



## The association between vitamin C dietary intake and its serum levels with anthropometric indices: A systematic review and meta-analysis



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### ABSTRACT

**Background:** studies showed inflammatory background of overweight and obesity. Prevalence of weight disorders has dramatically increased over the past few decades. Vitamin C is an antioxidant and may be associated with weight disorders. This study aims to systematically review the relationship between dietary and serum vitamin C levels with anthropometric indices.

**Methods:** A systematic search was conducted in Medline database (PubMed), Scopus, Embase, Web of Science, Cochrane library and Google Scholar up to the end of August 2021. All observational studies that assessed the relationship between dietary or circulating vitamin C levels and body mass index (BMI) and waist circumference (WC) on adults were included. The quality of included studies was assessed using the National Institute of Health quality assessment tool.

**Results:** Among 11,689 studies, 47 and 37 articles were included in the systematic review and meta-analysis, respectively. There was an inverse significant correlation between WC and serum vitamin C levels ( $r = -0.28$ , 95% CI:  $-0.35$ ,  $-0.21$ ,  $I^2 = 14.2\%$ ) and between BMI and serum vitamin C levels ( $r = -0.17$ , 95% CI:  $-0.25$ ,  $-0.09$ ,  $I^2 = 72.8\%$ ). Higher vitamin C consumption was significantly associated with lower BMI. There were no significant differences in serum vitamin C levels between normal-weight and overweight subjects, but serum vitamin C levels were significantly higher in obese subjects in comparison with normal-weight subjects.

**Conclusion:** Results showed that both dietary and serum vitamin C levels were inversely associated with BMI and WC. More well-designed clinical trials are needed to assess the effect of vitamin C supplementation in prevention and treatment of obesity.

### 1. Introduction

Weight disorders are associated with non-communicable diseases [1]. Prevalence of weight disorders, especially overweight and obesity has dramatically increased over the past few decades in various regions

[2–4]. It has been shown that overweight and obesity are associated with different complications such as cardiovascular disorders, diabetes mellitus, hypertension and metabolic syndrome and negatively affect various aspects of individuals quality of life [5–8].

Several factors including genetic, environment, socioeconomic

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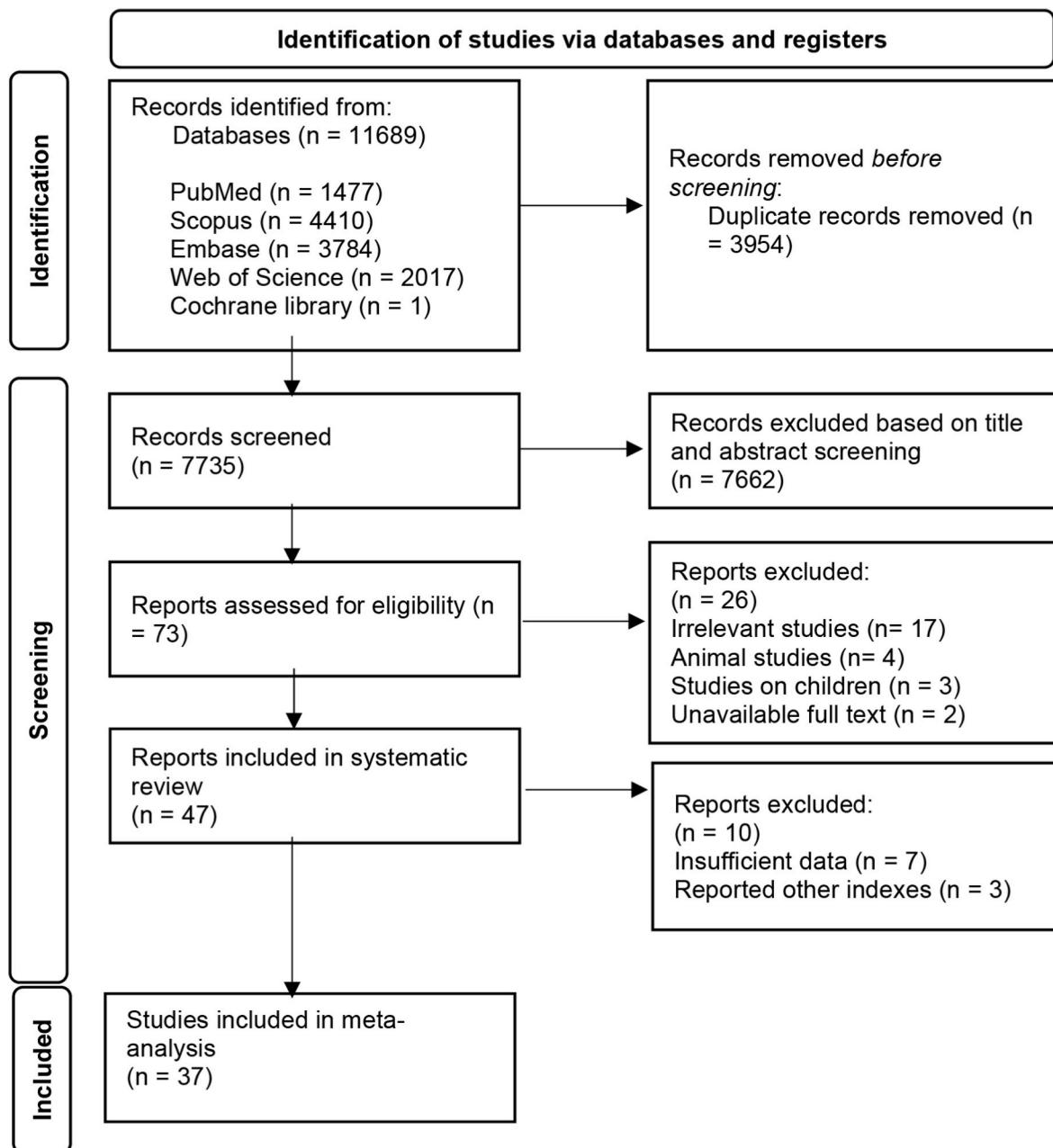


Fig. 1. PRISMA flow diagram of study selection process.

**Table 1**

Included studies, assessing Anthropometric indexes in different groups, categorized based on Ascorbic Acid intake or serum Ascorbic Acid level.

Author, year	Country	Study design	Population	N Subjects (male %)	Age <sup>a</sup> (year)	Ascorbic Acid intake <sup>a</sup> (mg/day) or serum Ascorbic Acid level (μmol/L)	N Subjects (lowest: highest group)	Anthropometric indexes		Outcome	
								Sample	(Lowest: highest group)		
Sinha et al., 1992 (41)	USA	Cross-sectional	Healthy people	68 (100)	40.6	blood	(35.7: 78.9)	(17: 17)	BW	(87.2: 78.5)	Groups with higher serum AA had significantly lower BW
Sargeant et al., 2000 (34)	England	Cross-sectional	Healthy people	3487 (0)	58.6	blood	(23.3: 80.8)	(457: 953)	BMI	(27.1: 25.1)	Groups with higher serum AA had significantly lower BMI and WHR
				2795 (100)	27.9	blood	(23: 80.7)	(809: 292)	WHR	(0.82: 0.78)	
Nam et al., 2003 (23)	South Korea	Case-control	IHD patients (case), healthy people (control)	250 (100)	53	food	(<141.8: >220.2)	(92: 71)	BMI	(23.7: 24.8)	Groups with higher AA intake had significantly higher BMI
Boekholdt et al., 2006 (35)	England	Case-control	Healthy people	2773 (63)	65.2	blood	(27.6: 77.1)	(870: 594)	BMI	(27: 25.6)	Groups with higher serum AA had significantly lower BMI
Azadbakht and Esmaillzadeh 2007 (29)	Iran	Cross-sectional	Healthy people	926 (0)	48	food	(<56: >116)	(231: 231)	WHR	N/A	Groups with higher AA intake had significantly lower WHR
Harding et al., 2008 (36)	Ten European countries	Cohort	Healthy people	12,016 (0)	58.1	blood	(≤43.7: ≥73.2)	(1963: 1963)	BMI	(27: 25.1)	Groups with higher serum AA had significantly lower BMI and WC
				9815 (100)	58.7	blood	(<31.8: >62.4)	(2403: 2403)	BMI	(26.7: 25.7)	
Myint et al., 2008 (37)	England	Cohort	Healthy people	20,649 (45)	58.4	blood	(28.2: 78.1)	(5298: 5343)	BMI	(26.9: 25.4)	Groups with higher serum AA had significantly lower BMI
				11,200 (0)	N/A	blood	(<41: >66)	(1895: 3957)	BMI	(27.1: 25.3)	
				9449 (100)	N/A	blood	(<41: >66)	(3403: 1386)	BMI	(26.8: 25.6)	
Cahill et al., 2009 (38)	Canada	Cross-sectional	Healthy people	979 (29)	22.6	blood	(6.2: 42.9)	(133: 521)	BMI	(23.1: 22.3)	Groups with higher serum AA had significantly lower BMI and WC
									WC	(75: 72.8)	
Kubota et al., 2010 (39)	Japan	Cross-sectional	Healthy people	1404 (0)	55.8	blood	(55.7: 92.5)	(281: 287)	BMI	(24: 23)	Groups with higher serum AA had significantly lower BMI
				778 (100)	58.2	blood	(42.3: 81.3)	(154: 155)	BMI	(23.8: 22.9)	
Ferraro et al., 2015 (26)	NHS I	Cohort	Healthy people	121,700 (0)	N/A	food	(<90: >1000)	N/A	BMI	(25.6: 24.9)	Groups with higher AA intake, had significantly lower BMI
	NHS II	Cohort	Healthy people	116,430 (0)	N/A	food	(<90: >1000)	N/A	BMI	(25.1: 23.9)	
	HPFS	Cohort	Healthy people	51,529 (100)	N/A	food	(<90: >1000)	N/A	BMI	(25.8: 25.1)	
Juhl et al., 2017 (40)	Denmark	Cross-sectional	T1DM women within 4-week of delivery	47 (0)	27	blood	(<26.6: >26.6)	(24: 23)	BMI	(29.2: 27.6)	There is no significant difference in BMI between 2 groups
Pearson et al., 2017 (25)	New Zealand	Cohort	Healthy people	368 (47)	N/A	blood	(<23: >23)	(47: 321)	BMI	(31.4: 28.1)	BMI, WC and BW is significantly lower in higher serum AA group
				250 (46)	N/A	food	(<110: >110)	(147: 103)	BMI	(28.5: 27.2)	
									WC	(94.6: 91.2)	
									BW	(82.2: 79.8)	There is no significant difference in BMI, WC and BW between 2 groups

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**Table 1 (continued)**

Author, year	Country	Study design	Population	N Subjects (male %)	Age <sup>a</sup> (year)	Ascorbic Acid intake <sup>a</sup> (mg/day) or serum Ascorbic Acid level (μmol/L)	N Subjects (lowest: highest group)	Anthropometric indexes		Outcome	
								Sample	(Lowest: highest group)		
Eshak et al., 2019 (24)	Japan	Cohort	Healthy people	12,092 (0) 7076 (100)	55.7 55.8	food food	(103: 202) (60: 185)	(3023: 3023) (1769: 1769)	BMI BMI	(22.8: 22.8) (22.6: 22.6)	There is no significant difference in BMI between 2 groups
Ivancovsky- Wajcman et al., 2019 (28)	Israel	Cross- sectional	People with risk of NAFLD	789 (52)	58.8	food	(<91.4: >91.4)	(526: 263)	BMI WC	(28.6: 28.3) (63.4: 58.8)	There is no significant difference in BMI and WC between 2 groups

Abbreviations: AA: Ascorbic Acid, BMI: Body Mass Index, BW: Body Weight, WC: Waist Circumferences, WHR: Waist to Hip Ratio, T1DM: Type 1 Diabetes Mellitus, NAFLD: Non-Alcoholic Fatty Liver Disease, IHD: Ischemic Heart Disease, NHS: Nurses' Health Study, HPFS: Health Professionals Follow-up Study, N: Number, N/A: Not Available.

<sup>a</sup> Values are Mean for age, BMI, BW, WHR, WC and Mean or Range for AA intake and serum AA level.

factors and nutritional status can be associated with weight disorders [9, 10].

Studies showed an association between overweight/obesity and increasing inflammatory markers such as tumor necrosis factor alpha (TNF-α), interleukin (IL-6, IL-4), leptin and macrophage chemoattractant protein-1 (MCP-1) [11–14]. Reactive Oxygen Species (ROS) have pivotal role in the development of obesity and its related complications [15,16]. Thus, antioxidant agents including carotenoids, vitamin E, vitamin C, zinc, magnesium, selenium may have protective effects on adverse complications of obesity and overweight [16].

Vitamin C (Ascorbic acid) is a water-soluble vitamin, which has different functions including wound healing, iron absorption, collagen synthesis and hemoglobin activation. It is considered as a cofactor for various enzymes in catecholamines and neurohormones formation [17]. Moreover, vitamin C is a powerful electron donor and scavenges the harmful free radicals. Recent studies confirmed its ability in diminishing oxidative stress and inflammatory reactions [17,18].

There are many studies that assessed the relationship between dietary or serum vitamin C status and anthropometric indices in different populations and regions. However, there are several discrepancies in their results. Some studies did not report any significant differences in serum vitamin C levels between normal, overweight, and obese participants [19,20], while others reported significant associations [21,22]. These discrepancies might be due to various reasons such as different sample size, regions of studies, nutritional status, and genetic factors. On the other hand, there are also controversies in the association of dietary vitamin C and anthropometric indices. Some investigations demonstrated the association between higher vitamin C intake and higher body mass index (BMI) [23], but some studies showed no significant difference [24,25] or showed the association between higher vitamin C intake and lower BMI [26]. Thus, we aim to conduct a systematic review and meta-analysis to better clarify the association between dietary and circulating vitamin C levels and anthropometric indices.

## 2. Materials and methods

### 2.1. Search strategy

The current systematic review and meta-analysis study was conducted according to PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [27]. The protocol was registered on PROSPERO (ID: CRD42021226063). A systematic literature search was performed in Medline database (PubMed), Scopus, Embase, Web of Science, Cochrane library up to end of August 2021 using the following search terms: ((“ascorbic acid” OR “vitamin C”) AND

(“body weight” OR “body mass index” OR “BMI” OR “waist circumference” OR “waist to hip ratio” OR “waist to height ratio” OR “body fat” OR “obesity” OR “overweight” OR “adiposity”). Grey literature was searched using Google Scholar. Search terms for systematic search in databases are shown in Table S1.

After removing duplicate papers, two independent reviewers (SMT and MHB) reviewed and screened the published papers based on title, abstract, and full text. Additionally, the references of related review articles were checked to find undetected appropriate studies. Any disagreement related to eligible records was resolved by the third reviewer (RK). Study selection process was demonstrated in Fig. 1.

### 2.2. Inclusion criteria

All observational studies (cross-sectional, case-control, and cohort) on individuals over 18 years that assessed the relationship between dietary intake or circulating vitamin C and anthropometric indices were included without restriction of race, age, gender, and publication date. Only English-language and human studies were included.

### 2.3. Exclusion criteria

Studies with following criteria were excluded: duplicated articles, conference proceedings, studies with insufficient data.

### 2.4. Data extraction

The following items were extracted from suitable and relevant studies: first author, country, publication date, study size, study design, age, gender, mean of serum vitamin C or vitamin C intake, BMI, WC, and other anthropometric indices such as WHR and weight if applicable. Data extraction was performed by two independent reviewers (SMT, MHB) and checked by the third reviewer (RK).

### 2.5. Quality assessment

The quality of included studies was assessed using National Institute of Health (NIH) quality assessment tool by two independent reviewers (SMT, MHB). Any discrepancy was resolved by third reviewer (RK). The scale consists of 14 questions for cohort and cross-sectional studies, and 12 questions for case-control studies. Based on risk of bias in different studies, quality of articles can be judged as “Poor”, “Fair”, and “Good”. Table S2 shows the quality assessment of cohort and cross-sectional studies and Table S3 shows quality assessment of case-control studies.

**Table 2**

Included studies, assessing Ascorbic Acid intake or serum levels in different groups, categorized based on body mass index, waist circumferences, or waist to hip ratio.

Author, year	Country	Study design	Population	N Subjects (male %)	Age <sup>a</sup> (year)	Anthropometric indexes <sup>a</sup>					N Subjects				Ascorbic Acid intake <sup>a</sup> (mg/day) or serum Ascorbic Acid level (μmol/L)				Outcome	
						Reported data	1st	2nd	3rd	4th	1st	2nd	3rd	4th	sample	1st	2nd	3rd	4th	
Ness et al., 1999 (42)	England	Cross-sectional	Healthy people	563 (0)	49.9	BMI	<20	20–24.9	25–29.9	>30	N/A	N/A	N/A	N/A	blood	57.6	49.5	44.3	42.9	Groups with higher BMI had significantly lower serum AA level
				455 (100)	50.4	BMI									blood	36	35	37.3	34.1	There is no significant difference in serum AA level among groups
Galan et al., 2005 (22)	France	Cross-sectional	Healthy people	1821 (0)	47.2	BMI	<25	25–30	>30	1471	268	82	blood	10.5		11.1	10.4		There is no significant difference in serum AA level among groups	
Johnston et al., 2007 (43)	USA	Cross-sectional	Healthy people	1307 (100)	52.1	BMI	<25	25–30	>30	692	546	69	blood	9.2		8.5	8.1		There is no significant difference in serum AA level among groups	
Vioque et al., 2007 (19)	Spain	Cross-sectional	Healthy people	118 (29)	38.7	BMI	18–24.9	25–29.9	30–34.9	>35	26	28	34	30	blood	54.4	46.4	38.3	37.2	Groups with higher BMI had significantly lower serum AA level
Aasheim et al., 2008 (44)	Norway	Cross-sectional	Healthy and severely obese people	106 (0)	40.4	BMI	23 ± 3	45 ± 7	30		76		blood	74		48			Serum AA was significantly lower in higher BMI group	
Van Guilder et al., 2008 (45)	USA	Case-control	normal weight and obese people	62 (100)	40	BMI	25 ± 3	45 ± 7	28		34		blood	63		48			There is no significant difference in serum AA between 2 groups	
Cahill et al., 2009 (38)	Canada	Cross-sectional	Healthy people	33 (66)	53.7	BMI	<25	25–30	>30	85	261	199	blood	124.1		45.8	45.4		There is no significant difference in serum AA and AA intake among groups	
Riess et al., 2009 (21)	USA	Cohort	patients undergoing elective abdominal surgery	979 (29)	22.6	BMI	<25	25–30	>30	85	787	192	blood	27.6		26			There is no significant difference in serum AA between 2 groups	
Schleicher et al., 2009 (46)	USA	Cross-sectional	Healthy people	266	N/A	BMI	19–24.9	25–29.9	30–34.9	>35	25	47	27	167	blood	52.2	46	43.7	39	Groups with higher BMI had significantly lower serum AA level
Mah et al., 2011 (47)	USA	Case-control	normal weight (control) and obese people (case)	2086 (100)	N/A	BMI	18.5–24.9	25–29.9	>30	636	635	742	blood	60.3		52.8	45		Groups with higher BMI had significantly lower serum AA level	
Garcia et al., 2012 (20)	Mexico	Cross-sectional	Healthy people	16 (100)	21	BMI	N/A	18–25	27–40		N/A	8	8		blood	N/A	43.7	27.2		Serum AA was significantly lower in obese people comparing to overweight
Nwagha et al., 2012 (48)	Nigeria	Cross-sectional	Primiparous non-pregnant women	513 (0)	N/A	BMI	<25	25–30	>30	105	194	214	blood	30.6		30.6	28.9		Serum AA was significantly lower in obese people	
Choi et al., 2013 (32)	South Korea	Case-control	Multiparous non-pregnant women	82 (0)	24.6	BMI	<20	20–25	25.1–30	>30	14	54	14	N/A	blood	60.4	89.5	98.5	N/A	N/A
			Healthy people	118 (0)	32.1	BMI					N/A	67	34	17	blood	N/A	68.7	70.3	66.4	
				9565 (0)	42.5	WC	<85	>85		7597	1968		food	109		102.3			AA intake of obese group was significantly higher than normal group	
				6849 (100)	43.2	WC	<90	>90		5215	1634		food	115		116.2			There is no significant difference in AA intake between 2 groups	

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**Table 2 (continued)**

Author, year	Country	Study design	Population	N Subjects (male %)	Age <sup>a</sup> (year)	Anthropometric indexes <sup>a</sup>				N Subjects				Ascorbic Acid intake <sup>a</sup> (mg/day) or serum Ascorbic Acid level (μmol/L)				Outcome		
						Reported data	1st	2nd	3rd	4th	1st	2nd	3rd	4th	sample	1st	2nd	3rd	4th	
Zavala et al., 2013 (49)	Mexico	Cross-sectional	Healthy people	280 (0)	37	BMI	<24.9		25–29.9	>30	52	104	124	blood	28.9	30.6	30.6	30.6	There is no significant difference in serum AA level among groups	
Jungert and Neuhäuser-Berthold 2015 (50)	Germany	Cross-sectional	Healthy people	270 (33)	72.3	BMI	<25		25–29.9	>30	117	98	55	blood	74	71	62	Groups with higher BMI had significantly lower serum AA level		
Singh and Singh 2015 (51)	India	Case-control	severe obese males (case) and normal males (control)	100 (100)	32.2	BMI	<27			>46	50		50	blood	47.1	38.6		Groups with higher BMI had significantly lower serum AA level		
Langlois et al., 2016 (52)	Canada	Cross-sectional	Healthy people	1615 (49)	N/A	BMI	<25		25–30	>30	615	586	414	blood	58	53	45	Serum AA of obese cases was significantly lower than normal cases		
Hitha et al., 2018 (53)	India	Cross-sectional	normal weight and obese people	300 (54)	N/A	BMI	<25		N/A	>30	150	N/A	150	blood	102.7	N/A	140.8	Serum AA was significantly higher in obese people		
Jia et al., 2018 (31)	China	Cross-sectional	Healthy people	11,375 (43)	N/A	BMI	<18.5	18.5–24	24–28	>28	469	5388	3938	1562	food	76.2	64.6	65.3	68.3	There is no significant difference of AA intake between different groups of BMIs
Adnan et al., 2019 (54)	Bangladesh	Case-control	normal weight (control) and obese people (case)	200 (38)	50.6	BMI	$22.9 \pm 1.7$		$33.8 \pm 2.7$		100	100		blood	46.2		32.4		Serum AA was significantly lower in obese people	
Amin et al., 2020 (55)	Bangladesh	Case-control	normal weight (control) and obese people (case)	140 (0)	36.9	BMI	$22.8 \pm 2.7$		$34.6 \pm 5.1$		70	70		blood	43.7		29.7		Serum AA was significantly lower in obese people	
Haidari et al., 2020 (30)	Iran	Cross-sectional	Healthy people	170 (0)	23.9	BMI WHR	<18.5 <0.8	18.5–24.9 >0.8	25–29.9 >30	6 115	104 55	5	food food	92.3 110.4	114.9 109	104 109	94.5	There is no significant difference of AA intake between different groups of BMIs and WHR		

Abbreviations: AA: Ascorbic Acid, BMI: Body Mass Index, WC: Waist Circumferences, WHR: Waist to Hip Ratio, N: Number, N/A: Not Available.

<sup>a</sup> Values are Mean for age, AA intake and Range for BMI, WC and WHR.

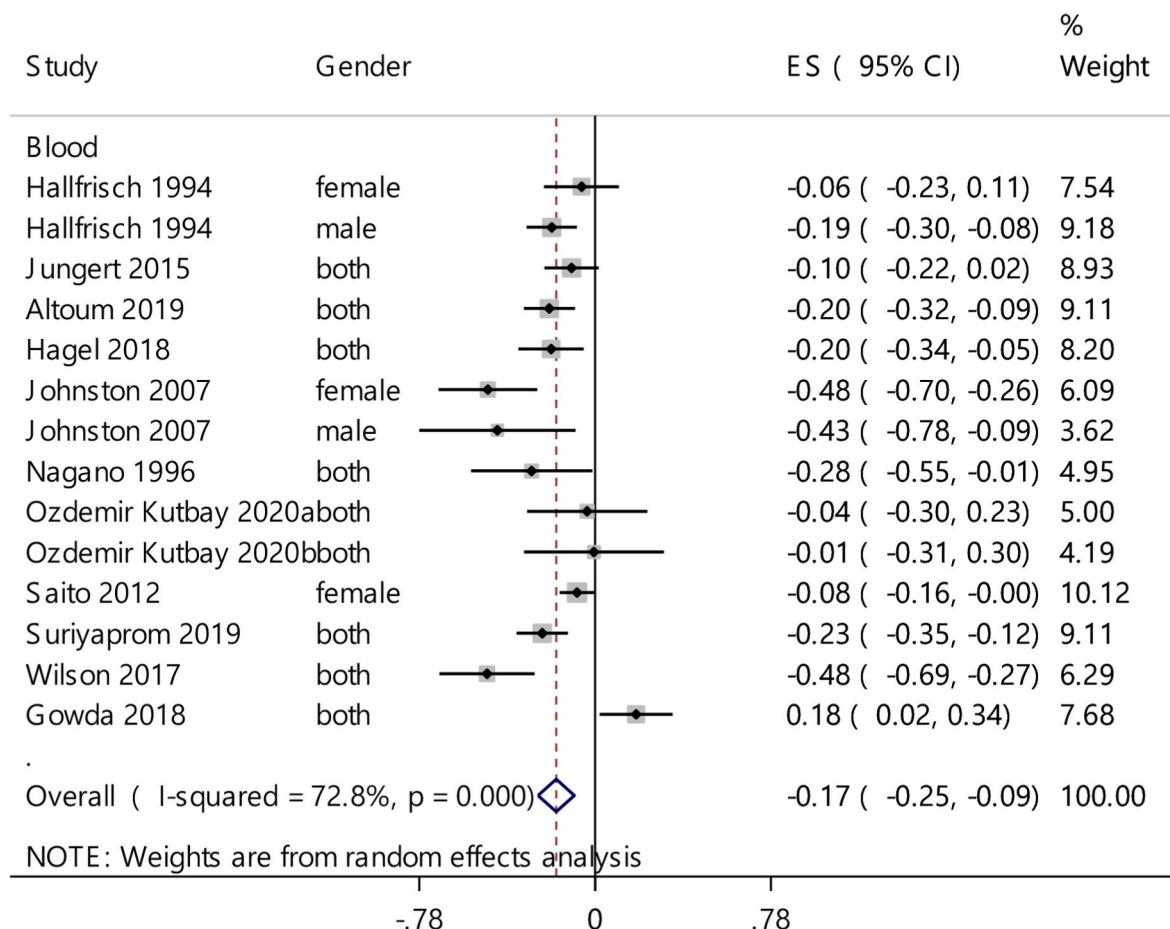
**Table 3**

Characteristic of included studies that assessed the correlation between anthropometric indices and serum or dietary vitamin C levels.

Author, year	Country	Study design	Population	N Subjects (male %)	Age <sup>a</sup> (year)	BMI <sup>a</sup>	AA <sup>a</sup>	Reported data	Outcome
Hallfrisch et al., 1994 (56)	USA	Cross-sectional	Healthy and sick people	316 (0)	59	24.5	76.7	BMI	No significant association was seen between serum AA and BMI
			Healthy and sick people	511 (100)	61	25.7	65.3	BMI	Serum AA was inversely associated with BMI
			Healthy people	142 (0)	N/A	N/A	N/A	BMI	No significant association was seen between serum AA and BMI
			Healthy people	314 (100)	N/A	N/A	N/A	BMI	Serum AA was inversely associated with BMI
Nagano et al., 1996 (57)	Japan	Cross-sectional	Patients with non-insulin-dependent DM	56 (50)	53.1	N/A	N/A	BMI	Serum AA was inversely associated with BMI
Toohey et al., 1996 (66)	USA	Cross-sectional	Healthy people	172 (26)	47.8	N/A	N/A	WC, WHR	Serum AA was inversely associated with WC and WHR
Drewnowski et al., 1997 (58)	France	Cross-sectional	Healthy people	837 (43)	42.6	23.4	47.8	BMI	Serum AA was inversely associated with BMI
Galan et al., 2005 (22)	France	Cross-sectional	Healthy people	1307 (100)	52.1	25.1	49.9	BMI	Serum AA was inversely associated with BMI
Johnston et al., 2007 (43)	USA	Cross-sectional	Healthy people	83 (0) 35 (100)	N/A N/A	N/A N/A	N/A	BMI, WC	Serum AA was inversely associated with BMI and WC
García et al., 2012 (20)	Mexico	Cross-sectional	Healthy people	513 (0)	N/A	N/A	N/A	BMI, WC, WHR	Serum AA was inversely associated with BMI and WHR, but there is no significant association with WC
Saito et al., 2012 (59)	Japan	Cross-sectional	Healthy people	655 (0)	75.7	22.9	50.5	BMI, BW	No significant association was seen between serum AA and BMI, BW
Jungert and Neuhäuser-Berthold 2015 (50)	Germany	Cross-sectional	Healthy people	270 (33)	72.3	26.6	71.4	BMI, BW, WC	Serum AA was inversely associated with BW and WC, but there is no significant association with BMI
Wilson et al., 2017 (60)	New Zealand	Cross-sectional	combination of people with T2DM, prediabetes, and NGT	89 (45)	59	30	49	BMI, WHR	Serum AA was inversely associated with BMI and WHR
Hitha et al., 2018 (53)	India	Cross-sectional	normal weight and obese people	300 (54)	N/A	N/A	N/A	BMI	No significant association was seen between serum AA and BMI
Hagel et al., 2018 (61)	Germany	Cross-sectional	Healthy people	188 (26)	52.6	24.3	N/A	BMI	No significant association was seen between serum AA and BMI
Abd Elgadir et al., 2019 (62)	Sudan	Cross-sectional	T2DM patients	300	50.2	29.5	N/A	BMI	No significant association was seen between serum AA and BMI
Maugeri et al., 2019 (33) (Dietary AA)	Czech	Cross-sectional	Healthy people	894 (46)	46.5	24.6	N/A	BMI, WHR	No significant association was seen between AA intake and BMI, WHR
Suriyaprom et al., 2019 (63)	Thailand	Case-control	patients with MS (case) and healthy people (control)	300 (44)	40.8	27.1	N/A	BMI, WC	Serum AA was inversely associated with BMI and WC in all study subjects
Coelho et al., 2020 (64)	Brazil	Cross-sectional	patients with diagnosed NAFLD	72	59	32.2	35.2	BMI	No significant association was seen between serum AA and BMI
Ozdemir Kutbay et al., 2020 (65)	Turkey	Case-control	Patients with Acromegaly	57 (49)	49.5	31	42.8	BMI, WC	No significant association was seen between serum AA and BMI, WC
Healthy people									
43 (37)									
49.6									
28.1									
78.3									

Abbreviations: AA: Ascorbic Acid, BMI: Body Mass Index, BW: Body Weight, WC: Waist Circumferences, WHR: Waist to Hip Ratio, DM: Diabetes Mellitus, T2DM: Type 2 Diabetes Mellitus, NGT: Normal Glucose Tolerance, MS: Metabolic Syndrome, NAFLD: Non-Alcoholic Fatty Liver Disease, N: Number, N/A: Not Available.

<sup>a</sup> Values are mean.



**Fig. 2.** Correlation of BMI and serum vitamin C levels.

## 2.6. Statistical analysis

Meta-analysis was conducted for three kind of effect sizes, correlation coefficient between anthropometrics indices and vitamin C intake and vitamin C levels in blood, the mean difference (MD) of vitamin C levels ( $\mu\text{mol/L}$ ) between normal weight and overweight/obese subjects and the mean difference (MD) of BMI and WC between low and high levels of vitamin C.

The association of anthropometric indices and vitamin C was evaluated in subgroups of vitamin C intake, serum vitamin C and gender groups if there was enough number of studies.

A random-effects meta-analysis was used to estimate effects because of underlying differences in study design and methodology. We assessed risk of publication bias overall by evaluating a funnel plot, asymmetry, and Begg's test. The between-study heterogeneity was assessed with the use of the  $I^2$  statistic. All statistical analyses were conducted in Stata 14 software (Stata Corp LP), and a 2-sided 0.05 level of significance was used in all cases.

## 3. Result

### 3.1. Study selection

Study selection process was summarized in Fig. 1. Based on the initial search, we found 11,689 papers and after excluding duplicates 7735 articles remained. After title and abstract screening, 73 articles remained for further assessment. Full texts of the relevant papers were reviewed carefully by three researchers. Finally, 47 articles had the eligibility for including in the systematic review and 37 articles were included in the meta-analysis. From 47 included articles, 31 articles had

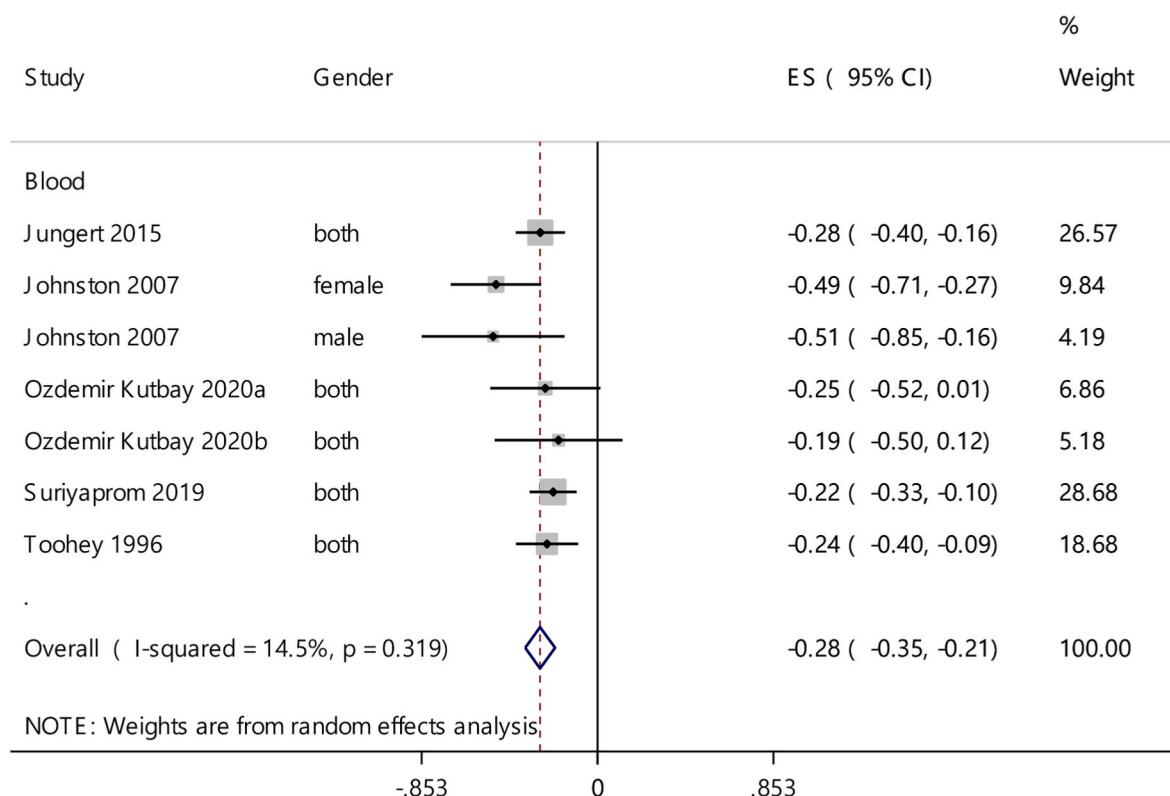
cross-sectional design, 6 articles had cohort design, and 10 articles had case-control design. Included studies in systematic review assessed different anthropometric indices including BMI, WC, WHR and body weight. Since the number of articles on BMI and WC were greater than others, so we selected them for meta-analysis.

### 3.2. Characteristics of studies that assessed vitamin C intake

Eleven studies investigated the association between vitamin C intake and anthropometric indices. Six studies assessed the mean differences of BMI [23–26,28], WC [25,28], WHR [29], and body weight [25] according to different groups of vitamin C intake. Four studies assessed mean vitamin C intake in different groups according to BMI [19,30,31], WC [32], and WHR [30] categories. One study assessed the relationship between dietary vitamin C with BMI and WHR [33]. These eleven studies had 340,440 participants in different years (from 2003 to 2020) and different countries. The sample size of included studies varies from 170 to 121,700. Two studies assessed only females [29,30], one study assessed only males [23], five studies assessed both genders [19,25,28,31,33], and three studies assessed males and females, separately [24,26,32]. Table 1-3 summarize the characteristics of included papers. From eleven studies, six papers were included in the mate-analysis.

### 4. Characteristics of studies that assessed serum vitamin C levels

Thirty-eight studies investigated serum vitamin C levels. Nine studies evaluated the mean differences of BMI [25,34–40], WC [25,36,38], WHR [34], and body weight [25,41] in different groups of serum vitamin C levels. Nineteen studies assessed serum vitamin C levels in different groups based on BMI categories [19–22,38,42–55]. Sixteen



**Fig. 3.** Correlation of WC and serum vitamin C levels.

studies assessed the association between serum vitamin C levels with BMI [20,22,43,50,53,56–65], WC [20,43,50,63,65,66], WHR [20,60,66], and body weight [50,59]. Overall, these 38 included studies had 71,784 participants. The lowest and highest sample sizes of included studies were 16 and 20,649, respectively. Six studies assessed only females [20, 40,48,49,55,59], three studies assessed only males [41,47,51], nineteen studies assessed both genders [19,21,25,35,38,45,50,52–54,57,58, 60–66] and eight studies assessed both genders separately [22,34,36,39, 42,44,46,56], and two studies assessed males and females together or separately [37,43]. Investigations were conducted in different years (from 1992 to 2020) and different countries. Tables 2 and 3 summarize the characteristics of included studies. From 38 articles, 32 papers were included in the meta-analysis.

#### 4.1. Correlation between anthropometric indices and serum vitamin C levels

Twelve studies reported the correlation coefficient of BMI with serum vitamin C levels. There was an inverse significant correlation between BMI and serum vitamin C levels ( $r = -0.17$ , 95% CI:  $-0.25$ ,  $-0.09$ ,  $I^2 = 72.8\%$ ) (Fig. 2). Funnel plot (Fig. S1) and Begg's test ( $p = 0.511$ ) show no evidence of publication bias. In sensitivity analysis, one study was dropped each time, the pooled correlation between BMI and serum vitamin C did not change substantially (the range of pooled effects was  $-0.15$  to  $-0.20$ , Fig. S2).

Fig. 3 shows forest plot of studies that reported correlation coefficients between WC and serum vitamin C levels. There was an inverse significant correlation between WC and serum vitamin C levels ( $r = -0.28$ , 95% CI:  $-0.35$ ,  $-0.21$ ,  $I^2 = 14.2\%$ ). There was no evidence of publication bias (Begg's  $p = 0.548$ ).

Mean differences of anthropometric indices according to different levels of serum vitamin C and vitamin C intake.

Higher vitamin C consumption was significantly associated with lower BMI ( $MD = -0.54 \text{ kg/m}^2$ , 95%CI:  $-0.15$ ,  $-0.93$ ;  $I^2 = 96.6\%$ ). The

heterogeneity decreased in male ( $MD = -1.86$ , 95%CI:  $-2.08$ ,  $-1.64$ ,  $I^2 = 30.7\%$ ) and female ( $MD = -1.13$ , 95%CI:  $-1.29$ ,  $-0.98$ ,  $I^2 = 28.9\%$ ) with separate subgroup analysis.

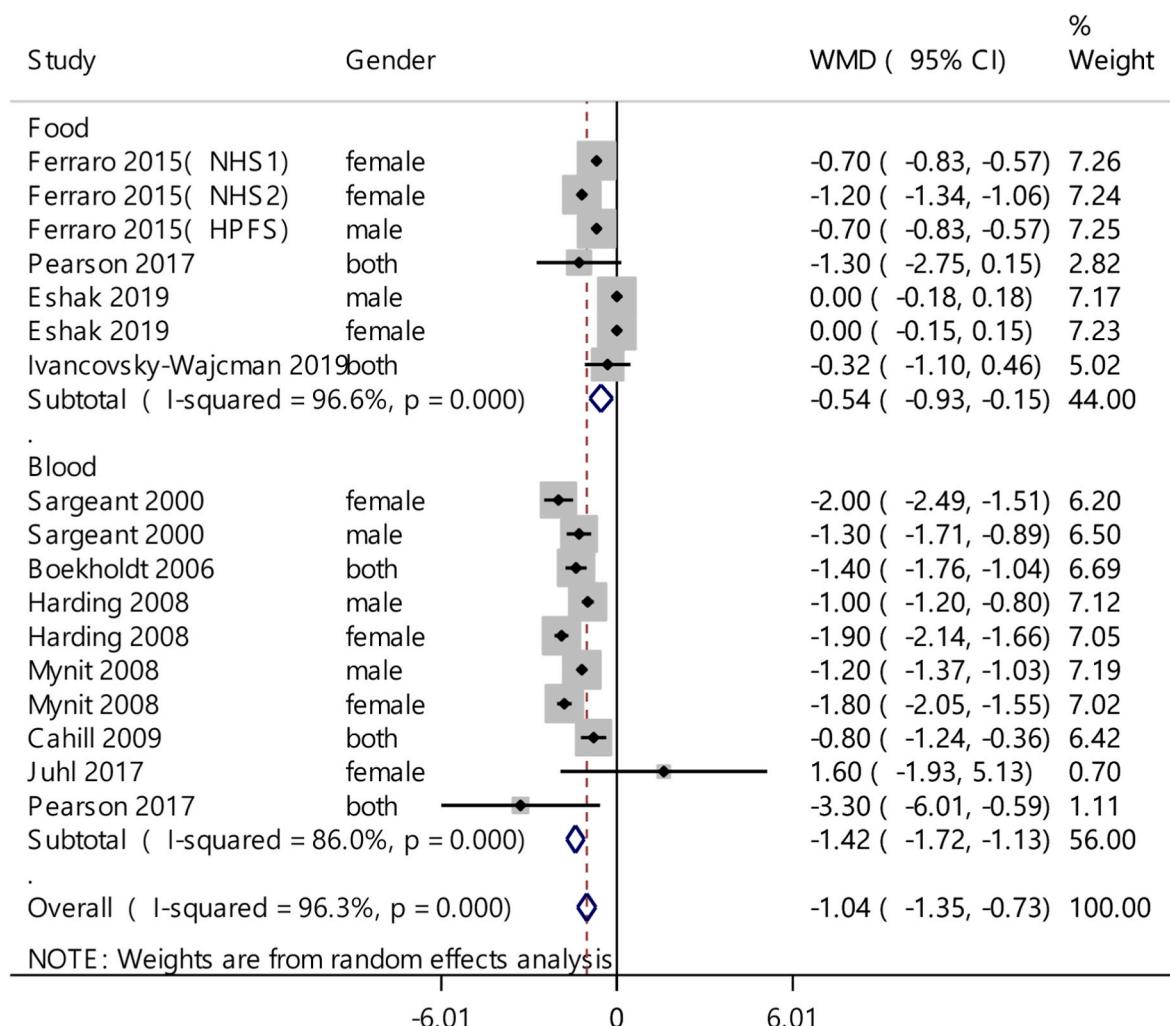
Higher serum vitamin C levels was associated with lower BMI (weighed mean difference ( $MD$ ) =  $-1.42 \text{ kg/m}^2$ , 95%CI:  $-0.73$ ,  $-1.35$ ;  $I^2 = 86.0\%$ ) (Fig. 4). There was no evidence of publication bias for serum vitamin C levels (Begg's  $p = 0.929$ ) and vitamin C intake (Begg's  $p = 0.453$ ). According to four studies that evaluated the difference of WC across serum vitamin C levels, individuals who had higher serum vitamin C levels in comparison with lower serum vitamin C levels had  $4.48 \text{ cm}$  lower WC ( $MD = -4.48$ , 95%CI:  $-2.85$ ,  $-6.11$ ,  $I^2 = 89.6\%$ ) (Fig. 5).

Mean difference of serum vitamin C levels in obese and overweight groups compared with normal weight group.

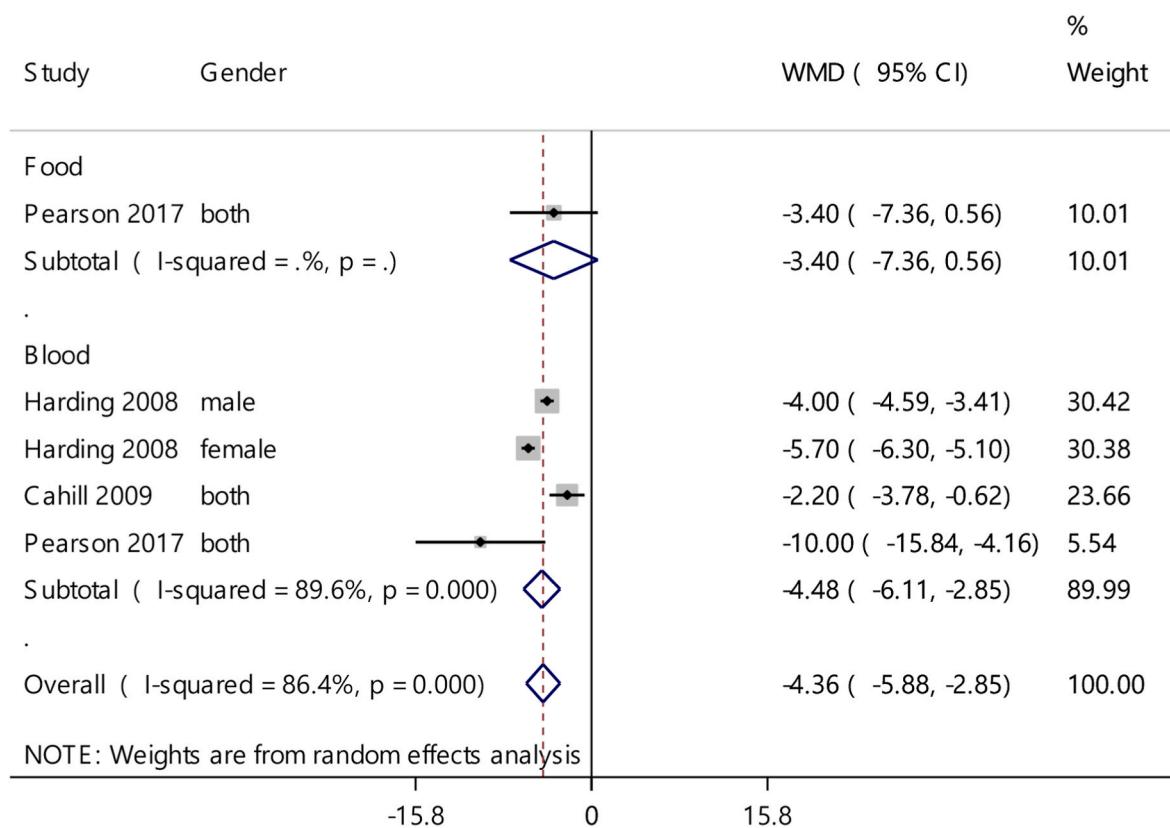
Seventeen studies reported the mean difference of serum vitamin C levels between normal weight, overweight and obese people. There was not any significant difference in mean serum vitamin C levels between normal and overweight groups ( $MD = 0.60 \mu\text{mol/L}$ , 95% CI:  $-3.57$ ,  $4.87$ ,  $I^2 = 94.6\%$ ) (Fig. 6), but there was significant difference in mean serum vitamin C levels between normal and obese people ( $MD = 7.03$ , 95%CI:  $3.80$ ,  $10.26$ ,  $I^2 = 91.7\%$ ) (Fig. 7). The heterogeneity decreased in male ( $MD = 8.48$ , 95%CI:  $5.88$ ,  $11.09$ ,  $I^2 = 45.7\%$ ) and female ( $MD = 8.32$ , 95%CI:  $1.48$ ,  $15.15$ ,  $I^2 = 94.6\%$ ) with separate subgroup analysis. There was no evidence of publication bias for serum vitamin C levels (Begg's  $p = 0.329$ ) and vitamin C intake (Begg's  $p = 0.317$ ) respectively.

#### 5. Discussion

The present study assessed the association between dietary and circulating vitamin C levels with anthropometric indices. Findings showed an inverse correlation between BMI and WC with serum vitamin C levels. Higher vitamin C consumption and serum vitamin C levels were significantly associated with lower BMI. Individuals who had higher serum vitamin C levels in comparison with lower serum vitamin C levels



**Fig. 4.** Mean difference BMI between high and low levels of vitamin C in serum and intake.



**Fig. 5.** Mean difference WC between low and high levels of vitamin C in serum and intake.

had lower WC.

Although, some studies did not find any significant association between BMI [50,53,59,61,62,64,65] or WC [20,65] and serum vitamin C levels, most studies reported an inverse relationship between BMI and WC with serum vitamin C levels [22,43,57,58,60,63,66]. These discrepancies mainly might be due to different regions of the study and different samples.

Our analysis shows higher levels of serum vitamin C in normal weight subjects in comparison with obese subject. This may be due to higher levels of inflammatory adipokines in obese subjects in comparison with overweight and normal weight subjects [67,68]. One cross-sectional study on 300 obese and non-obese subjects with both gender indicated significantly higher circulating vitamin C level in obese participants comparing to normal weight subjects [53]. Some studies assessed serum vitamin C levels in men and women separately. Their results demonstrated lower serum vitamin C levels in men in comparison with women. It might be due to several reasons such as volumetric dilution effect, because of higher fat-free mass in males, higher dietary intakes of vitamin C in females and differences in health habits, including physical activity, smoking, alcohol consumption and even hormonal status [22,32,36,39,42,46].

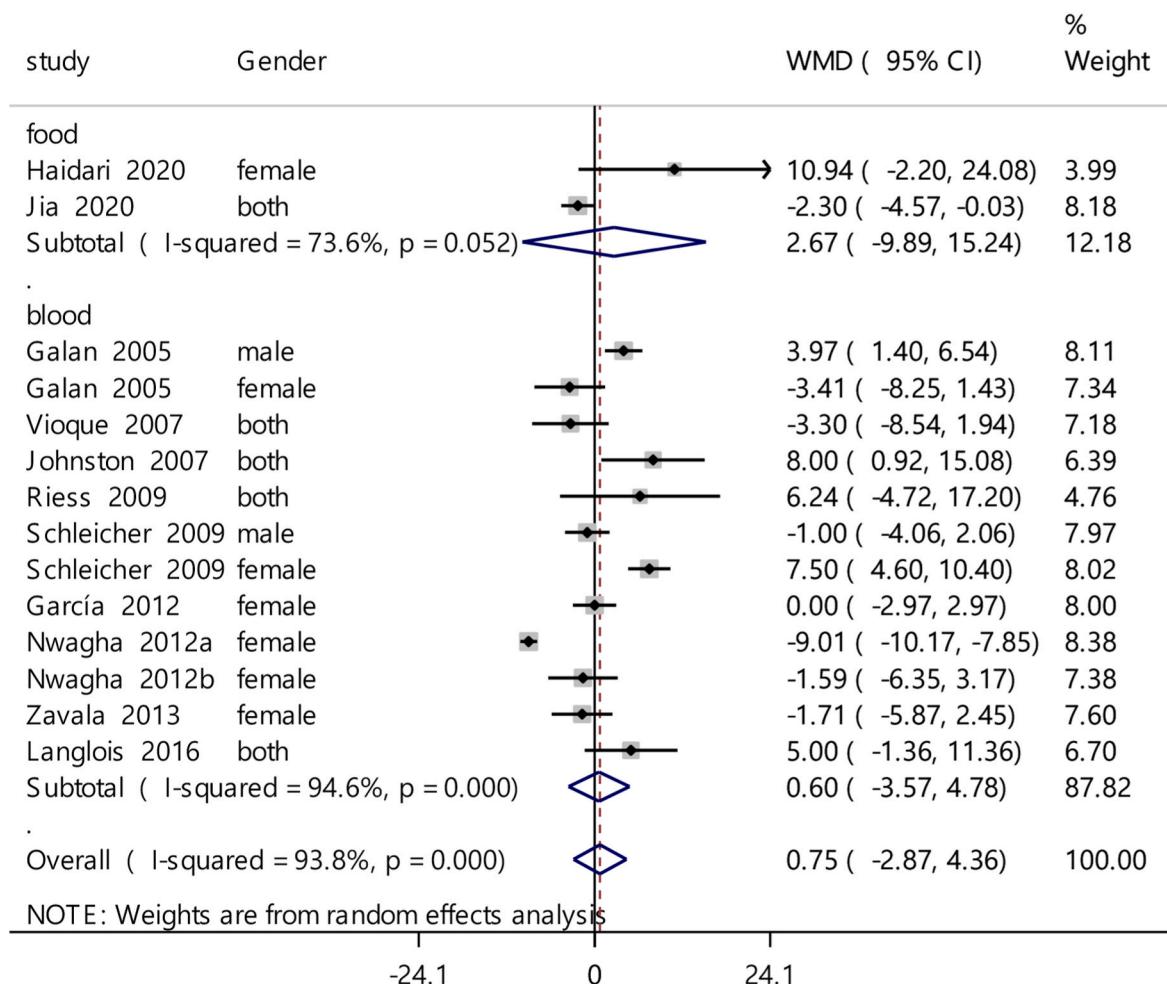
Our results showed that subjects with higher vitamin C consumption had significantly lower BMI. However, one case-control study on patients with coronary artery disease in Seoul, Korea showed that men with higher BMI had higher vitamin C intake [23]. Some studies did not show any significant differences between vitamin C consumption and weight [24,25,28]. These disagreements in the results of studies might be due to lack of adjustment in the amount of energy intake of participants [19,30,31].

Evidence has suggested a change in different immune cells count in obese individuals, tending to an overall decrease in immune system function. In obese people, there is a shift in macrophages from M2 (anti-inflammatory) to M2 (pro-inflammatory). This alteration is

correspondent with some manifestations of obesity such as inflammation and insulin resistance [69,70]. On the other hand, numerous studies in the field of immunometabolism, demonstrated an increase in inflammatory biomarkers in obesity. TNF- $\alpha$ , as one of the main pro-inflammatory cytokines in obesity, activates c-Jun N-terminal kinase (JNK) and I $\kappa$ B kinase (IKK $\beta$ ) intracellular pathways, which are responsible for insulin resistance [71]. There is a positive association between the severity of obesity, and the level of inflammatory biomarkers [72]. Moreover, weight loss in obese and overweight individuals, reduced the level of inflammatory molecules [73,74]. According to the chronic inflammatory background for obesity, numerous studies have evaluated the efficacy of different antioxidant agents in ameliorating obesity and its comorbidities [75,76].

Serum vitamin C level is associated with dietary consumption of vitamin C. Vitamin C has biological antioxidant effects that can decrease levels of oxidative stress. So, vitamin C can prevent chronic diseases. There are different suggestions for the amount of vitamin C consumption. According to a review study on numerous observational and clinical trial studies, 200 mg per day is the optimum dietary intake of vitamin C for the majority of the adult population [77]. While, another study based on European Food Safety Authority (EFSA), recommends that a 60 kg person should intake 110 mg vitamin C per day, which attain the serum vitamin C level to 50  $\mu$ mol/L. According to the results of this study, people with higher body weight have to consume higher amounts of vitamin C in order to attain the sufficient serum vitamin C levels. It is suggested to consume an additional amount of 10 mg per day for every 10 kg increase in body weight [78]. This amount of vitamin C can maximize the vitamin's potential health benefits with the least risk of inadequacy or adverse health effects. Most health agencies recommend a maximum daily vitamin C intake of 1–2 g/day [77]. Fresh fruits and vegetables are the major source of vitamin C. In contrast, meat, eggs, grains, and dairy contain low levels of vitamin C [79].

There are some mechanisms that explain the reason of the



**Fig. 6.** Mean difference of serum vitamin C levels between normal weight and overweight subjects.

association between vitamin C and anthropometric measurements [80]. First, vitamin C is an antioxidant agent which neutralizes free radicals. Consequently, oxidative stress reduces and obesity and its complications are prevented [81]. Second, vitamin C inhibits hypoxia and adipose tissue expansion because of its protective effects against ROSs. Evidence has suggested that hypoxia plays a pivotal role in development of obesity [82]. Third, vitamin C affects the function of antioxidant enzymes groups including paraoxonases (PON) and peroxiredoxins (PRDX) which play an important role in protection against obesity [81]. Vitamin C may affect adipocytes differentiation. It prevents mature adipocytes formation through inhibition of glycerol phosphate dehydrogenase (GPDH) activity [83]. On the other hand, vitamin C is a competitive adenylate cyclase inhibitor which reduces intracellular cyclic adenosine monophosphate (cAMP). Intracellular cAMP levels support adipogenesis [84].

Results of a recent meta-analysis on vitamin C and metabolic syndrome (MetS) revealed that both dietary and circulating vitamin C inversely associated with MetS incidence [80]. Thus, prevention of vitamin C deficiency in populations at higher risk of metabolic disorders such as hypertension, impaired glucose tolerance, dyslipidemia, and obesity can be useful. The serum vitamin C level of 70 μmol/L is considered optimal for health, and vitamin C supplementation could be utilized to reach the optimal level of circulating vitamin C [85,86]. However, there are limited randomized clinical trials (RCTs) on the effect of vitamin C supplementation on anthropometric indices which reported inconsistent results [87–89]. Further RCTs on various populations are needed to clarify the exact relationship between vitamin C supplementation and anthropometric indices.

Our study has several strengthens. This is the first meta-analysis and

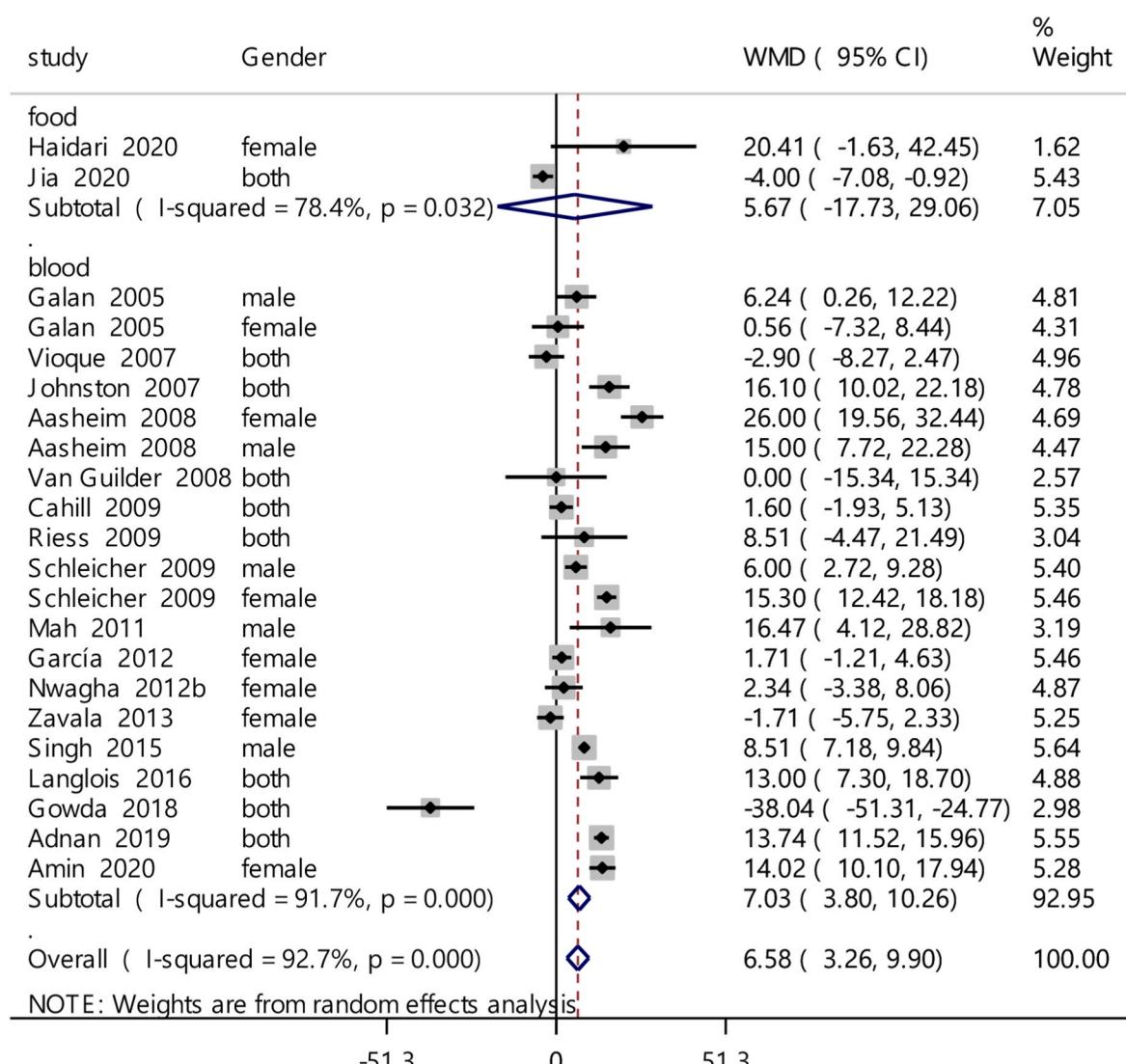
comprehensive review on observational studies that assessed the relationship between dietary and circulating vitamin C levels and anthropometric indices. Second, most of the included studies have high quality and there is no publication bias. Third, our study clarifies the importance of vitamin C in control and prevention of metabolic disorders such as obesity. The limitation of the present study is heterogeneity in the results. It might be due to different regions of studies (from approximately 23 countries), different populations and differences in demographic features of included studies.

## 6. Conclusion

The results of the current meta-analysis demonstrated an inverse association between serum vitamin C levels and BMI and waist circumference. Higher vitamin C consumption was significantly associated with lower BMI. There was significant differences in mean serum vitamin C levels between normal and obese people. Thus, vitamin C supplementation might prevent metabolic disorders. However, more well-designed clinical trials are needed to assess the efficiency of vitamin C supplementation in prevention and treatment of metabolic disorders.

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**Fig. 7.** Mean difference of vitamin C levels between normal weight and obese subjects.

#### Author contribution

SMT, MHB and RK contributed to the conception and design of the research. SMT, MHB, ZY and RK reviewed the literature, and drafted the manuscript. MY contributed to the analysis of data. SMT, MHB and RK contributed to the interpretation of the data and revision. All authors read and approved the final manuscript, and accept its content.

#### Availability of data

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

#### Declaration of competing interest

The authors declare that they have no conflict of interest.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ctcp.2023.101733>.

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