols. J Agric Food Chem. 2006; 54: 10262-10268.
28. Sugatani J, Yamakawa K, Tonda E, Nishitani S, Yoshinari K, Degawa M, et al. The induction of human UDP-glucuronosyltransferase 1A1 mediated through a distal enhancer module by flavonoids and xenobiotics. Biochem Pharmacol. 2004; 67: 989-1000.
29. Matthews J, Gustafsson JA. Estrogen receptor and aryl hydrocarbon receptor signaling pathways. Nucl Recept Signal. 2006; 4: e16.
30. Ohtake F, Baba A, Fujii-Kuriyama Y, Kato S. Intrinsic AhR function underlies cross-talk of dioxins with sex hormone signalings. Biochem Biophys Res Commun. 2008; 370: 541-546.
31. Thompson HJ, Heimendinger J, Sedlacek S, Haegele A, Diker A, O'Neill C, et al. 8-Isoprostane F2alpha excretion is reduced in women by increased vegetable and fruit intake. Am J Clin Nutr. 2005; 82: 768-776.
32. Miller ER 3rd, Appel LJ, Risby TH. Effect of dietary patterns on measures of lipid peroxidation: results from a randomized clinical trial. Circulation. 1998; 98: 2390-2395.
33. Dragsted LO, Pedersen A, Hermetter A, Basu S, Hansen M, Haren GR, et al. The 6-a-day study: effects of fruit and vegetables on markers of oxidative stress and antioxidative defense in healthy nonsmokers. Am J Clin Nutr. 2004; 79: 1060-1072.
34. Kolomvotsou AI, Rallidis LS, Mountzouris KC, Lekakis J, Koutelidakis A, Efstathiou S, et al. Adherence to Mediterranean diet and close dietetic supervision increase total dietary antioxidant intake and plasma antioxidant capacity in subjects with abdominal obesity. Eur J Nutr. 2013; 52: 37-48.

SciMedCentral

35. van den Berg R, van Vliet T, Broekmans WM, Cnubben NH, Vaes WH, Roza L, Haenen GR, et al. A vegetable/fruit concentrate with high antioxidant capacity has no effect on biomarkers of antioxidant status in male smokers. J Nutr. 2001; 131: 1714-1722.

36. Paterson E, Gordon MH, Niwat C, George TW, Parr L, Waroonphan S, et al. Supplementation with fruit and vegetable soups and beverages increases plasma carotenoid concentrations but does not alter markers of oxidative stress or cardiovascular risk factors. J Nutr. 2006; 136: 2849-2855.

37. Young JF, Nielsen SE, Haraldsdóttir J, Daneshvar B, Lauridsen ST, Knuthsen P, et al. Effect of fruit juice intake on urinary quercetin excretion and biomarkers of antioxidative status. Am J Clin Nutr. 1999; 69: 87-94.

Cite this article

Hirata A, Ohnaka K, Tanaka M, Wang Z, Morita M, et al. (2014) A Dietary Pattern Characterized by a High Consumption of Vegetables and Fruits is related to lower Concentrations of Serum Bilirubin in Japanese women. J Endocrinol Diabetes Obes 2(1): 1013.