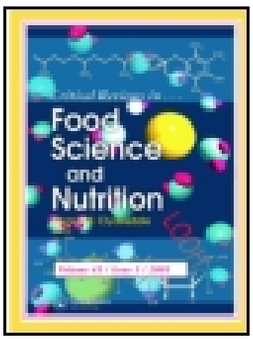

Critical Reviews in Food Science and Nutrition

ISSN: 1040-8398 (Print) 1549-7852 (Online) Journal homepage: http://www.tandfonline.com/loi/bfsn20

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To cite this article: Najmeh Maharlouei, Reza Tabrizi, Kamran B. Lankarani, Abbas Rezaianzadeh, Maryam Akbari, Fariba Kolahdooz, Maryam Rahimi, Fariba Keneshlou & Zatollah Asemi (2018): The effects of ginger intake on weight loss and metabolic profiles among overweight and obese subjects: A systematic review and meta-analysis of randomized controlled trials, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2018.1427044

To link to this article: https://doi.org/10.1080/10408398.2018.1427044

Published online: 02 Feb 2018.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2018.1427044

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The effects of ginger intake on weight loss and metabolic profiles among overweight and obese subjects: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

This systematic review and meta-analysis of randomized controlled trials (RCTs) was performed to summarize the effect of ginger intake on weight loss, glycemic control and lipid profiles among overweight and obese subjects. We searched the following databases through November 2017: MEDLINE, EMBASE, Web of Science, and Cochrane Central Register of Controlled Trials. The relevant data were extracted and assessed for quality of the studies according to the Cochrane risk of bias tool. Data were pooled using the inverse variance method and expressed as Standardized Mean Difference (SMD) with 95% Confidence Intervals (95% CI). Heterogeneity between studies was assessed by the Cochran Q statistic and I-squared tests (I^2). Overall, 14 studies were included in the meta-analyses. Fourteen RCTs with 473 subjects were included in our meta-analysis. The results indicated that the supplementation with ginger significantly decreased body weight (BW) (SMD −0.66; 95% CI, −1.31, −0.01; P = 0.04), waist-to-hip ratio (WHR) (SMD −0.49; 95% CI, −0.82, −0.17; P = 0.003), hip ratio (HR) (SMD −0.42; 95% CI, −0.77, −0.08; P = 0.01), fasting glucose (SMD −0.68; 95% CI, −1.23, −0.05; P = 0.03) and insulin resistance index (HOMA-IR) (SMD −1.67; 95% CI, −2.86, −0.48; P = 0.006), and significantly increased HDL-cholesterol levels (SMD 0.40; 95% CI, 0.10, 0.70; P = 0.009). We found no detrimental effect of ginger on body mass index (BMI) (SMD −0.65; 95% CI, −1.36, 0.06; P = 0.074), insulin (SMD −0.54; 95% CI, −1.43, 0.35; P = 0.23), triglycerides (SMD −0.27; 95% CI, −0.71, 0.18; P = 0.24), total- (SMD −0.20; 95% CI, −0.58, 0.18; P = 0.30) and LDL-cholesterol (SMD −0.13; 95% CI, −0.51, 0.24; P = 0.48). Overall, the current meta-analysis demonstrated that ginger intake reduced BW, WHR, HR, fasting glucose and HOMA-IR, and increased HDL-cholesterol, but did not affect insulin, BMI, triglycerides, total- and LDL-cholesterol levels.

KEYWORDS

Ginger; weight loss; metabolic profiles; overweight; meta-analysis

1. Introduction

Obesity is defined as excessive fat accumulation which is a public health concern during recent decades (Amato et al. 2013). Globally, more than 1.6 billion adults are overweight; it has been reported that by 2030, in the USA up to 86% of people will be overweight or obese (Ginter and Simko 2014). Obesity has a number of serious complications for people and healthcare system (Martins et al. 2008) including, coronary heart diseases (CHD), hypertension, type 2 diabetes mellitus (T2DM), and non-metabolic such as osteoarthritis and cancers (Kromhout 1983; Lynch et al. 2009). Insulin resistance and metabolic syndrome occurrence up to 30% and between 20% and 45% of obese patients, respectively (Engin 2017).

Common treatments for managing obesity and metabolic disorders in obese patients include lifestyle changes such as weight loss, appropriate diet, and increased physical activity (Villareal et al. 2011). Ginger is one of the most widely used spices and medicinal plants around the world to manage body weight, insulin resistance and lipid profiles (Azimi et al. 2014; Shidfar et al. 2015; Ebrahimzadeh Attari et al. 2016). Ginger intake may reduce body weight and improve metabolic profiles through increased expression of glucose transporter type 4, glucose uptake by cells, increased insulin receptors, elevated pancreatic beta cells' functions, and also modifying the adipokines concentrations (Li et al. 2012b). Despite reported anti-obesity, glucose- and lipid-lowering effects of ginger in some clinical trials (Mahluji et al. 2013a; Azimi et al. 2014; Shidfar et al. 2015; Ebrahimzadeh Attari et al. 2016), few studies did not show any additional effect of supplementation with ginger on body weight (BW), body mass index (BMI), glycemic control and

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some lipid profiles (Atashak et al. 2011a; Pape et al. 2011). Therefore, effect of ginger intake for reducing body fat, and promoting weight lost, and improving glycemic control and lipid profiles remains controversial. Discrepancies in findings might be the result of differences in study design, characteristics of study populations, dosage of ginger used, co-supplementation with other compositions, and duration of the studies.

Despite several randomized controlled trials (RCTs), we are aware of no systematic review and meta-analysis of RCTs about the effect of ginger supplement on weight lost, and improving glycemic control and lipid profiles. This meta-analysis was performed to summarize the available evidence of RCTs to establish the effect of ginger supplement on weight lost, glycemic control and lipid profiles among overweight and obese subjects.

2. Methods

2.1. Search strategy and selection studies

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline were conformed to design, analysis, and reporting of this study. Eligible RCTs were identified using Cochrane Library, Embase, Medline, and Web of Science databases for relevant articles published up to November 2017, and by manually searching the reference list of the retrieved articles. Databases of International Standard Randomized Controlled Trial Number Register and Meta-register for RCTs were also searched for all ongoing trials. Studies retrieved that examined the association between supplementation with ginger and body composition, and metabolic profiles by using the following MeSH and text words: patients ["obese" OR "overweight"], intervention ("ginger" OR "Zingiber officinale" AND "supplementation" OR "intake"), and outcomes ["body mass index (BMI)" OR "body weight (BW)" OR "waist-to-hip ratio (WHR)" OR "hip ratio (HR) "OR "glucose" OR "insulin" OR "homeostasis model assessment of insulin resistance (HOMA-IR)" OR "triglycerides (TG)" OR "total cholesterol (TC)" OR "low-density lipoprotein cholesterol (LDL-cholesterol)" OR "high-density lipoprotein cholesterol (HDL-cholesterol)"]. The search was limited to studies in human and published in English. Additional manual search such as reference lists of related studies; former review studies were reviewed to increase sensitivity in search strategy. Two authors (RT &MA) independently read the abstracts of all identified studies to exclude those that were clearly not relevant. The full texts of the remaining articles were read to determine if they met the study inclusion criteria. In case of discrepancy, consensus was reached or resolved by discussion with a third author (ZA). Trials were included for meta-analysis that met the following criteria: 1) original trials, 2) human trials in design, 3) intervention and control groups received of ginger supplementation and placebo, respectively and 4) the trials reported mean changes or mean difference of body composition and/or metabolic profiles with standard deviation (SD) for the intervention and control groups.

2.2. Data extraction and quality assessment

Two authors (NM and MA) independently have extracted data and have assessed the quality of all RCTs by using standard forms and the Cochrane Collaboration risk of bias tool, respectively. This tool is based on information on the following domains: randomization generation, allocation concealment, blinding of subjects and outcome assessment, incomplete outcome data, and selective outcome reporting, and other sources of bias. When there was disagreement among them, it resolved by discussion with third author (ZA). Eligible studies were reviewed and the following data were abstracted: 1) first authors' name 2) publication year 3) age, sex, and body composition and/or metabolic profiles of study participants and associated measures of variance 4) study location 5) number of participants in the intervention and control groups 6) study design 7) type and doses of ginger supplement 8) duration of the intervention.

2.3. Data analysis

Statistical analyses were performed using STATA version 12.0 (Stata Corp., College Station, TX) and RevMan V.5.3 software (Cochrane Collaboration, Oxford, UK). Heterogeneity of effect size across trials was estimated by Cochran's Q test and I-square statistic. I-square higher than 50 percent with p-value <0.05 represented significant heterogeneity. The standardised mean difference (SMD) with 95% confidence interval (CI) calculated by inverse variance method and Cohen statistics. Because of different indications among trials used random-effects models for meta-analysis the effect of ginger on body composition and metabolic profiles in our study. Heterogeneity in body composition and metabolic profiles was assessed by conducting stratified meta-analysis. Subgroup analyses were conducted to assess the source of heterogeneity between studies. Predefined subgroups were created based on dosage of ginger supplement ($\leq$ 1,000 mg/d, $>$1,000 mg/d), population study (obese or overweight vs. obese with other disease), type of intervention (ginger vs. ginger plus other nutrient), gender (female vs. male vs. both), the duration of study ($\leq$8 weeks vs. $>$8 weeks).In addition, sensitivity analyses were performed to examine the contribution of a particular study to the pooled SMDs. Egger's test were used to detect the existence of potential publication bias for the primary outcome measure. P-values <0.05 were considered as statistically significant.

3. Results

3.1. Search results

Our initial search found 923 potential citations. After screening trials, 14 trials were proved to be eligible for meta-analysis. Figure 1 shows the details of step by step study identification and selection. The key characteristics of the RCTs are summarized in Table 1. Trials were published between 2011 and 2017. These 14 selected studies included 473 randomized participants: 255 were allocated to the ginger supplementation group and 218 were allocated to the placebo group. The number of participants in these trials ranged from 16 to 70. Two studies were designed as parallel groups and 12 studies were designed as the randomized double-blind. Four trials have reported changes on BMI (Ebrahimzadeh Attari et al. 2015a; Afzalpour et al. 2017; Banitalebi 2017; Taghizadeh et al. 2017), BW (Ebrahimzadeh Attari et al. 2015a; Afzalpour et al. 2017; Banitalebi 2017; Taghizadeh et al. 2017), WHR (Ebrahimzadeh Attari et al. 2015a; Afzalpour et al. 2017; Banitalebi 2017; Taghizadeh et al. 2017), triglycerides (Atashak et al. 2014; Ebrahimzadeh Attari et al.

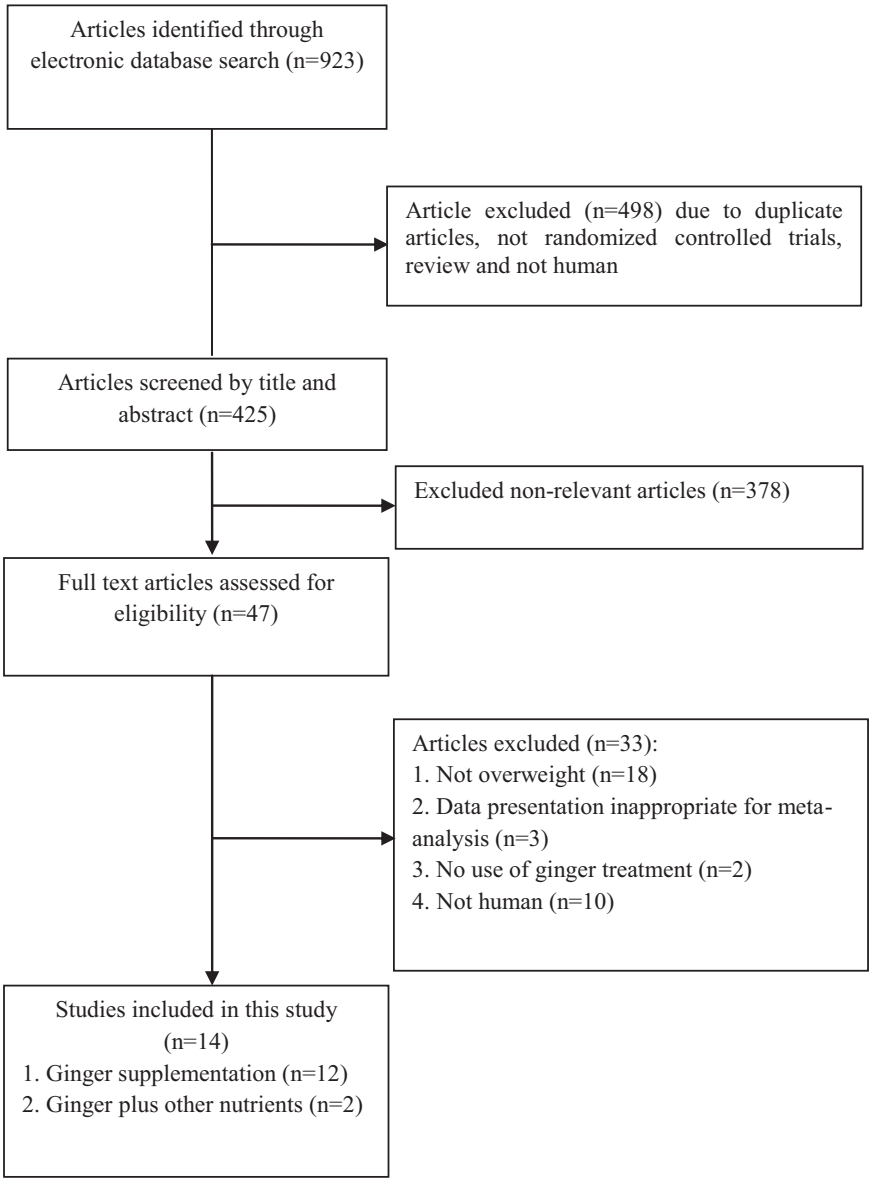


Figure 1. Literature search and review flowchart for selection of studies.

2015a; Karimi et al. 2015; Taghizadeh et al. 2017), LDL-cholesterol (Atashak et al. 2014; Ebrahimzadeh Attari et al. 2015a; Karimi et al. 2015; Taghizadeh et al. 2017), and HDL-cholesterol (Atashak et al. 2014; Ebrahimzadeh Attari et al. 2015a; Karimi et al. 2015; Taghizadeh et al. 2017), six on glucose (Lopez et al. 2013; Atashak et al. 2014; Alizadeh et al. 2015; Ebrahimzadeh Attari et al. 2015a; Banitalebi 2017; Taghizadeh et al. 2017), five on insulin (Atashak et al. 2014; Alizadeh et al. 2015; Ebrahimzadeh Attari et al. 2015a; Banitalebi 2017; Taghizadeh et al. 2017), HOMA-IR (Atashak et al. 2014; Alizadeh et al. 2015; Ebrahimzadeh Attari et al. 2015a; Banitalebi 2017; Taghizadeh et al. 2017), and total cholesterol (Lopez et al. 2013; Atashak et al. 2014; Ebrahimzadeh Attari et al. 2015a; Karimi et al. 2015; Taghizadeh et al. 2017) and three on HR (Lopez et al. 2013; Ebrahimzadeh Attari et al. 2015a; Banitalebi 2017). The ginger powder was the main type of intervention (thirteen out of fourteen) and ginger extract was used in one study (Taghizadeh et al. 2017). The ginger supplement was administered to the individuals in doses ranging from 200 to 3000 mg/day with duration of supplementation ranged between 2 and 12 weeks in the included trials. The quality of the included trails was assessed as described in the Cochrane Handbook for Systematic Reviews of Interventions and the results of risk of bias are summarized in Figure 2.

3.2. Main outcomes

Pooled estimates of the standardized difference means between intervention and placebo groups are shown in Table 2. The effects of ginger supplementation on body composition and glycemic control based on subgroup analysis are shown in Table 3. The findings of subgroup analyses showed that the effects were different in some of specific strata of suspected variables.

3.3. Effects of ginger supplementation on body composition

The effects of ginger supplementation on body composition are shown in Figure 3. Meta-analysis of data from 4 RCTs indicated a significant effect of supplementation with ginger on reduction of BW (SMD −0.66; 95% CI, −1.31, −0.01; P =

Table 1. Characteristics of included studies.

Authors (Ref)	Intervention/control (sample size)	Duration (wk)	Subject type	Age (years)	Intervention (name and daily dose)
Ebrahimzadeh Attari et al. (2015)	39/31	12	Obese women	18–45	2 g ginger rhizomes powder/day
Ebrahimzadeh Attari et al. (2016)	39/31	12	Obese women	18–45	2 g ginger rhizomes powder/day
Ebrahimzadeh Attari et al. (2015a)	39/31	12	Obese women	18–45	2 g ginger rhizomes powder/day
Atashaket al.(2011b)	8/8	10	Obese men	18–30	4 capsules (each capsule containing 250 mg/day ginger-root powder)
Atashaket al. (2012)	8/8	10	Obese men	20–30	4 capsules (each capsule containing 250 mg/day ginger-root powder)
Atashaket al. (2014)	8/8	10	Obese men	18–30	4 capsules (each capsule containing 250 mg/day ginger-root powder)
Taghizadeh et al. (2017)	25/25	8	Obese women	18–50	Supplements containing green tea, capsaicin and ginger (50 mg/day ginger extracts)
Banitalebi et al. (2017)	12/10	10	Obese women with diabetes mellitus	45–60	4 capsules (each capsule containing 250 mg/day ginger-root powder)
Alizadeh et al. (2015)	10/10	6	Obese women with breast cancer	40–55	4 capsules (each capsule containing 750 mg/day ginger powder)
Karimi et al. (2015)	10/10	6	Obese women with breast neoplasm	40–55	4 capsules (each capsule containing 750 mg/day ginger powder)
Vahdat Poor et al. (2016)	12/10	2	Overweight girls	23–28	2 g/day ginger powder
Afzalpour et al. (2017)	10/10	10	Overweight women	20–30	3 g/day ginger powder
Afzalpour et al. (2016)	8/8	10	Overweight women	20–30	3 g/day ginger powder
Lopez et al. (2013)	27/18	8	Overweight men and women	21–45	500 mg/day Zingiber officinale

0.04), WHR (SMD −0.49; 95% CI, −0.82, −0.17; P = 0.003), and HR (SMD −0.42; 95% CI, −0.77, −0.08; P = 0.01).

In stratified analyses by the dosage of ginger, the ≤1,000 mg/day category (SMD: −0.66; 95%CI: −1.31, −0.01; I^2:76.9%) had a significant effect on body weight reduction compared to the >1,000 mg/day category (Table 3). Body weight did not affect by the type of intervention, population study, gender and the duration of study after ginger intake.

We found no detrimental effect of ginger supplement on BMI (SMD −0.65; 95% CI, −1.36, 0.06; P = 0.074). In stratified analyses by the dosage of ginger, only the ≤1,000 mg/day category (SMD: −0.86; 95%CI: −1.68, −0.03; I^2:79.6%) had an effect on BMI reduction; while the >1,000 mg/day category had no effect (SMD: −0.07; 95%CI: −0.80, 0.95) (Table 3). Further analyses revealed that there was a significant reduction in BMI for the category of ginger plus other compositions

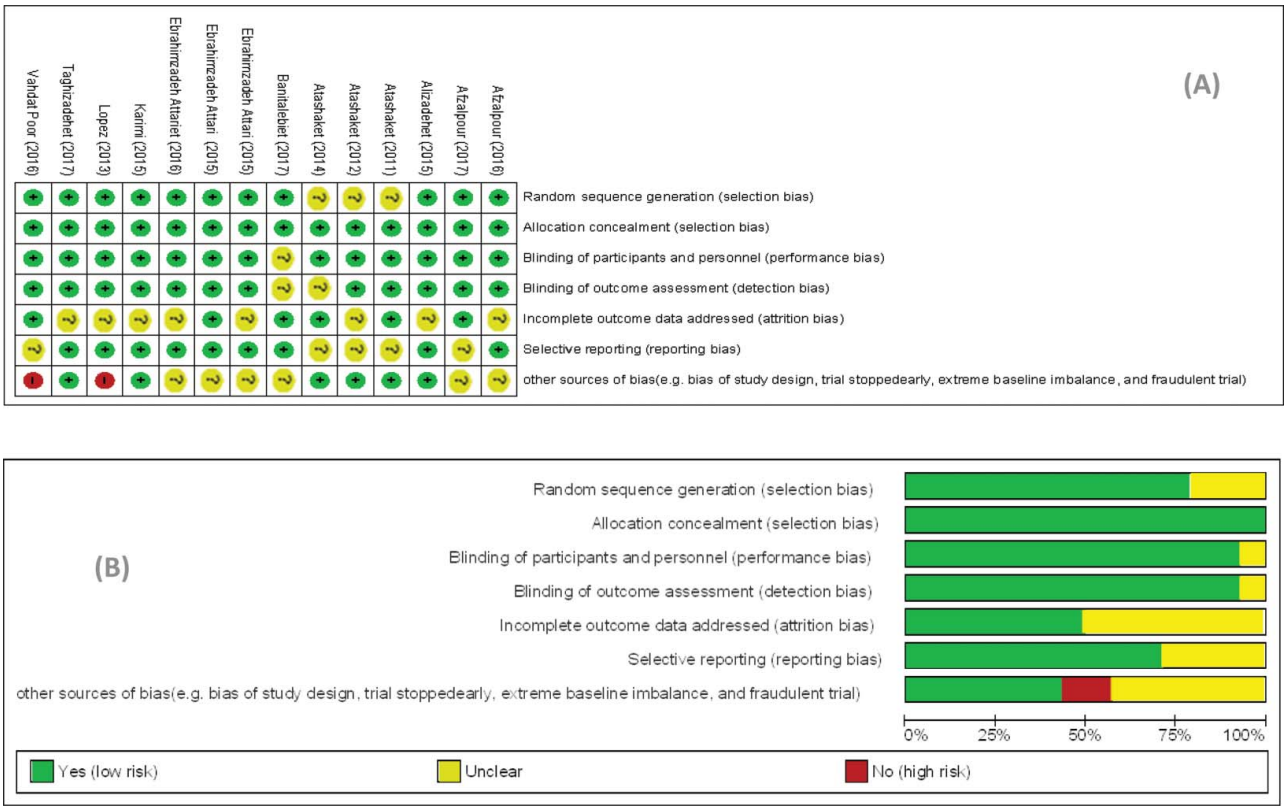


Figure 2. The methodological quality of included trials on effect of ginger on body composition and metabolic profiles based on review authors' judgments about each risk of bias item presented as percentages across all included studies (A) and each risk of bias item for each included study (B).

Table 2. Estimation of the standardized difference means of related indictors with CI 95% between the intervention and placebo groups.

Variable			Number of study	Standardized mean difference	CI 95%	Heterogeneity		
						I^2 (%)	Q	P-value
Body composition	BMI	Intervention group (after vs. before)	4	−0.19	−0.49, 0.11	0.0	0.66	0.882
		Placebo group (after vs. before)	4	−0.04	−0.35, 0.28	0.0	0.25	0.969
		Change intervention group vs. placebo group	4	−0.65	−1.36, 0.06	76.6	12.80	0.005
	Body weight	Intervention group (after vs. before)	4	−0.14	−0.41, 0.13	0.0	0.41	0.938
		Placebo group (after vs. before)	4	0.00	−0.30, 0.30	0.0	0.09	0.993
		Change intervention group vs. placebo group	4	−0.66	−1.31, − 0.01	76.9	13.01	0.005
	WHR	Intervention group (after vs. before)	4	−0.27	−0.57, 0.03	0.0	0.65	0.884
		Placebo group (after vs. before)	4	−0.08	−0.42, 0.26	0.0	0.25	0.969
		Change intervention group vs. placebo group	4	−0.49	−0.82, − 0.17	0.0	1.81	0.613
	HR	Intervention group (after vs. before)	3	−0.15	−0.47, 0.16	0.0	0.01	0.993
		Placebo group (after vs. before)	3	−0.01	−0.37, 0.35	0.0	0.00	0.998
		Change intervention group vs. placebo group	3	−0.42	−0.77, −0.08	0.0	0.13	0.939
Glycemic control	Glucose	Intervention group (after vs. before)	6	−0.59	−1.23, 0.06	81.1	26.41	<0.0001
		Placebo group (after vs. before)	6	−0.12	−0.52, 0.28	47.1	9.45	0.092
		Change intervention group vs. placebo group	6	−0.68	−1.23, − 0.05	78.2	22.95	<0.0001
	Insulin	Intervention group (after vs. before)	5	0.01	−0.56, 0.58	70.1	13.36	0.010
		Placebo group (after vs. before)	5	0.13	−0.18, 0.43	0.0	2.48	0.649
		Change intervention group vs. placebo group	5	−0.54	−1.43, 0.35	86.2	28.91	<0.0001
	HOMA-IR	Intervention group (after vs. before)	5	−0.70	−1.17, −0.22	54.6	8.81	0.066
		Placebo group (after vs. before)	5	0.12	−0.19, 0.42	0.0	3.70	0.448
		Change intervention group vs. placebo group	5	−1.67	−2.86, −0.48	89.9	39.51	<0.0001
Lipid profiles	Triglycerides	Intervention group (after vs. before)	4	−0.33	−0.68, 0.02	14.8	3.52	0.318
		Placebo group (after vs. before)	4	−0.12	−0.45, 0.20	0.0	1.96	0.581
		Change intervention group vs. placebo group	4	−0.27	−0.71, 0.18	41.2	5.10	0.164
	Total cholesterol	Intervention group (after vs. before)	5	−0.21	−0.47, 0.06	0.0	0.65	0.958
		Placebo group (after vs. before)	5	−0.11	−0.40, 0.18	0.0	1.33	0.856
		Change intervention group vs. placebo group	5	−0.20	−0.58, 0.18	39.0	6.55	0.161
	LDL-cholesterol	Intervention group (after vs. before)	4	−0.13	−0.41, 0.15	0.0	0.36	0.948
		Placebo group (after vs. before)	4	−0.13	−0.44, 0.17	0.0	0.85	0.838
		Change intervention group vs. placebo group	4	−0.13	−0.51, 0.24	33.0	4.48	0.214
	HDL-cholesterol	Intervention group (after vs. before)	4	0.15	−0.13, 0.43	0.0	0.62	0.892
		Placebo group (after vs. before)	4	0.05	−0.25, 0.36	0.0	1.16	0.762
		Change intervention group vs. placebo group	4	0.40	0.10, 0.70	0.0	0.87	0.831

administration (SMD: −1.60; 95%CI: −2.24, −0.96), while there was no effect when the studies administrated only ginger (SMD: −0.32; 95%CI: −0.70, 0.06). In stratified analyses by the duration of study, the ≤ 8 weeks category (SMD: −1.60; 95%CI: −2.24, −0.96) had a significant effect on BMI reduction compared to the >8 weeks category (SMD: −0.32; 95%CI: −0.70, 0.06). There was no difference in the effect of ginger supplementation on BMI in subgroup analyses by the study population.

3.4. Effects of ginger supplementation on glycemic control

The findings showed that ginger supplementation among subjects with overweight and obese participants significantly decreased fasting glucose (SMD −0.68; 95% CI, −1.23, −0.05; P = 0.03), and HOMA-IR (SMD −1.67; 95% CI, −2.86, −0.48; P = 0.006) (Figure 4). We found no significant effect of ginger supplementation on insulin levels (SMD −0.54; 95% CI, −1.43, 0.35; P = 0.23) (Table 2).

In stratified analyses by the dosage of ginger, the ≤1,000 mg/day category had a significant effect on reducing glucose levels (SMD: −0.83; 95%CI: −1.57, −0.08; I^2:82.0%), while the >1,000 mg/day category showed no effect (SMD: −0.04; 95%CI: −0.92, 0.84) (Table 3). Fasting glucose levels did not influence by the study population, type of intervention, gender and the duration of study after supplementation with ginger.

In stratified analyses by the dosage of ginger, the >1,000 mg/day category had a considerable effect on reducing insulin levels (SMD: −1.25; 95%CI: −2.21, −0.28); the ≤1,000 mg/day category showed no effect (SMD: −0.37; 95%CI: −1.36, 0.61; I^2:87.2%) (Table 3). In addition, in the category of ginger plus other compositions administration insulin levels significantly decreased (SMD: −0.65; 95%CI:

Table 3. The effects of ginger supplementation on body composition and glycemic control based on subgroup analysis.

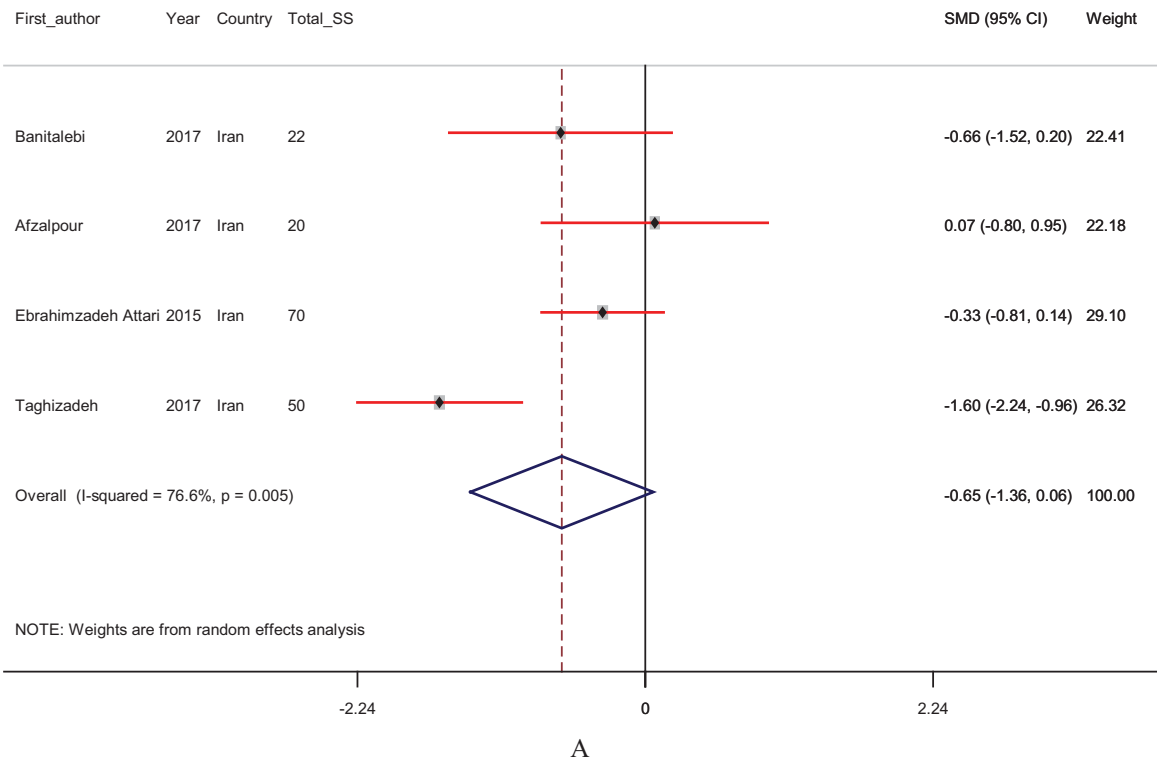
Variable		Number of SMD included	Subgroups	Pooled effect estimate	95% CI	I^2 (%)	Overall I^2 (%)
BMI	Dosage of ginger (mg/day)	3	≤ 1000 (mg/d)	−0.86	−1.68, −0.03	79.6	76.6
		1	> 1000 (mg/d)	0.07	−0.80, 0.95	—	
	Study population	3	Obese or overweight	−0.64	−1.59, 0.31	84.4	
		1	Obese with other diseases	−0.66	−1.52, 0.20	—	
	Type of intervention	3	Ginger	−0.32	−0.70, 0.06	0.0	
		1	Ginger plus other compositions	−1.60	−2.24, −0.96	—	
	Gender	4	Female	−0.65	−1.36, 0.06	84.2	
		—	Male	—	—	—	
		—	Both	—	—	—	
	Duration of study (week)	1	≤ 8 weeks	−1.60	−2.24, −0.96	—	
		3	> 8 weeks	−0.32	−0.70, 0.06	0.0	
Body weight	Dosage of ginger (mg/day)	4	≤ 1000 (mg/d)	−0.66	−1.31, −0.01	76.9	76.9
		—	> 1000 (mg/d)	—	—	—	
	Study population	4	Obese or overweight	−0.69	−1.52, 0.15	84.6	
		—	Obese with other diseases	−0.57	−1.43, 0.29	—	
	Type of intervention	2	Ginger	−0.36	−0.77, 0.06	0.0	
		2	Ginger plus other compositions	−0.90	−2.30, 0.49	90.1	
	Gender	3	Female	−0.82	−1.68, 0.04	81.4	
		—	Male	—	—	—	
		1	Both	−0.20	−0.80, 0.40	—	
	Duration of study (week)	2	≤ 8 weeks	−0.90	−2.30, 0.49	90.1	
		2	> 8 weeks	−0.36	−0.77, 0.06	0.0	
Glucose	Dosage of ginger (mg/day)	5	≤ 1000 (mg/d)	−0.83	−1.57, −0.08	82.0	78.2
		1	> 1000 (mg/d)	−0.04	−0.92, 0.84	—	
	Study population	3	Obese or overweight	−0.29	−0.59, 0.00	0.0	
		1	Obese with other diseases	−1.71	−5.05, 1.64	94.1	
	Type of intervention	4	Ginger	−1.04	−2.24, 0.16	86.7	
		2	Ginger plus other compositions	−0.31	−0.72, 0.10	0.0	
	Gender	4	Female	−0.80	−1.76, 0.16	85.9	
		1	Male	−1.04	−2.09, 0.02	—	
		1	Both	−0.27	−0.86, 0.33	—	
	Duration of study (week)	3	≤ 8 weeks	−0.26	−0.63, 0.11	0.0	
		3	> 8 weeks	−1.44	−3.20, 0.32	90.7	
Insulin	Dosage of ginger (mg/day)	4	≤ 1000 (mg/d)	−0.37	−1.36, 0.61	87.2	86.2
		1	> 1000 (mg/d)	−1.25	−2.21, −0.28	—	
	Study population	3	Obese or overweight	−0.39	−1.70, 0.91	91.2	
		2	Obese with other diseases	−0.78	−1.63, 0.07	43.2	
	Type of intervention	4	Ginger	−0.53	−1.71, 0.65	88.0	
		1	Ginger plus other compositions	−0.65	−1.21, −0.08	—	
	Gender	4	Female	−0.32	−1.25, 0.62	86.7	
		1	Male	−1.57	−2.71, −0.43	—	
		—	Both	—	—	—	
	Duration of study (week)	3	≤ 8 weeks	−0.30	−1.65, 1.04	88.2	
		2	> 8 weeks	−0.81	−1.34, −0.29	91.0	
HOMA-IR	Dosage of ginger (mg/day)	4	≤ 1000 (mg/d)	−1.88	−3.32, −0.44	91.6	89.9
		1	> 1000 (mg/d)	−0.86	−1.78, 0.06	—	
	Study population	3	Obese or overweight	−2.47	−3.78, −1.17	85.8	
		2	Obese with other diseases	−0.46	−1.18, 0.25	25.0	
	Type of intervention	4	Ginger	−1.70	−3.36, −0.03	92.4	
		1	Ginger plus other compositions	−1.60	−2.24, −0.96	—	
	Gender	4	Female	−1.53	−2.92, −0.13	92.2	
		1	Male	−2.34	−3.64, −1.03	—	
		—	Both	—	—	—	
	Duration of study (week)	2	≤ 8 weeks	−1.30	−2.01, −0.59	40.6	
		3	> 8 weeks	−1.98	−4.21, 0.26	94.2	

−1.21, −0.08); while we found no effect among studies which supplemented with ginger alone (SMD: −0.53; 95%CI: −1.71, 0.65; I^2:88.0%). Compared to the female (SMD: −0.32; 95%CI: −1.25, 0.62; I^2:86.7%), male (SMD: −1.57; 95%CI: −2.71, −0.43) showed a significant reduction in their insulin levels after supplemented with ginger. In stratified analyses by the duration of study (>8 weeks, vs. ≤8 weeks), only the >8 weeks category of ginger supplementation showed a significant effect on decreasing insulin levels (SMD: −0.81; 95%CI: −1.34, −0.29; I^2:91.0%). Insulin levels did not influence by study population after ginger intake.

3.5. Effects of ginger supplementation on lipid profiles

Ginger supplementation significantly increased HDL-cholesterol levels (SMD 0.40; 95% CI, 0.10, 0.70; P = 0.009). We found no significant effect of ginger supplementation on triglycerides (SMD −0.27; 95% CI, −0.71, 0.18; P = 0.24), total- (SMD −0.20; 95% CI, −0.58, 0.18; P = 0.30), and LDL-cholesterol (SMD −0.13; 95% CI, −0.51, 0.24; P = 0.48) (Table 2 & Figure 5).

In stratified analyses by the dosage of ginger (≤1,000 vs. >1,000 mg/day), only the ≤1,000 mg/day category had a significant reduction in HOMA-IR (SMD: −1.88; 95%CI: −3.32,



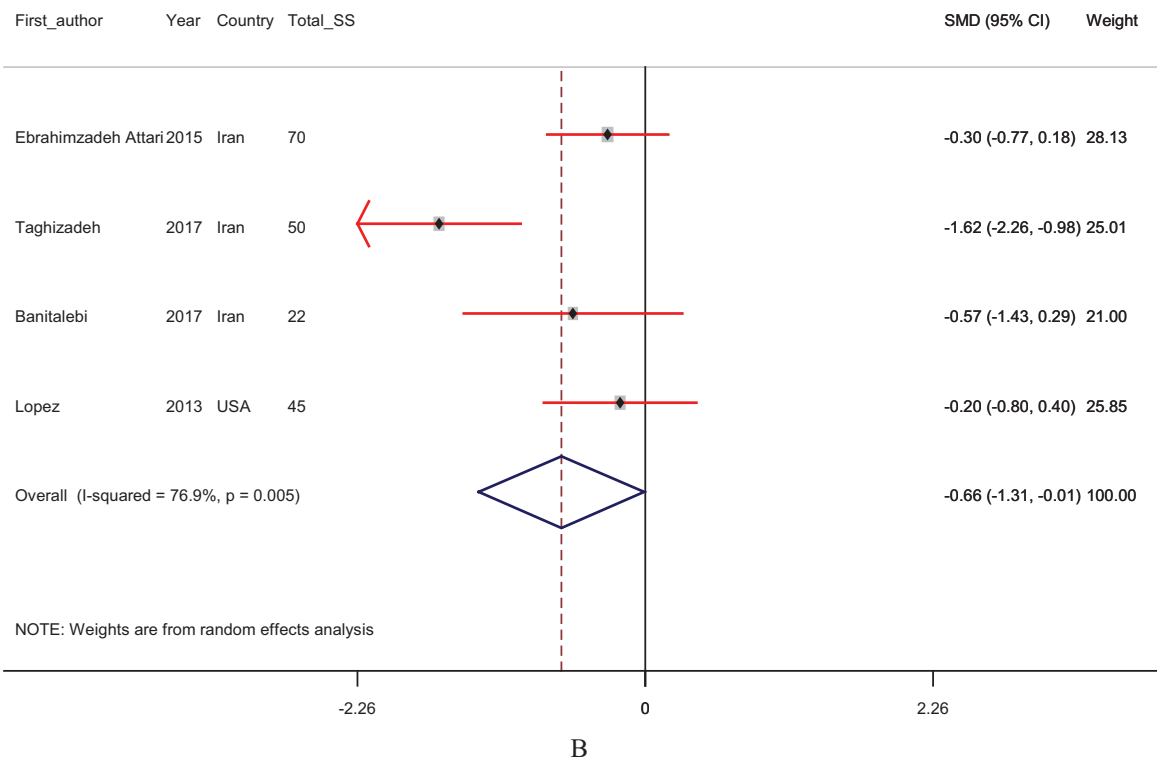
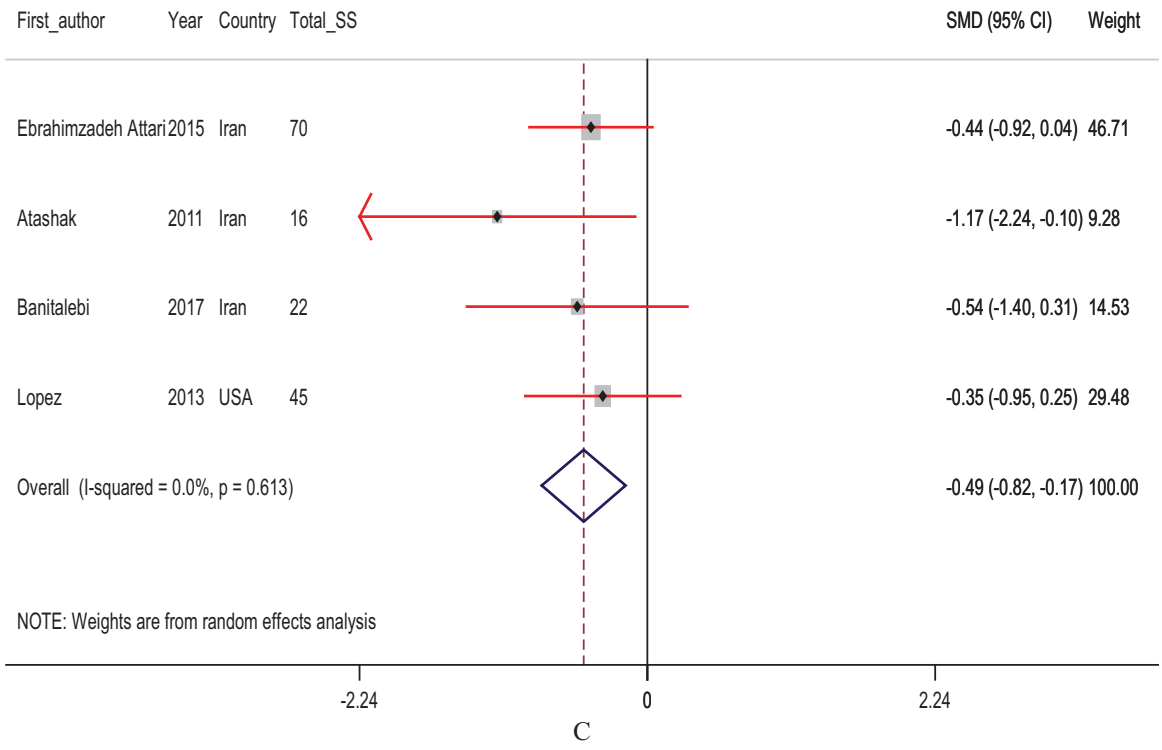


Figure 3a. A–D. Meta-analysis body composition standardized mean differences estimates for (A) BMI, (B) for weight, (C) for WHR, and (D) for HR in ginger supplements and placebo groups (CI=95%).

−0.44; I^2:91.6%) (Table 3). Supplementation with ginger among obese or overweight patients showed a considerable reduction in their HOMA-IR (SMD: −2.47; 95%CI: −3.78, −1.17; I^2:85.8%); we found no effect among those with obesity plus other diseases. The effect of ginger supplementation on HOMA-IR reduction were similar among categories of supplementation with ginger plus other compositions (SMD: −1.60; 95%CI: −2.24, −0.96) and ginger alone (SMD: −1.70; 95%CI: −3.36, −0.03; I^2:92.4%). Effect of ginger supplementation on reduction of HOMA-IR levels were greater among males (SMD: −2.34; 95%CI: −3.64, −1.03), compared to females (SMD: −1.53; 95%CI: −2.92, −0.13; I^2:92.2%). In



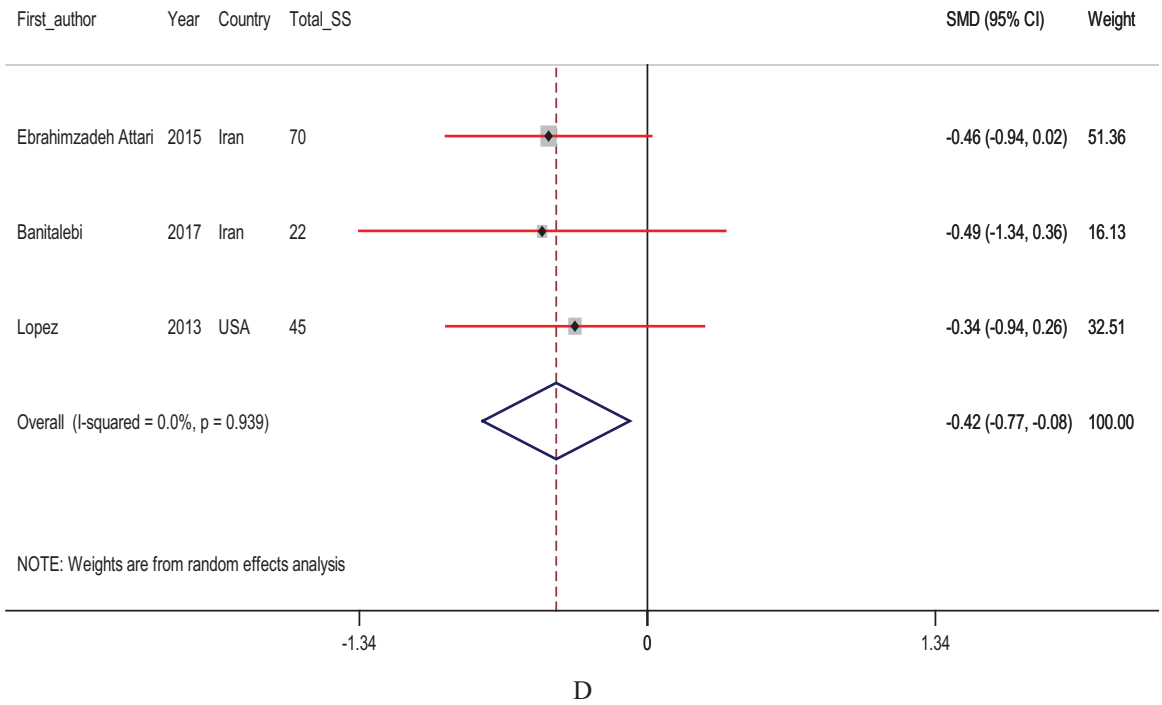
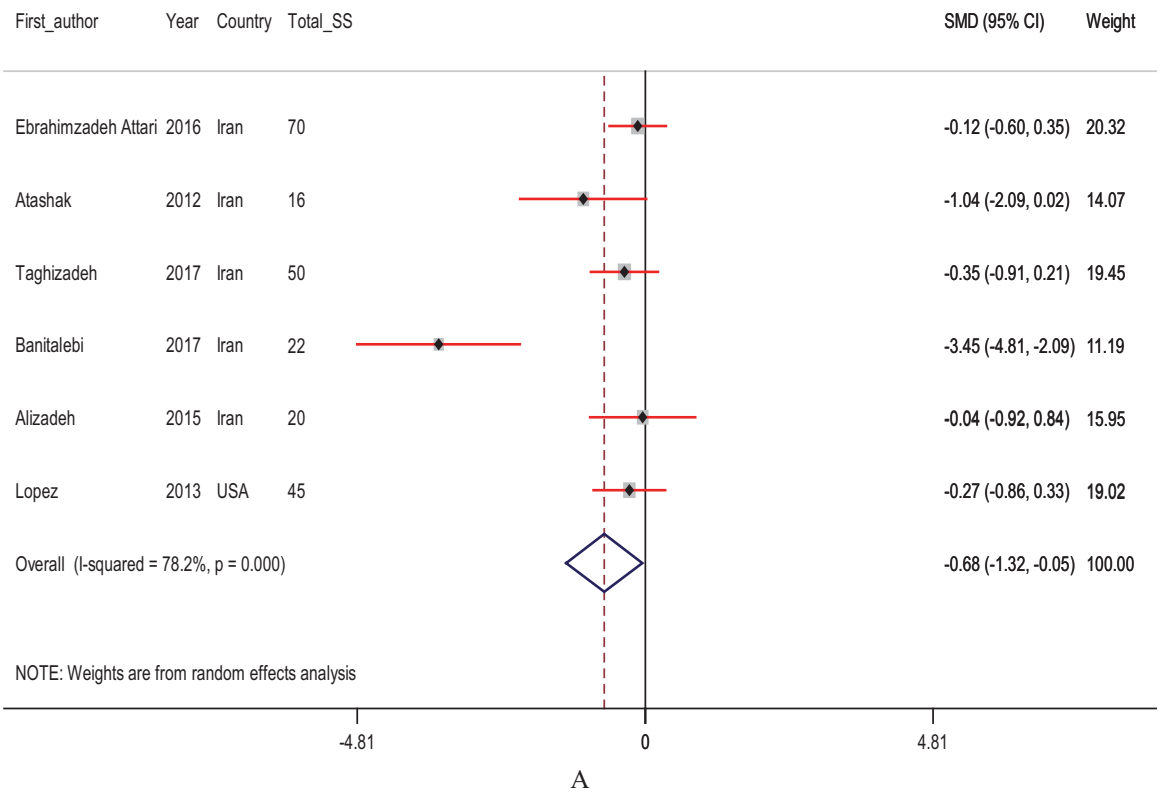


Figure 3b. (Continued).

stratified analyses by the duration of study (>8 weeks, vs. ≤8 weeks), only the ≤ 8 weeks category (SMD: −1.30; 95%CI: −2.01, −0.59; I^2:40.6%) had a significant decrease in HOMA-IR.

In sensitivity analysis, to explore the effect of each study on the strength of association between ginger supplementation and body composition, the pooled SMDs were estimated after excluding each trial from the analysis. We found no significant difference between the pre- and post-sensitivity pooled SMDs for WHR. The lower and higher pooled SMD of the sensitivity analysis for WHR was −0.55 (95% CI:−0.94, −0.16) after omitting the Lopez et al. (2013) and −0.42 (95% CI: −0.76, −0.08) after omitting Atashak et al. (2011b). But after omitting Afzalpour et al. (2017) for BMI, Taghizadeh et al. (2017) and Lopez et al. (2013) studies for BW, and Ebrahimzadeh Attari et al. (2015a) for HR, we found significant differences between pre- and post-sensitivity pooled SMDs for results on body composition (Table 4).



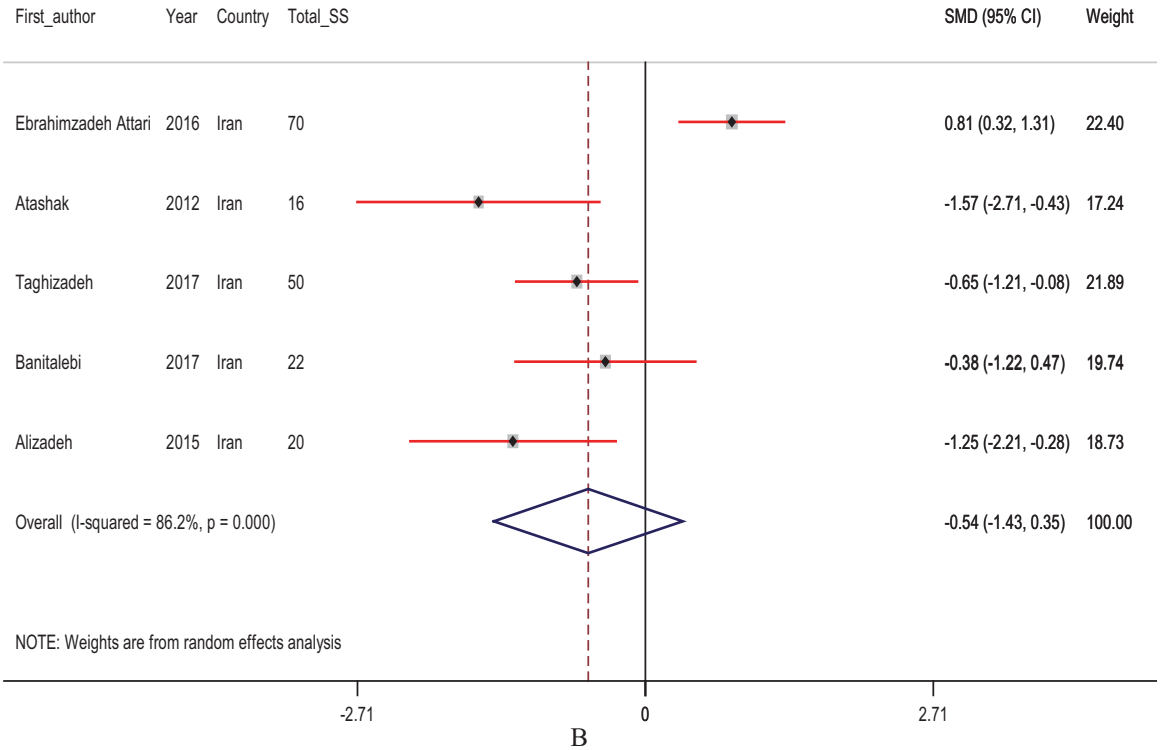


Figure 4a. A–C. Meta-analysis lipid profiles standardized mean differences estimates for (A) fasting glucose, (B) for insulin, (C) for HOMA-IR in ginger acid supplements and placebo groups (CI=95%).

Sensitivity analyses were conducted and the findings for HOMA-IR remained consistent with pooled SMD; for fasting glucose, we found significant difference between the pre- and post-sensitivity pooled SMD (−0.59 (95%CI: −0.88, −0.29) and −0.63 (95%CI:−1.34, 0.07), respectively) after excluding Atashak et al. (2011b). For insulin we observed a significant difference between pre −0.54 (95% CI: −1.43, −0.35) and post-sensitivity pooled SMD −0.83 (95% CI:−1.29, −0.36) after excluding Ebrahimzadeh Attari et al. (2015a) (Table 4).

Egger's regression test used to detect publication bias among included studies into meta-analysis. Egger's regression tests indicated no significant publication bias for meta-analyses of

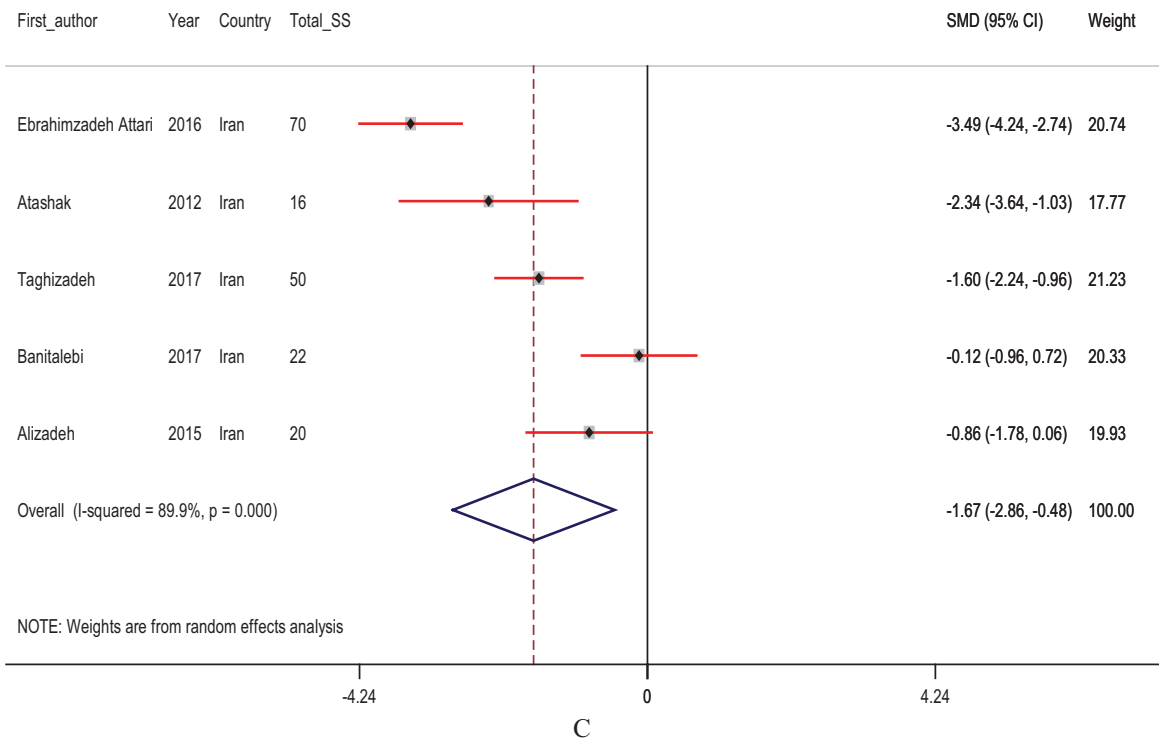


Figure 4b. (Continued).

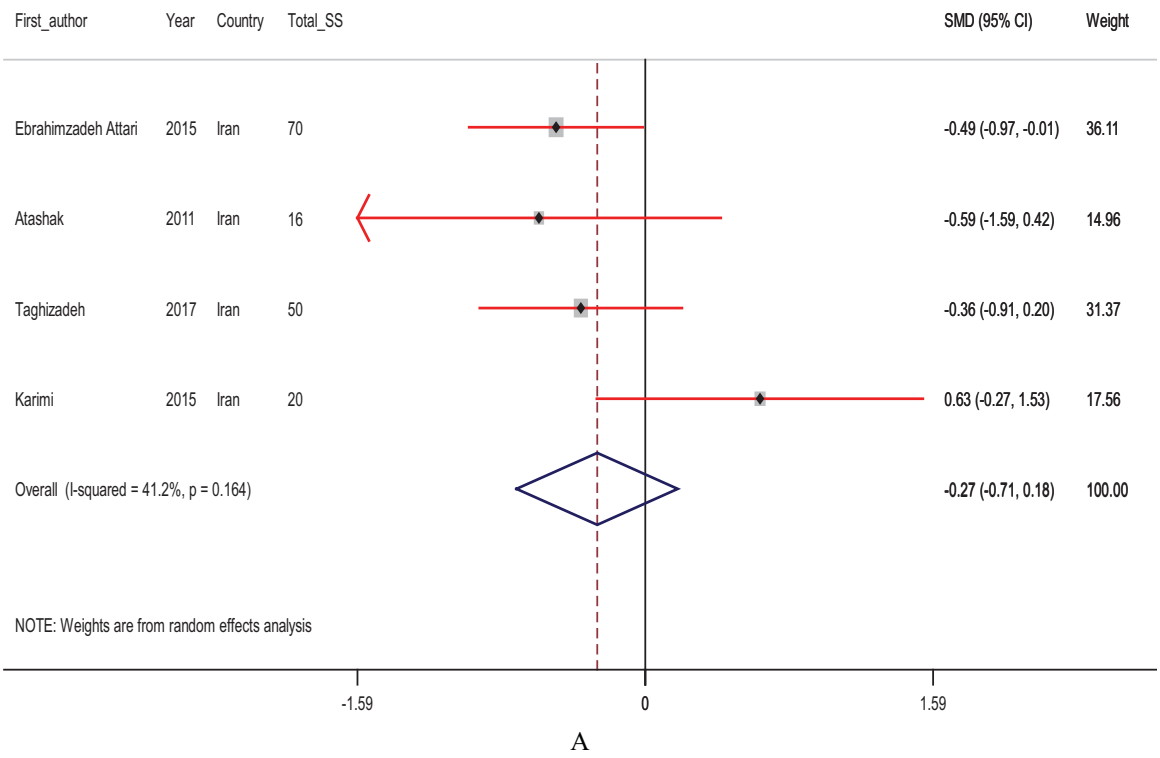
assessing ginger effect on BMI (B = −0.09, P = 0.98), BW (B = −3.17, P = 0.64), WHR (B = −1.84, P = 0.19), HR (B = −0.04, P = 0.96), glucose (B = −4.61, P = 0.06), insulin (B = −6.16, P = 0.11), and HOMA-IR (B = 1.08, P = 0.89).

4. Discussion

This systematic review and meta-analysis is the first report of the effect of ginger supplementation on weight, BMI, body fat and metabolic profiles. This meta-analysis showed that ginger intake reduced weight, WHR, HR, fasting glucose and HOMA-IR, and increased HDL-cholesterol, but did not affect insulin, BMI, triglycerides, total- and LDL-cholesterol levels. It must be kept in mind that differences in types of supplement used, for example ginger as powder or extracts are important for interpreting the findings. In a study by Weng et al. (2010), it was observed that 6-shogaol and 6-gingerol, two active compounds found in ginger, had both anti-invasive activities against hepatoma cells through regulation of matrix metalloproteinase-9 and metalloproteinase protein-1 and that 6-shogaol could further regulate urokinase-type plasminogen activity. In another study, 6-gingerol, 8-gingerol, and 10-gingerol, the three analogues, had a strong and relatively equal efficacy in the treatment of colitis (Zhang et al. 2017). In our meta-analysis study, all studies except one (Taghizadeh et al. 2017) have used ginger rhizomes (Zingiber officinale) as powder.

Obesity is associated with many metabolic and non-metabolic disorders such as CHD, T2DM, and certain types of cancer (Kromhout 1983; Lynch et al. 2009). The current meta-analysis of RCTs demonstrated that ginger ingestion resulted in a significant decrease in weight, WHR and HR, but did not affect BMI. However, some meta-analysis study have reported the beneficial effects of herbal drugs on weigh and BMI reduction, data on the effect of ginger supplementation on weight, BMI, body fat are limited. In a meta-analysis study, intake of tea or tea extraction reduced the waist circumference in individuals with T2DM patients (Li et al. 2016). Data on ginger supplementation on weight loss are controversial. Adherence to the eight-week weight loss program among overweight subjects who were received METABO containing ginger, primarily raspberry ketone, caffeine, capsaicin, garlic, and Citrus aurantium led to the reduction in body fat (Lopez et al. 2013). A significant reduction in BMI was also observed following supplementation with 2 g/day of ginger for 12 weeks among obese women (Ebrahimzadeh Attari et al. 2015b). However, ginger supplementation (1 g/day) for 10 weeks among obese men did not cause any change in their BMI and/or body composition (Atashak et al. 2011a). It has been suggested that increasing thermogenesis and energy expenditure, as well as increasing the lipolysis of white adipose tissue by ginger (Pulbutr and Rattanakiat 2010) may result in body fat and/or weight reduction.

Our meta-analysis of RCTs documented that ginger intake resulted in a significant decrease in fasting glucose and HOMA-IR, but did not affect insulin levels. In line with our meta-analysis, Mazidi et al. (2016) demonstrated that ginger supplementation significantly improved glycemia indexes. In addition, Mahluji et al. (2013b) demonstrated that ginger supplementation for 2 months among patients with T2DM significantly reduced HOMA-IR; however, no significant change was observed in fasting glucose. Ginger supplementation for 6 weeks to obese women with breast neoplasm have resulted in a reduction of insulin, glucose and insulin resistance (Karimi et al. 2015). However, Bordia et al. (1997) demonstrated that ginger



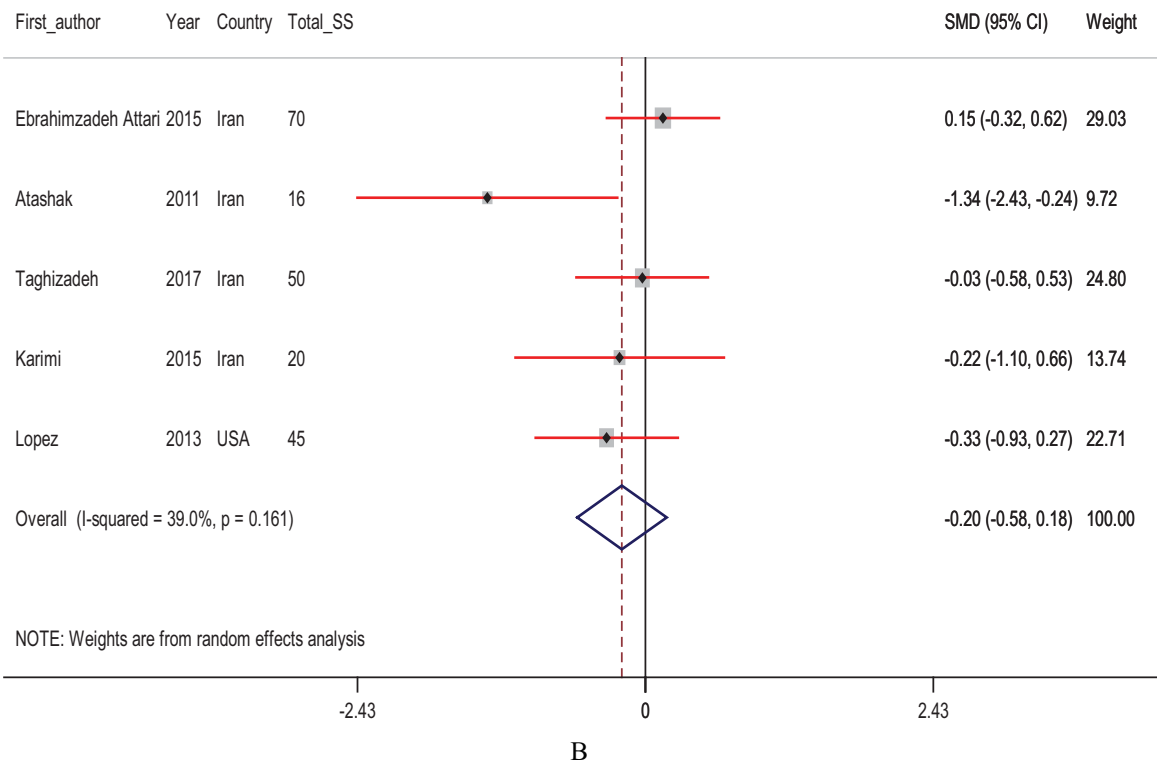
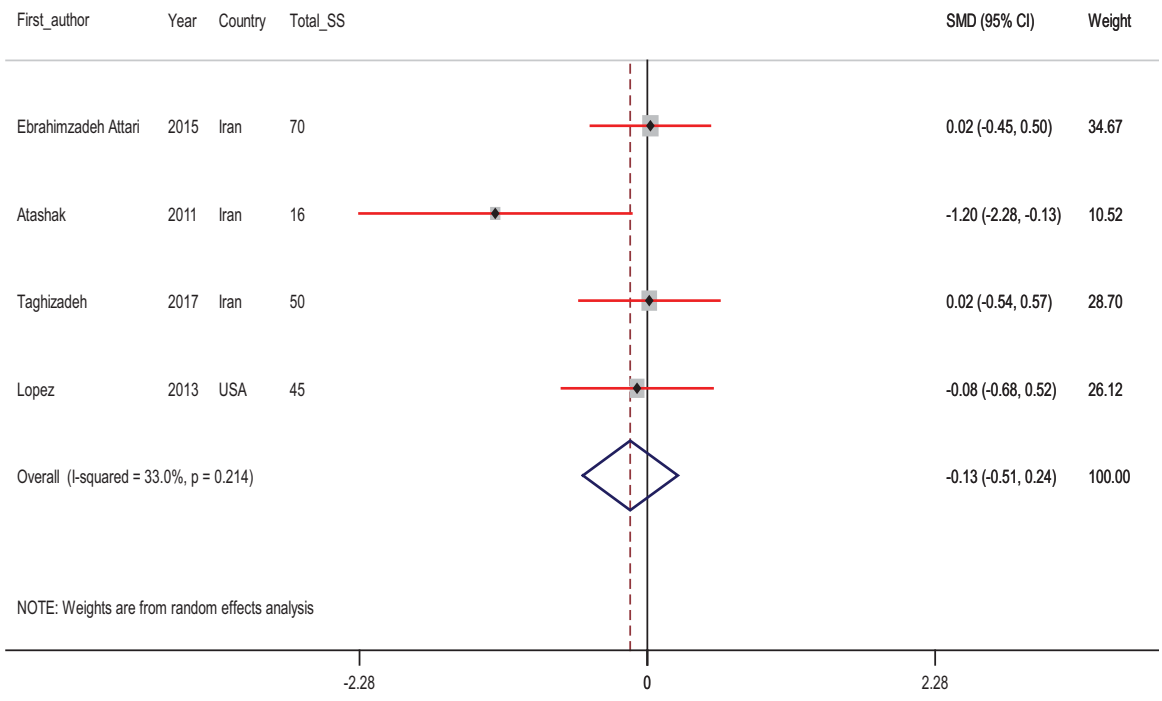


Figure 5a. A–D. Meta-analysis lipid profiles standardized mean differences estimates for (A) triglycerides, (B) for total-, (C) for LDL-, and (D) for HDL-cholesterol in ginger supplements and placebo groups (CI=95%).

supplementation had no significant effect on fasting glucose. An interesting observation in the current meta-analysis was that ginger administration did not affect insulin levels despite of reduced fasting glucose and HOMA-IR. This may have few reasons. The study duration may be one possible explanation for such discrepancy. The short duration of RCTs may cause the inverse effect on insulin. In addition, the dosage of ginger may affect insulin levels. It was proposed that the hypoglycemic effects of ginger may be due to its content of phenols, polyphenols, and flavonoids (Shanmugam et al. 2011). In vitro studies on the mechanism of the effect of ginger on glucose homeostasis parameters have indicated that the active constituents of ginger such as 6-gingerol and 8-gingerol increased cellular glucose uptake through elevating gene expression of glucose



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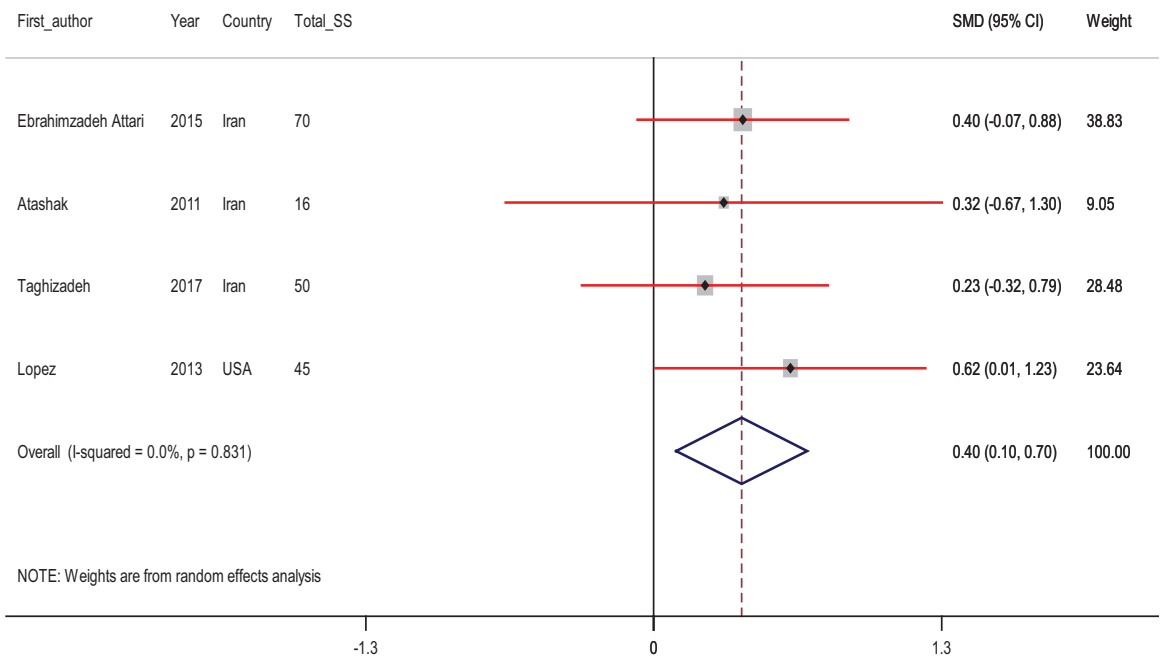

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Figure 5b. (Continued).

transporter type 4 (Li et al. 2012a; Son et al. 2015). In addition, ginger mat reduce blood glucose by antagonistic activity against serotonin receptors (Al-Amin et al. 2006). The 6-gingerol and 6-shogaol in ginger may improve glycemic control by upregulating adiponectin and peroxisome proliferator-activated receptor-γ, which in turn decrease insulin resistance (Isa et al. 2008).

This meta-analysis of RCTs showed that ginger supplementation was effective in increasing HDL-cholesterol, but did not influence other lipid profiles. In a meta-analysis study conducted by Mazidi et al. (2016), it was observed that ginger supplementation to healthy and patient's people significantly improved triglycerides and HDL-cholesterol levels, but did not affect other lipid profiles. Ginger supplementation for 6 weeks among obese women was associated with a significant reduction in triglycerides and LDL-cholesterol, and significantly increased HDL- and HDL-/LDL-cholesterol (Karimi et al. 2015). In another study, total cholesterol levels significantly decreased following the

Table 4. The assess of association between ginger supplementation, body composition and metabolic profiles based on sensitivity analysis.

	Pre-sensitivity analysis				Post-sensitivity analysis		
Variable	No. of studies included	Pooled SMD (random effect)	95% CI	Upper & lower of effect size	Pooled SMD (random effect)	95% CI	Excluded studies
BMI	4	-0.65	-1.36, 0.06	Upper	−0.31	−0.69, 0.05	Taghizadeh
				Lower	−0.85	−1.67, −0.03	Afzalpour
Body weight	4	-0.66	-1.31, −0.01	Upper	0.30	−0.64, 0.03	Taghizadeh
				Lower	−0.82	−1.68, 0.03	Lopez
WHR	4	-0.49	-0.82, −0.17	Upper	−0.42	−0.76, −0.08	Atashak
				Lower	−0.55	−0.94, −0.16	Lopez
HR	3	-0.42	-0.77, −0.08	Upper	−0.38	−0.87, 0.10	Ebrahimzadeh Attari
				Lower	−0.46	−0.88, −0.05	Lopez
Glucose	6	-0.59	-0.88, −0.29	Upper	−0.63	−1.34, 0.07	Atashak
				Lower	−0.87	−1.70, −0.03	Ebrahimzadeh Attari
Insulin	5	-0.54	-1.43, 0.35	Upper	−0.53	−1.40, 0.35	Atashak
				Lower	−0.83	−1.29, −0.36	Ebrahimzadeh Attari
HOMA-IR	5	-1.67	-2.86, −0.48	Upper	−1.16	−2.02, −0.30	Ebrahimzadeh Attari
				Lower	−2.06	−3.24, −0.89	Banitalebi
Triglycerides	4	-0.27	-0.71, 0.18	Upper	−0.12	−0.79, 0.54	Ebrahimzadeh Attari
				Lower	−0.45	−0.79, −0.11	Karimi
Total cholesterol	5	-0.20	-0.58, 0.18	Upper	−0.05	−0.34, 0.23	Atashak
				Lower	−0.33	−0.77, 0.10	Ebrahimzadeh Attari
LDL-cholesterol	4	-0.13	-0.51, 0.24	Upper	−0.006	−0.31, 0.30	Atashak
				Lower	−0.26	−0.84, 0.30	Ebrahimzadeh Attari
HDL-cholesterol	4	0.40	0.10, 0.70	Upper	0.46	0.11, 0.81	Taghizadeh
				Lower	0.32	−0.01, 0.66	Lopez

supplementation of ginger (1 g/day) in obese men after 10 weeks of resistance training (Atashak et al. 2011a), but unchanged other lipid profiles. Hepatic overexpression of apoA-I and apoA-II after ginger intake may explain the observed increase in HDL-cholesterol concentrations (Tangirala et al. 1999). In addition, increasing HDL-cholesterol levels is not only attributed to the upregulation of its apolipoproteins but also to niacin present in ginger which causes reduction in the catabolic rate of HDL-cholesterol (Al-Noory et al. 2013).

Overall, the current meta-analysis demonstrated that ginger intake reduced weight, WHR, HR, fasting glucose and HOMA-IR, and increased HDL-cholesterol, but did not affect insulin, BMI, triglycerides, total- and LDL-cholesterol levels. Additional prospective studies investigating the effect of ginger supplementation on weight, BMI, body fat loss and metabolic profiles are necessary.

Conflict of interest

None.

Funding

The current study was founded by a grant from the Vice-chancellor for Research, Shiraz University of Medical Sciences, Shiraz, and Iran.

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