REVIEW ARTICLE

https://doi.org/10.1590/1806-9282.20211111

Omentin-1 circulating levels as predictor of heart diseases: a systematic review and meta-analysis

Jijun Wang[1], Xiaoqing Zhuo[2], Zhiyong Jiang[3]*

INTRODUCTION

Cardiovascular disorders (CVDs) are considered a significant global health problem. These disorders are the leading cause of mortality and disability, with more than three-quarters reported from developing countries[1,2]. Development of tools, guidelines, and designing models based on the prediction factors was conducted to prevent and control CVDs[3-5]. Several comorbidities and genetic and biochemical factors have been considered in the prediction systems of CVDs[6,7]. Some adipose tissue biomarkers including adipokines have been hypothesized as the predictive factors of the occurrence of CVDs[5,8,9]. Previous reports revealed the probable role of omentin-1 as the established adipokines of atherosclerosis in healthy men and in patients with type 2 diabetes mellitus (T2DM)[10-12].

There are conflicting studies about the role of omentin-1, the visceral adipose tissue adipokine[13], on the development of CVDs. A cross-sectional association of cardiometabolic parameters and omentin-1 showed that this adipokine is a cardioprotective factor. Inverse association of omentin-1 and carotid intima thickness in patients with metabolic syndromes[14] and a similar inverse correlation between this adipokine and cardiovascular events within individuals with T2DM were also investigated[14,15]. Given the previous conflicting reports, this systematic review and meta-analysis aimed to investigate the association between circulation omentin-1 and the occurrence of CVD.

METHODS

We conducted our meta-analysis based on observational studies, and it was reported according to MOOSE (Meta-analysis of Observational Studies in Epidemiology) checklist.

Search strategy

Online databases of MEDLINE/PubMed, Scopus, EMBASE, and Web of Science (ISI) were systematically searched for all observational studies until February 24, 2021. In addition to Google Scholar, the reference lists of previous all relevant review articles, including narrative or systematic reviews and selected studies, were manually checked to obtain further studies missed in online searches.

Study selection

After undertaking a comprehensive literature search, the selection process was conducted individually by two investigators (JW and XZ), and discrepancies were resolved by consensus or discussion with a third author (ZJ). Studies were selected if they met the following predefined inclusion criteria: those conducted on human with observational designs (cross-sectional, case-control, nested case-control, or cohort); those published in the English language without date restrictions; those that investigated the association of serum/plasma omentin-1 levels with heart diseases (e.g., heart failure, ischemic heart disease, coronary artery disease [CAD], acute coronary artery syndrome, slow coronary flow, and myocardial infarction), cardiomyopathies (e.g., dilated cardiomyopathy, obstructive hypertrophic cardiomyopathy, and atrial fibrillation); and those that reported sufficient data on mean [corresponding standard deviation (SD) or standard error (SE)] or median [interquartile range (IQR)] of these measurements in both case and control groups. We excluded studies that were animal studies, *in vivo*, *in vitro*, case reports, case series, meeting abstracts, reviews, letters, editorials, and studies that did not have a control group.

Data extraction and quality assessment

From the selected studies, we extracted the primary data. After extracting the data by two individual authors (JW and XZ), a third author (ZJ) checked for more accuracy. The Newcastle-Ottawa Scale (NOS) was used to assess each selected study (Table 1)[16].

[1]The Third Hospital of Jinan, Department of Cardiology – Jinan, China.
[2]Shandong Provincial ENT Hospital, Shandong Second Provincial General Hospital, Department of Cardiovascular Medicine – Jinan, China.
[3]The Fourth People's Hospital of Jinan, Department of Traditional Chinese Medicine – Jinan, China.
*Corresponding author: woaicoffee369@sina.com
Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on January 13, 2022. Accepted on February 01, 2022.

Table 1. Main characteristics of included studies.

First author	Publication year	Country	Type of study	Sample size (case/control)	Mean age (case/control)	Gender M/F (control vs. case)	Body fluid	Case population	Control population	Quality scores
Shang et al.[22]	2011	China	Case-control	107/46	62.56±9.35 64.41±8.14	26/20 65/42	Serum	CAD	Healthy subjects	6
ZHONG et al.[23]	2011	China	Case-control	127/26	59.81±9.88 61.85±12.05	38/14 90/37	Serum	ACS	Healthy subjects	6
Wang et al.[24]	2014	China	Case-control	59/31	75.85±50.05 73.90±64.44	20/11 36/23	Plasma	CHD	Healthy subjects	7
ZHONG et al.[23]	2011	China	Case-control	28/26	59.81±9.88 60.61±15.02	38/14 15/13	Serum	SAP	Healthy subjects	8
Huang et al.[25]	2016	China	Case-control	100/45	52 ± 12 54 ± 13	25/20 72/28	Plasma	Dilated cardiomyopathy	Healthy subjects	8
Tao et al.[26]	2016	China	Cross-sectional	220/115	58.43±9.55 59.75±10.03	61/54 113/107	Serum	AF	Individuals for routine checkup in hospital	7
Stejskal et al.[27]	2016	Czech Republic	Case-control	61/40	35.5±9.4 42.7±6.9	72.7% male 82.5% female	Serum	Premature CAD	Healthy subjects	7
Motawi et al.[20]	2017	Egypt	Case-control	45/15	54.6±3.1 53.7±7.6	14/16 23/22	Serum	CAD	Healthy subjects	6
Motawi et al.[20]	2017	Egypt	Case-control	45/15	54.6±3.1 55.3±6	14/16 11/34	Serum	CAD	Healthy subjects	7
Abd-Elbaky et al.[28]	2016	Egypt	Case-control	80/80	38.6±4.2 40.3±2.5	All men	Serum	CVD	Healthy, nonobese controls	5
El-Mesallamy et al.[29]	2011	Egypt	Case-control	22/15	52.6±11.61 59±9.38	14/1 18/4	Serum	IHD	Healthy subjects	7
Kadoglou et al.[30]	2015	Greece	Case-control	78/32	63.1± 9 66.2± 14.4	25/7 63/15	Serum	AMI	Healthy subjects	8
Biscetti et al.[31]	2020	Italy	Cohort	84/123	74.584 75.244	79/44 65/19	Serum	CAD	Patients without CAD	6
Shibata et al.[32]	2011	Japan	Case-control	78/61	61.3±39.83 63.6±72.42	All men	Plasma	CAD	Healthy subjects	6
Narumi et al.[33]	2014	Japan	Case-control	136/20	65±16 72±12	11/20 76/136	Serum	HF	Subjects without signs of significant heart disease	7
Nazar et al.[40]	2017	Pakistan	Case-control	250/100	49.7±6.4 51.3±6.38	71% male 63.2% male	Serum	CAD	Healthy subjects	6
Nazar et al.[34]	2020	Pakistan	Case-control	250/220	55.43±4.90 53.29±5	157/93	Serum	CAD	Healthy subjects	6
Baig et al.[35]	2020	Saudi Arabia	Case-control	122/52	53.38±5.99 54.94±9.08	105/17 34/18	Serum	AMI	Healthy subjects	6
Onur et al.[36]	2013	Turkey	Case-control	110/83	66.2+11.9 68.2+10.2	All women	Serum	CAD	Patients without CAD	6
Yıldız et al.[21]	2018	Turkey	Cohort	50/25	37.7±9.6 36.6±13	24/26 25/25	Serum	Nonobstructive hypertrophic cardiomyopathy	Without HCM	7
Yıldız et al.[21]	2018	Turkey	Cohort	37/25	37.7±9.6 40.9±12.1	24/26 20/17	Serum	Obstructive hypertrophic cardiomyopathy	Without HCM	7

Statistical analysis

Mean differences and their SDs in blood omentin-1 levels between cases and controls were considered ESs, and these were expressed as weighted mean difference (WMD) and corresponding 95% confidence interval (CI) in our meta-analysis. A random-effects model was used to pool ESs with DerSimonian and Laird method. Between-study heterogeneity was quantified by chi-square test and inconsistency index (I^2) statistic. A $p<0.1$ with $I^2>50\%$ represented significant heterogeneity across included studies[17]. Furthermore, to detect the source of heterogeneity, additional analyses, including subgroup and sensitivity analyses, were conducted. Egger's regression asymmetry test[18,19] and visual-filled funnel plot were used to assess the evidence of potential publication bias. The data were analyzed using STATA version 16.0 software (STATA Corp, College Station, TX, USA).

RESULTS

Literature search and study characteristics

A total of 873 records were identified using our search strategies. As shown in Figure 1, 855 records were excluded step by step due to the aforementioned reasons. Finally, the remaining 18 articles (or 21 studies) were investigated for our meta-analysis[20-36]. It should be noted, however, that out of all these 18 articles, 9 studies reported data on CAD, and the rest addressed other heart diseases. Overall, the included studies, published from 2011 to 2020, contained 2089 cases and 1195 controls. Seventeen studies were conducted using a case-control design, three studies employed a cohort design, and one studies had a cross-sectional design. Six studies were performed in China, four in Egypt, three in Turkey, two studies in Japan and Pakistan, and finally one in Czech Republic, Greece, Italy, and Saudi Arabic. However, the main characteristics of each included study are summarized in Table 1.

Meta-analysis results for omentin-1 levels

Figure 2 is a forest plot that indicated the individual and pooled WMD of blood omentin-1 levels between cases with heart diseases and controls. Based on 21 qualified studies, the pooled result using the random-effects model showed that the omentin-1 levels among cases were significantly lower than controls (WMD: -15.20 ng/mL; 95%CI -16.38, -14.01; $p<0.001$).

Due to considerable heterogeneity across included studies ($I^2=99.73\%$, $p<0.001$), we conducted additional analyses. The subgroup findings based on potential modifying variables, including continent, study design, body fluid, type of heart disease, and quality status. The pooled WMDs were remained significant in the different strata of all subgroup analyses. Moreover, publication year ($\beta=-10.39$, $p=0.431$) and total sample size ($\beta=-0.12$, $p=0.741$) had no statistically significant effects on omentin-1 levels in circulating between cases with heart diseases and controls.

Sensitivity analysis was conducted based on the heterogeneity statistic (I^2: 25%) and there was no significant change in pooled ES (WMD: -0.25 ng/mL; 95%CI -0.30, -0.19). Furthermore, in sensitivity analysis, after excluding each study using the leave-one-out method, the pooled WMD remained stable.

Publication bias

We found evidence of potential publication bias across included studies using visual-filled funnel plots and the results of Egger's asymmetry test for omentin-1 ($p<0.001$). Therefore, after considering censure studies using nonparametric trim-and-fill analysis, we found that the pooled WMD for omentin-1 (WMD: -15.19 ng/mL; 95%CI -16.38, -14.01) was still significant.

DISCUSSION

Findings demonstrated a significantly lower circulating level of omentin-1 in patients with CVDs. This outcome was also confirmed by subgroup analysis due to the significant heterogeneity among included studies after modifying the continent, study design, body fluid, type of heart disease, and quality status.

Omentin-1 has a modulator and vasodilator effect on endothelium. Its probable association with chronic inflammatory disease, obesity, insulin resistance, and CADs was reported in several studies. The results obtained from a meta-analysis on six studies conducted by Agasthi et al. were in consistent with the present study, indicating a significant negative association between serum level of omentin-1 and risk of CAD with a standard mean difference (SMD) of -2.27[37]. Epicardial fat tissue, which was described as distributed visceral fat in coronary arteries in a meta-analysis study by Li et al., was considerably higher in patients with diabetes[38]. Following these results, in a meta-analysis study by Ashabi et al., omentin-1 had a significantly lower serum level in patients with T2DM and IGT after pooled analysis of 28 included case-control studies[39]. Summarizing these two studies' results might reveal the probable negative association between omentin-1 and epicardial fat tissue, which

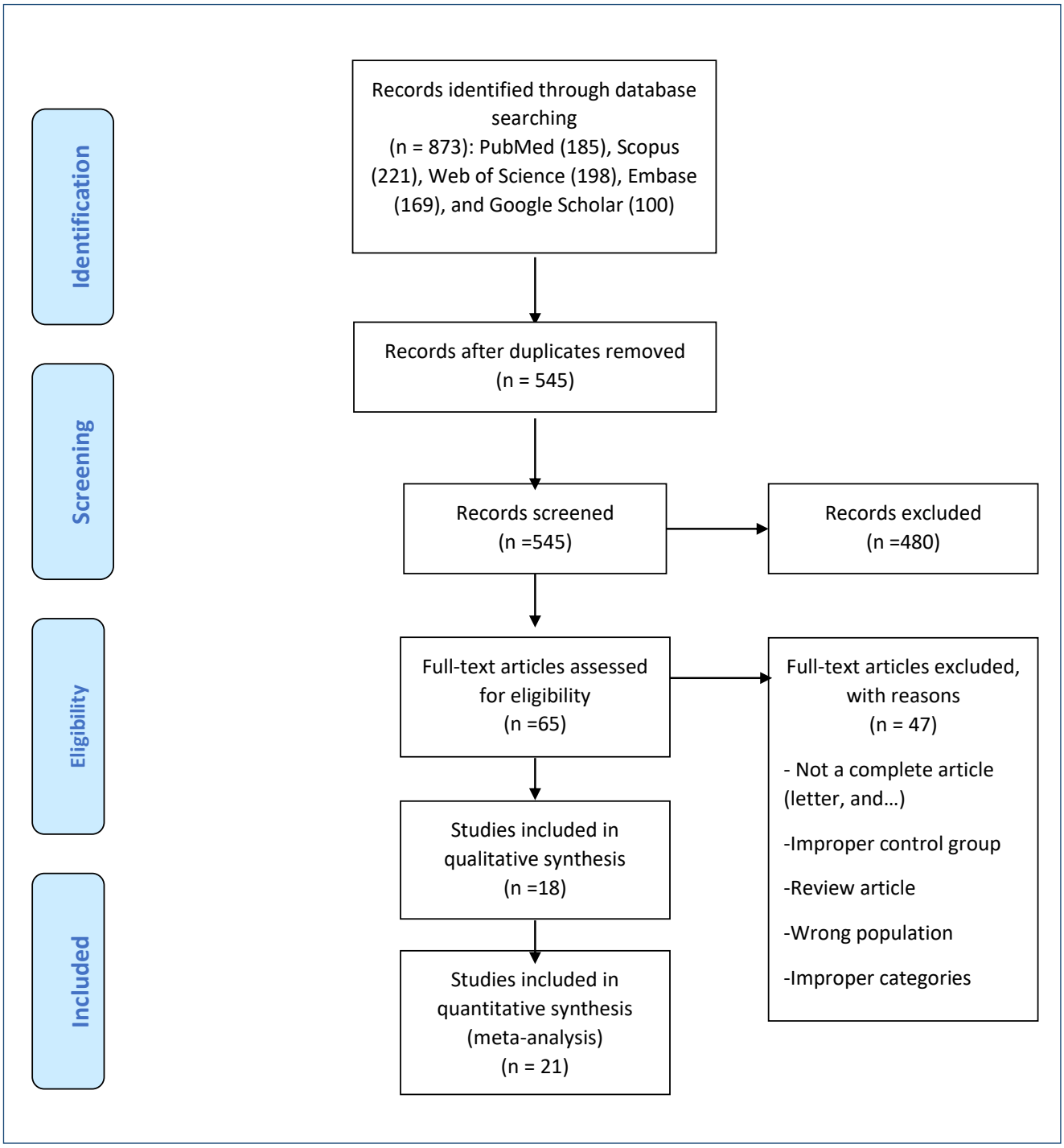

Figure 1. Flowchart of study identification and selection process.

could involve coronary arteries as atherosclerosis and could result in CADs in patients with diabetes.

This study has several limitations. There was significant heterogeneity by evaluating the role of omentin-1 in predicting CVDs. In this study, we did not evaluate the effect of duration and the role of therapeutic management of underlying CVDs on omentin-1 levels. Moreover, the role of this adipokine should be assessed for predicting more arrhythmias than atrial fibrillation. The results of this meta-analysis should be interpreted by considering these limitations.

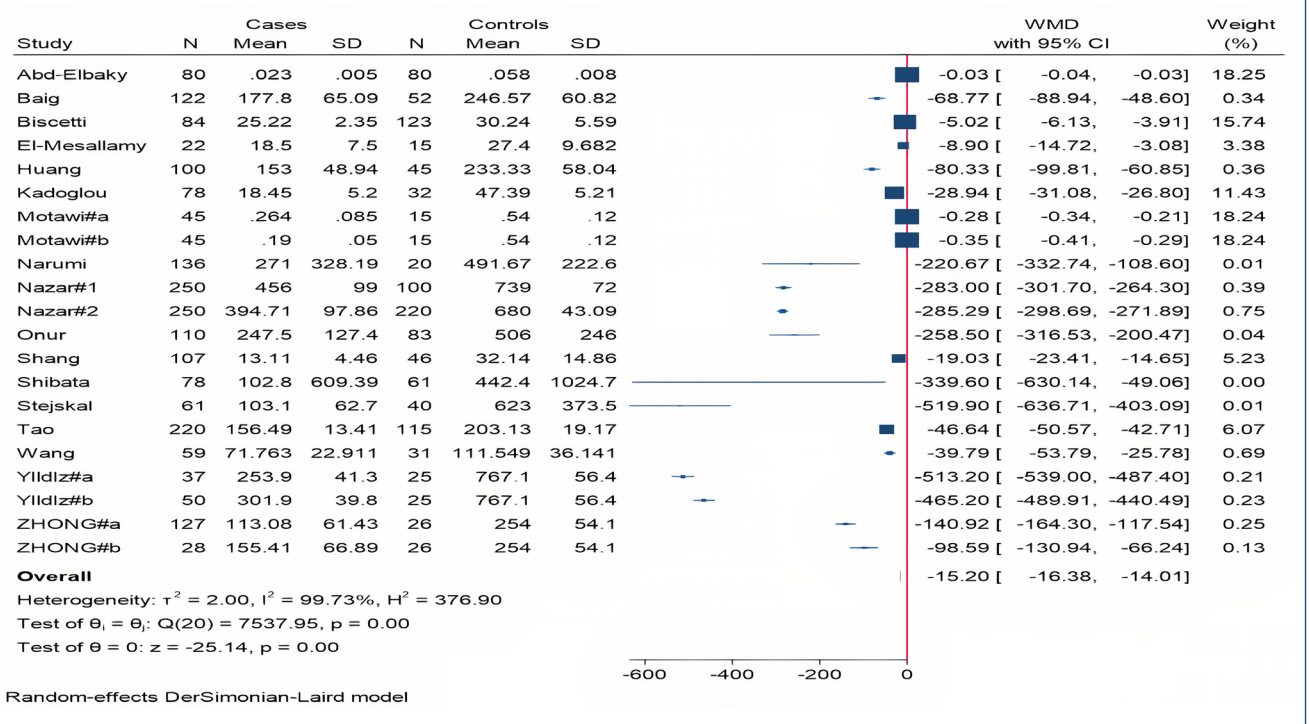

Figure 2. Forest plot of pooled estimates of the weighted mean differences of circulating omentin-1 levels between cases with heart diseases and controls.

CONCLUSIONS

The findings of this study about the effect of diabetes on omentin-1 circulating levels coincided with their CVD changes. Therefore, this adipokine could be the independent prediction factors of CVDs in a population with or without diabetes/MetS. Nonetheless, omentin-1 was shown to have a negative association with prediction of CVDs.

AUTHORS' CONTRIBUTIONS

JW: Conceptualization, Data curation, Formal Analysis, Writing – original draft, and Writing – review & editing. **XZ**: Conceptualization, Data curation, Formal Analysis, and Writing – original draft. **ZJ**: Conceptualization, Data curation, Formal Analysis, Investigation, Supervision, Writing – original draft, and Writing – review & editing.

REFERENCES

1. Sangy S, Bahaoddini A, Tavassoli A. Evaluation of histopathological changes of osteoarthritis on the cardiovascular system by gavage of hydro alcoholic extract of wild anemone (Papaver Rhoeas L.) in male rats. Prog Chem Biochem Res. 2020;3(4):402-11. https://doi.org/10.22034/PCBR.2020.114303
2. Teimouri H, Obeidavi Z, Pouria A, Jafari Z, Safari M, Rashidzadeh S, et al. Investigating the impact of body mass index on the outcomes of coronary artery bypass graft surgery: a single referral center experience. Int J Adv Biol Biomed Res. 2016;4(3):305-11. https://doi.org/10.26655/IJABBR.2016.9.10
3. World Health Organization. Hearts: technical package for cardiovascular disease management in primary health care. 2016. Available from: https://www.who.int/cardiovascular_diseases/hearts/Hearts_package.pdf
4. Wangchuk D, Virdi NK, Garg R, Mendis S, Nair N, Wangchuk D, et al. Package of essential noncommunicable disease (PEN) interventions in primary health-care settings of Bhutan: a performance assessment study. WHO South East Asia J Public Health. 2014;3(2):154-60. https://doi.org/10.4103/2224-3151.206731
5. Halim S, Jasmi NA, Ridzuan P, Anna D, Abdullah S, Sina T. Novel potential *Centella asiatica* extract in ameliorating neurotoxicity induced oxidative stress in chronic morphine dependant rat model. Int J Med Toxicol Legal Med. 2020;23(3 and 4):79-83. https://doi.org/10.5958/0974-4614.2020.00050.9
6. Akbari H, Asadikaram G, Vakili S, Masoumi M. Atorvastatin and losartan may upregulate renalase activity in hypertension but not coronary artery diseases: the role of gene polymorphism. J Cel Biochem. 2019;120(6):9159-71. https://doi.org/10.1002/jcb.28191

7. Hudiyawati D, Ainunnisa K, Riskamala G. Self-care and its related factors among patients with congestive heart failure in Surakarta, Indonesia. J Med Chem Sci. 2021;4(4):364-73. https://doi.org/10.26655/JMCHEMSCI.2021.4.7
8. Mahajan K, Kandoria A, Bhardwaj R, Negi PC, Asotra S, Gupta G. Clinical and coronary angiographic profile in women presenting with anginal chest pain: results from a single-center prospective observational study. J Nat Sci Biol Med. 2019;10(1):60. https://doi.org/10.4103/jnsbm.JNSBM_172_18
9. Abid H, Abid Z, Abid S. Atherogenic indices in clinical practice and biomedical research: a short review: atherogenic indices and cardiovascular diseases. Baghdad J Biochem Appl Biol Sci. 2021;2(2):59-69. https://doi.org/10.47419/bjbabs.v2i02.52
10. Patil VC, Avhad AB, Kulkarni AR, Pandere KA. High-sensitive C-reactive protein in patients with coronary artery disease. J Nat Sci Biol Med. 2020;11(1):39.
11. Sowndarya K, Joseph JA, Shenoy A, Hegde A. Evaluation of triglyceride/high-density lipoprotein ratio as a surrogate marker for insulin resistance in healthy young males. J Nat Sci Biol Med. 2021;12:213.
12. Kumar A. Potential biomarkers to detect inflammation leading to coronary artery disease. J Nat Sci Biol Med. 2020;11(1):1-1.
13. Cheng X. Elucidating the pathophysiological significance of circulating omentin levels: is higher better? Atherosclerosis. 2016;251:522-24. https://doi.org/10.1016/j.atherosclerosis.2016.06.042
14. Liu R, Wang X, Bu P. Omentin-1 is associated with carotid atherosclerosis in patients with metabolic syndrome. Diabetes Res Clin Pract. 2011;93(1):21-5. https://doi.org/10.1016/j.diabres.2011.03.001
15. Greulich S, Chen WJ, Maxhera B, Chen WJ, Maxhera B, Rijzewijk LJ, et al. Cardioprotective properties of omentin-1 in type 2 diabetes: evidence from clinical and in vitro studies. PLoS One. 2013;8(3):e59697. https://doi.org/10.1371/journal.pone.0059697.
16. Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute; 2011.
17. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-58. https://doi.org/10.1002/sim.1186
18. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629. https://doi.org/10.1136/bmj.315.7109.629
19. Begg CB, Berlin JA. Publication bias and dissemination of clinical research. J Natl Cancer Inst. 1989;81(2):107-15. https://doi.org/10.1093/jnci/81.2.107
20. Motawi TMK, Mahdy SG, El-Sawalhi MM, Ali EN, El-Telbany RFA. Serum levels of chemerin, apelin, vaspin, and omentin-1 in obese type 2 diabetic Egyptian patients with coronary artery stenosis. Can J Physiol Pharmacol. 2018;96(1):38-44. https://doi.org/10.1139/cjpp-2017-0272
21. Yıldız SS, Sahin I, Cetinkal G, Aksan G, Kucuk SH, Keskin K, et al. Usefulness of serum Omentin-1 levels for the prediction of adverse cardiac events in patients with hypertrophic cardiomyopathy. Med Princ Pract. 2018;27(2):107-14. https://doi.org/10.1159/000487396
22. Shang F-J, Wang J-P, Liu X-T, Zheng Q-S, Xue Y-S, Wang B, et al. Serum omentin-1 levels are inversely associated with the presence and severity of coronary artery disease in patients with metabolic syndrome. Biomarkers. 2011;16(8):657-62. https://doi.org/10.3109/1354750X.2011.622789
23. Zhong X, Zhang H-Y, Tan H, Zhou Y, Liu FL, Chen FQ, et al. Association of serum omentin-1 levels with coronary artery disease. Acta Pharmacol Sin. 2011;32(7):873-8. https://doi.org/10.1038/aps.2011.26
24. Wang X-H, Dou L-Z, Gu C, Wang X-Q. Plasma levels of omentin-1 and visfatin in senile patients with coronary heart disease and heart failure. Asian Pac J Trop Med. 2014;7(1):55-62. https://doi.org/10.1016/S1995-7645(13)60192-3
25. Huang Y, Lin Y, Zhang S, Wang Z, Zhang J, Chang C, et al. Circulating Omentin-1 levels are decreased in dilated cardiomyopathy patients with overt heart failure. Dis Markers. 2016;2016:6762825. https://doi.org/10.1155/2016/6762825
26. Tao S, Huang Y-Q, Cai A-P, Huang C, Zhang Y, Tang S-T, et al. Association of serum omentin-1 concentrations with the presence of atrial fibrillation. Med Sci Moni: Int Med J Exp Clin Res. 2016;22:4749-54. https://doi.org/10.12659/msm.898202
27. Stejskal D, Vaclavik J, Smekal A, Svobodova G, Richterova R, Svestak M. Omentin-1 levels in patients with premature coronary artery disease, metabolic syndrome and healthy controls. Short communication. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2016;160(2):219-21. https://doi.org/10.5507/bp.2016.019
28. Abd-Elbaky AE, Abo-ElMatty DM, Mesbah NM, Ibrahim SM. Omentin and apelin concentrations in relation to obesity, diabetes mellitus type two, and cardiovascular diseases in Egyptian population. Int J Diabet Dev Ctries. 2016;36(1):52-8. https://doi.org/10.1007/s13410-015-0416-y
29. El-Mesallamy H, El-Derany M, Hamdy N. Serum omentin-1 and chemerin levels are interrelated in patients with Type 2 diabetes mellitus with or without ischaemic heart disease. Diabet Med. 2011;28(10):1194-200. https://doi.org/10.1111/j.1464-5491.2011.03353.x
30. Kadoglou NPE, Tahmatzidis DK, Giannakoulas C, Kapelouzou A, Gkontopoulos A, Parissis J, et al. Serum levels of novel adipokines, omentin-1 and chemerin, in patients with acute myocardial infarction: KOZANI STUDY. J Cardiovasc Med (Hagerstown). 2015;16(5):341-46. https://doi.org/10.2459/jcm.0000000000000053
31. Biscetti F, Nardella E, Rando MM, Cecchini AL, Angelini F, Cina A, et al. Association between omentin-1 and major cardiovascular events after lower extremity endovascular revascularization in diabetic patients: a prospective cohort study. Cardiovasc Diabetol. 2020;19(1):170. https://doi.org/10.1186/s12933-020-01151-z
32. Shibata R, Ouchi N, Kikuchi R, Takahashi R, Takeshita K, Kataoka Y, et al. Circulating omentin is associated with coronary artery disease in men. Atherosclerosis. 2011;219(2):811-14. https://doi.org/10.1016/j.atherosclerosis.2011.08.017
33. Narumi T, Watanabe T, Kadowaki S, Kinoshita D, Yokoyama M, Honda Y, et al. Impact of serum omentin-1 levels on cardiac prognosis in patients with heart failure. Cardiovasc Diabetol. 2014;13(1):84. https://doi.org/10.1186/1475-2840-13-84
34. Nazar S, Qamar A, Mughal A, Butt F. Association of serum Vitamin D and omentin-1 in patients with coronary artery disease. Prof Med J. 2020;27(6):1237-43. https://doi.org/10.29309/TPMJ/2020.27.06.4201
35. Baig M, Alghalayini KW, Gazzaz ZJ, Atta H. Association of serum Omentin-1, chemerin, and leptin with acute myocardial infarction and its risk factors. Pak J Med Sci. 2020;36(6):1183-88. https://doi.org/10.12669/pjms.36.6.2372
36. Onur I, Oz F, Yildiz S, Oflaz H, Sigirci S, Elitok A, et al. Serum Omentin 1 level is associated with coronary artery disease and its severity in postmenopausal women. Angiology. 2014;65(10):896-900. https://doi.org/10.1177/0003319713511322

37. Agasthi P, Aloor S, Axiyan M, Onwuanyi A. Association between serum omentin-1 level and coronary artery disease: a meta-analysis. Arteriosc Thromb Vasc Biol. 2015;35(suppl_1):A548. Available from: https://www.ahajournals.org/doi/abs/10.1161/atvb.35.suppl_1.548

38. Li Y, Liu B, Li Y, Jing X, Deng S, Yan Y, et al. Epicardial fat tissue in patients with diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2019;18(1):3. https://doi.org/10.1186/s12933-019-0807-3

39. As Habi A, Sadeghi M, Arab A, Hajianfar H. The association between omentin and diabetes: a systematic review and meta-analysis of observational studies. Diabetes Metab Syndr Obes. 2019;12:1277-86. https://doi.org/10.2147/DMSO.S206981

40. Nazar S, Farhan S, Tasneem U. Association of serum Omentin-1 levels with coronary artery disease (CAD) in a local population of Karachi-A multicenter study. Ann Abbasi Shaheed Hosp Karachi Med Dent Coll. 2017;22(1):31-6. Available from: http://annals-ashkmdc.org/index.php/ashkmdc/article/view/94