REVIEW ARTICLE

A Review on the Evaluation of Serum Adipokine (adiponectin, leptin) Levels in Cardiovascular Disease: A Systemic Review

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ABSTRACT

Background: This review enumerates current knowledge of adipose tissue and reveals processes by which adipocytes affect obesity and cardiovascular illness. Obesity, according to growing evidence, is a crucial factor that influences cardiometabolic phenotypes. However, the pathogenic mechanisms are still unknown. As per recent reports, adipose tissue interacts with a variety of organs, including the lungs, heart, and kidneys, by secreting multiple cytokines known as adipokines.

Aim and Objectives: The current study examines the adipokine (adiponectin and leptin) profiles of adipocytes from the adipose tissue and biochemical and clinical parameters in patients with heart disease (CVD).

Methods: Relevant articles were retrieved by screening the following databases: Medline (PubMed, Scopus), Web of Science. Keyword searches included 'adiponectin', 'leptin', AND 'cardiovascular disease', from 2013-2023 (May). The retrieved studies were subjected through a screening procedure to identify case-control, cohort and epidemiological studies that contained the required data. Per preferred reporting items for systematic reviews and (PRISMA) guidelines, we conducted the systematic review.

Results: A total of 2377 studies were found relevant, out of which only 90 fulfilled the inclusion criteria. From these 90 studies we reviewed 50 articles that are included in the systematic review.

Conclusion: The dysfunction of adipose tissue triggered an alteration in the secretory profile of adipokines, which serves as a signal of metabolic disorder. An imbalance in pro- and anti-inflammatory adipokine formation exacerbates cardiometabolic diseases and CVD challenges.

Keywords: Adipokines, Adiponectin, Cardiovascular disease, Leptin, Obesity

Highlights

- The systemic review enumerates the impact of adipokines levels for better understanding of cardiovascular disorders and to find the effect of these adipokines in inflammation and different cardiovascular aetiologies.
- In long-term studies, an abnormal profile of serum adipokines in cardiovascular disease is associated with systemic inflammation and signifies the occurrence of serious cardiovascular complications.
- Low adiponectin levels were linked to a greater incidence of cardiovascular illnesses and overall mortality in CVD patients, while high leptin levels were linked to a high risk of cardiovascular illness in CVD patients.

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INTRODUCTION

In accordance with the most current Global Burden of Disease Study data, cardiovascular disease is considered as major cause of fatality and has given a negative impact on the standard of life globally and is only spreading inprevalence. In developed countries, cardiovascular disease is the main factor in fatalities. Cardiovascular diseases, including myocardial infarction and stroke, are more likely to happen by smoking, poor nutrition, an aging population, a lack of exercise, arterial hypertension, or diabetes.[1]

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Adipose tissue secretes a variety of bioactive metabolites known as "adipokines," making it an active endocrine organ. Many adipokines, including adiponectin, leptin, and resistin, tremendously influence inflammatory processes, metabolic homeostasis, and energy balance. One of the main connections among obesity and cardiovascular disease is the malfunction of adipose tissue, which is characterized by the invasion of inflammatory cells and abnormal generation of adipokines. Adipose tissue performs a variety of key metabolic sensing functions, including sensitivity to insulin, glucose and lipid metabolism, and cardiovascular homeostasis are all regulated, in addition to its conventional function as a storage organ for extra energy.[2]

Because of its levels' antagonistic relationship with obesity, adiponectin stands out among the other adipokines. Adiponectin also has anti-inflammatory, insulin-sensitizing, and anti-atherogenic properties. Adiponectin has been proven in both laboratory and clinical trials to have a preventive effect against type 2 diabetes. Adiponectin values and the risk for type 2 diabetes are inversely correlated, in accordance with the new systematic review and meta-analysis. Adiponectin may protect against dyslipidemia, metabolic syndrome, and several forms of cancer, according to expanding research (breast, colon, prostate, and others). A higher risk of myocardial infarction has been linked to decreased plasma concentrations of adiponectin, as it copmprise coronary artery disease, hypertension, left ventricular hypertrophy, and other conditions.[3]

An adipokine called leptin also promotes oxidative stress, inflammation, thrombosis, arterial stiffness, angiogenesis, and atherogenesis in addition to regulating food intake through appetite suppression. These leptin-induced actions could increase the risk of developing cardiovascular conditions. Leptin is a hormonal peptide that is mostly released by adipocytes and controls appetite by acting on the hypothalamus. It is also involved in food intake regulation. Leptin is a "anorexigenic" hormone as a result. However, the development of leptin resistance makes obesity characterized by hyperleptinemia. In addition to obesity, high leptin levels are also linked to insulin resistance and hypertension.[4]

The mechanism by which leptin exerts its physiological action is the leptin receptor (LEPR), which is found on chromosome lp31. A molecule called LEPR, is found in many tissues, can mediate the significant effect of the hormone leptin on the body's overall energy homeostasis. Thrombosis, angiogenesis, and cardiac hypertrophy are just a few of the cardiac and vascular effects that leptin has been shown to control peripherally. Additionally, it affects the regulation of metabolism, immunity, and reproduction. Inflammatory response, oxidative stress, atherogenesis, and thrombosis are stimulated, which encourages vascular dysfunction, arterial stiffness, and the growth and vulnerability of atherosclerotic plaques. Leptin also controls angiogenesis, reproduction, and bone homeostasis.[4]

Cardiovascular diseases are multidimensional and involve many different pathways, including uncoupling of eNOS, production of reactive oxygen species, unusual regulation of calcium homeostasis, signaling linked to harmful phosphorylation pattern, and ineffective counter-regulatory processes at the humoral, cellular, and tissue levels. Early research has also suggested that cells from the immune system and inflammatory signals are vital in the onset of cardiovascular disease.[1]

Because it promotes thrombocyte activation, vasoconstriction, leukocyte activation/infiltration, and smooth muscle cell proliferation (intima-media thickness) in the vessel wall, endothelial dysfunction is a potential indicator of the formation of atherosclerosis, hypertension, and future cardiovascular events. In recent years, three key factors in the vascular process of aging that may trigger endothelial dysfunction have been identified: worsening nitric oxide signaling, oxidative stress, and inflammation.[1]

MATERIAL AND METHODS

Search strategy and eligibility criteria

We screened Medline (PubMed and Scopus), Web of science, and Google scholar mainly for reports published from January 1, 2012, to May 2023. We performed searches using terms such as "Adipokines" and "cardiovascular disease" from the Medical Subject Headings. Search terms were investigated and effectively enhanced in accordance with the databases. We included studies with plasma adiponectin values at baseline and all-cause fatalities and/or major cardiovascular morbidity and mortality as results that lasted for more than a year. Additional articles were identified via the review of references.

The systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards. All associated studies that were found were included in our review. Additional publications were found by hand-searching bibliographies of relevant studies, including the most recent reviews. Publications were then anthologized according to selection and elimination procedures and finally screened for the full-text article for additional clarity of the selection procedure.

Inclusion Criteria

- Cross-sectional, Case-control or cohort epidemiological researches were included.
- Studies were taken after 2012
- Studies with the association of cardiovascular disease with adipokines (adiponectin,leptin) levels were included.

Exclusion Criteria

- Other systemic reviews were excluded.
- Non-English papers were excluded because of the structural language barrier.
- Studies with all-cause death and/or morbidity were also excluded.
- All co-morbidities other than metabolic syndrome were excluded (coronary arterial stenosis, studies on type 1 diabetes or chronic renal failure, and studies of genetic variants in adiponectin-related genes).

Study Selection

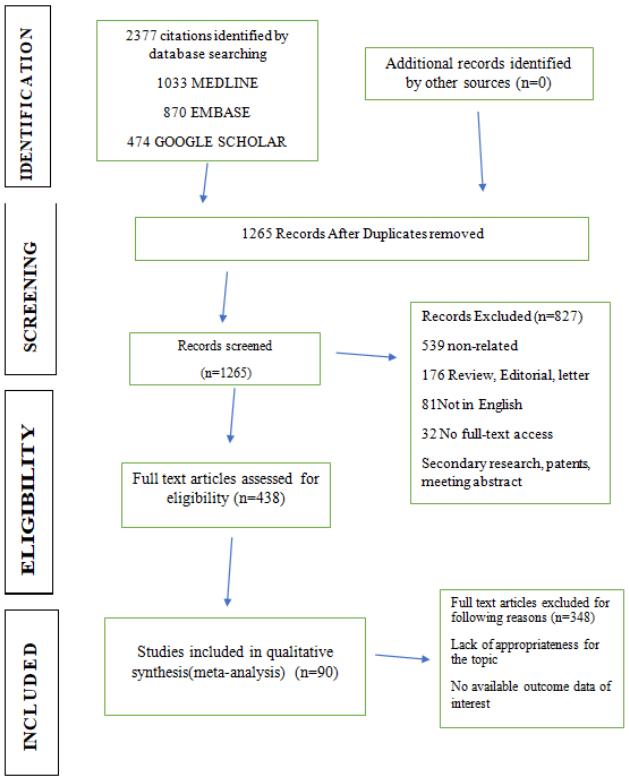
We intend to study the association of linking adipokines with inflammation and cardiovascular disease. The study underwent review by both reviewers in sequence and any disagreements were settled by a third reviewer. The manuscript's title was first checked for repeated phrases and abstracts before being compared to the inclusion and exclusion criteria. To determine eligibility, the remaining full-text papers were reviewed.

Analytic Process

The current systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The syntax used in this paper corresponds to ICS definitions. Criteria outlined in the Standards for the Reporting of Diagnostic Accuracy (STARD) and the Consolidated Standards of Reporting Trials (CONSORT) were used to assess the quality of included literature and reduce selection bias. From the beginning to May 2023, the PubMed and Embase databases were searched.

Literature Search

Flowchart 1 depicts a schematic representation of the articles included in our systematic review. During the preliminary search, a total of 2377 articles were found (1033 Medline 870 Embase, 474 Google scholar). After removing 1265 duplicates, 438 studies were chosen for further review. We then excluded 1574 articles by studying their abstracts and titles, and the remaining 90 full-text studies were scrutinized for eligibility.



Flowchart: 1 Schematic representation for the selection of studies included in the systemic review

RESULTS

Among the 90 studies that met the inclusion criteria, we have reviewed 50 articles that are shown in three different tables. Table 1 shows 19 individual studies of adiponectin, Table 2 depicts 18 reviewed articles for leptin among cardiovascular disease and 13 combined studies of leptin, adiponectin and LAR are depicted in Table 3. The findings revealed that higher serum leptin levels (Hyperleptinemia) correspond to an increased rate of cardiovascular disease, as well as a higher leptin/adiponectin (L/A) ratio (4 studies) in patients in contrast with controls. In 18 studies, the level of adiponectin in CVD patients was significantly lower (hypoadiponectinemia) than in the healthy controls. Moreover, 4 articles revealed an elevation in adiponectin levels among cardiometabolic diseases. Lastly, 11 studies didn't show any meaningful correlation among these parameters in CVD.

DISCUSSION

Cardiovascular disease (CVD) includes pathologies such as coronary heart disease (CHD), cerebrovascular disease (CVD), peripheral arterial disease (PAD), rheumatic and congenital heart disease, and venous thromboembolism. CVD is responsible for 31% of all fatalities worldwide, predominantly because of CHD and strokes.[5]

It is becoming more widely accepted that adipose tissue serves as an endocrine organ that may remotely tell other tissues to change their metabolic cycle. This signaling is carried out by adipocytes produced by specialized cells known as adipokines, including molecules like leptin, adiponectin, chemerin, and others. Adipokines have a variety of metabolic impacts, such as controlling blood pressure, hunger, fibrosis, inflammation, and insulin sensitivity, given the diverse range of metabolic effects, there is a lot of interest in how adipokines affect cardiovascular risk and various novel mechanisms through which they affect coronary heart disease (CHD) have recently been discovered.[6]

Adipokines are hormones that the fat tissue produces. They contribute to the equilibrium of energy, the regulation of thermogenesis, reproduction of sugar and fat metabolism, and immunity. They also impact cardiovascular function, either immediately through paracrine actions on the arterial wall or indirectly through changed serum and tissue levels of adipokines in proportion to the body's total adipose tissue mass. Pro-inflammatory and anti-inflammatory adipokines are produced in equilibrium under normal conditions. This equilibrium is disturbed with increasing obesity, especially perivascular and visceral obesity, and adipocytes overloaded with triacylglycerols and energy produce more pro-inflammatory adipokines, which have various detrimental cardiovascular effects.[7]

According to recent research, adipokines may play a role in the etiology of cardiovascular diseases. As a result of the notable discovery of leptin and adiponectin, which solidified adipose tissue as a proficient and highly functional endocrine organ, an entirely novel phase in research on adipose-mediated

Table 1: Showing the studies of adiponectin levels in cardiovascular disease

S. No	*References*	*Publicationyear*	*Study population*	*Studydesign*	*Samplesize*	*Outcomes*
1	Mitsuyama SK, *et al*.[12]	2019 (3-year follow-up)	Japan	Cohortstudy	1,228	They discovered baseline characteristics of patients classified by serum total adiponectin quartile. The prevalence of combined cardiovascular and renal issues by serum HMW adiponectin quartile or HMW/total adiponectin ratio.
2	Tu WJ, *et al*.[13]	2020	China	Cohortstudy	4274	Adiponectin levels in the blood were linked to an increased risk of Significant Detrimental Cardiovascular and Cerebrovascular incidents.
3	Ruijter HMD, *et al*.[14]	2014	Netherlands	Case- control study		Adiponectin levels were found to be higher in patients with severe heart failure, regardless of CAD, when compared to healthy subjects.
4	Khorasani ZM, *et al*.[15]	2020	Iran	Cross-sectional study	90	They discovered that the plasma adiponectin level in type 2 diabetes, insulin resistance, hypertension, MI, and dyslipidemia is less than 4 µg/mL. The present investigation discovered that low serum adiponectin values are associated with a higher incidence of CAD in type 2 diabetics.
5.	JeonJY,*et al*.[16]	2015 (9 year follow-up)	Korea	Observational-Cohort study	349	The overall prevalence of cardiovascular diseases did not differ substantially between the three adiponectin groups based on total, middle-molecular weight, high-molecular-weight, or high-molecular-weight/total adiponectin.
6.	Nomura H, *et al*.[17]	2021	Japan			In men, higher adiponectin levels were linked to a rise in cardiovascular events.
7.	Mukama T,*et al*.[18]	2022 (15-year follow-up)	Europe	CohortStudy	510,000	A significant relationship between adiponectin and mortality was observed in the presence of high NT-proBNP levels. Their findings support the hypothesis that NT-proBNP could unravel the contradiction of adiponectin.
8.	Zaidi H, *et al*.[19]	2021		Case- Control Study	137	After one year, no significant difference in alterations in the analyzed markers was observed between the intervention and control groups.
9.	Persson J, *et al*.[20]	2015		Cross-sectional study	3430	Adiponectin concentrations were found to be contrary to the advancing mean common carotid IMT in men, but not in women.
10.	Zhang YQ, *et al*.[21]	2022		Case-control study	269	Reduce serum CTRP9, tAPN, LMW, and HMW levels have been linked with a higher likelihood of ischemic stroke in non-hyperlipidemic individuals.
11.	Zhang HL, *et al*.[22]	2015		Cross- section al study	347	Serum adiponectin level was negatively correlated with CHD progression with CHD progression.
12.	Xia K, *et al*.[23]	2012		Case- control study	87	Adiponectin levels are lower in CHD subjects, and substantially lower in CHD patients with improper metabolism of glucose.
13.	MatsushitaY, *et al*.[24]	2014	Japan	Cross- section al study	6996	The most significant association was found between adiponectin levels and levels of high-density lipoprotein cholesterol. VFA and adiponectin levels were both associated with metabolic risk factor grouping.
14.	Schrieks IC, *et al*.[25]	2018		Cohortstudy	6998	In descriptive cohorts, adiponectin correlates negatively with incident coronary heart disease (CHD), while free fatty acids (FFAs) are positively associated.

15.	GhanbariAA, *et al*.[26]	2013	Cross- section al study	1015	The levels of adiponectin are contrary related to CHD progression and glucose intolerance, but positively related to heart failure progression.
16.	Stojanovic S, *et al*.[27]	2021	Cross- section al study	130	When juxtaposed with the controls , serum adiponectin levels were significantly lower in the CAD+MetS group (p 0.001) and the CAD-MetS group (p 0.01).
17.	Ketlogetswe KS, *et al*.[28]	2014	Cohortstudy	493	Adiponectin concentrations were reduced in HIV-infected men and were associated with the extent of subclinical atherosclerosis, regardless of traditional cardiovascular disease (CVD) risk variables.
18.	Wang Z, *et al*.[29]	2019	Observational Cohortstudy	227	Our findings show that adiponectin levels are related to stroke severity.
19.	Wang G, *et al*.[30]	2022	Cross- section al study	8610	Variants of rs2241766 and rs266729 were linked to lower levels of adiponectin and HDL-C, in addition to higher levels of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C).

Table 2: Shows the studies for leptin levels in cardiovascular disease

S.No	*References*	*PublicationYear*	*Study- Population*	*Study-design*	*Sample-size*	*Outcomes*
1	Vavruch C, *et al.*[31]	2015 (3-year follow-up)	Sweden	Prospective study	720	They discovered that an increased risk associated with elevated leptin levels was also statistically significant when carotid-femoral PWV and IMT were added to the calculations when serum adiponectin levels were less than 4 µg/mL.
2	Nalini D,*et al*.[32]	2015	Chennai	Case-control study	200	Leptin levels in the bloodstream were discovered to be higher in both obese healthy individuals and AMI patients regardless of BMI. Furthermore, leptin has been considered to be directly associated with serum triglycerides, insulin and TNF-α in AMI subjects.
3	Saber H,*et al*.[33]	2015 (follow-up 10 years)	Framingham (Boston)	Cohort study	757	The levels of leptin were not found to be directly related to the chance of incident stroke in general, but there was a negative correlation with stroke in the top waist/hip ratio quartile.
4	Yang H,*et al*.[34]	2017	China	Case-control study	257 CVD patientsand 26710 controls	The results of their study suggest that elevated leptin levels aren't necessarily correlated with an increased risk of CHD or stroke.
5	Sina G,*et al*.[35]	2022	Iran	Retrospective Cross-sectional study		The average serum leptin level was 290.44 ng/ml (82.9-1600 ng/ml). They demonstrated that there is definitely no significant connection between human serum leptin and coronary artery disease risk factors, age, or gender; additionally, none of the measurable myocardial perfusion scan parameters correlate with serum leptin.
6	Chen J,*et al*.[36]	2021	China	Cohort study	223	Leptin was found to be considerably linked to CV incidents among RA patients. Serum leptin levels that are elevated may be an effective prognostic factor for estimating The consequences of cardiovascular disease in RA patients.
7	Chen TH, *et al*.[37]	2018	Taiwan	Cross-sectional	60	Raised leptin levels are a risk factor for PAD in the elderly.

8	Du Y, *et al*.[38]	2018	China	Case-control study	394	Serum leptin concentration was higher in female patients and independently related to CRP, WBCC, and its subsets, indicating a potential relationship among leptin and inflammation in female CAD patients.
9.	Hanboly NH, *et al*.[39]	2018	Cairo (Egypt)	Case-control study	100	Serum leptin levels in the ACS group were significantly higher than in the normal controls (P= 0.001). Although the difference was not statistically significant, leptin levels were higher in the eventful group compared to the uneventful group.
10.	Qin Z, *et al*.[40]	2021	China	Prospective	165	Serum leptin concentrations are predictive of cardiovascular outcomes and overall mortality in MHD patients. The effects of serum leptin concentration on the onset of LVH and PVD could be a possible mechanism. 10.1016/j.cca.2021.06.003
11.	Liu Y, *et al*.[41]	2019	China	Case-Control study	397	Human serum leptin levels were higher in 200 CAVD patients than in 197 non-CAVD controls.
12.	Martin SS, *et al*.[42]	2015	US	Prospective Cohort Study	13,789	Leptin levels are not related to the occurrence of cardiovascular diseases.
13.	ChristenT, *et al*.[43]	2023	Netherlands	Cross-sectionalstudy	6107	In exploratory research, leptin was found to be merely linked to heart function and subclinical cardiovascular illness, but the relationships were diminished when total body fat was taken into account.
14.	AljaloudKS, *et al*.[44]	2022		Cross-sectionalstudy	55	Low active individuals had higher levels of leptin and hsCRP irrespective of body composition status.
15.	Montazer ifar F, *et al*.[45]	2016		Case-control study	80	When compared to healthy controls, CAD patients had higher levels of leptin and CRP (p 0.001), cholesterol (p 0.05), triglyceride (p 0.01), and WC (p 0.05).
16.	Zonneveld MH, *et al*.[46]	2021		Cross-sectionalstudy	5623	There was a 135 mm3 (95% CI 2;268) higher volume of the amygdala per log ng/mL higher serum leptin, independent of BMI, but no correlation with cognitive tests or other brain volumes was found.
17.	Caffo O,*et al*.[47]	2021	North Florida	Church based longitudnal study	89	Serum leptin levels were found to be directly associated with sex (being female) (r = 0.623, p 0.001).
18.	Wang H,*et al*.[48]	2020	China	Cross-sectionalstudy	384	The frequency of the G allele at rs2167270 was considerably increased in patients with CAD than in controls. Compared to the AA genotype, the AG genotype at rs7799039 was found to be linked with a significantly lower risk of CAD.

tissue cross-talk has begun. The fact that both obesity-associated hyperleptinemia and hypoadiponectinemia are significant indicators to predict cardiovascular conclusions suggests that adiponectin and leptin play a vital role in obesity-associated cardiovascular diseases.

It is true that maintaining healthy levels of adiponectin and leptin is crucial for maintaining cardiovascular function. Heart failure is brought on by insufficient leptin and adiponectin signaling. However, a contradictory relationship between high leptin and adiponectin values and cardiovascular disease pathophysiology is arising. We address the underlying processes for the new conflict of adiponectin and leptin action, as well as the potential use of partial leptin reduction in together with boosting the adiponectin/leptin ratio, in the context of avoiding or curing cardiovascular conditions.[8]

Leptin has a connection to obesity and may have a role in many of the cardiovascular problems that go along with it. In addition to stimulating the sympathetic nervous system, it supports atherosclerosis, ROS production, angiogenesis, hypertension, and vascular remodeling. Studies have demonstrated that this hormone can predict stroke without the use of conventional risk factors and that patients with

Table 3: Shows the studies for levels of Leptin and Adiponectin in Cardiovascular Disease

S. No	*References*	*Publication Year*	*Study- Population*	*Study-design*	*Sample-size*	*Outcomes*
1	Yan H, *et al*.[49]	2022	China	Cross- sectional study	80	They discovered elevated leptin levels while serum diminished adiponectin levels; and these levels were statistically significant and distinct from the participants of the control group.
2	Anaszewicz M, *et al*.[50]	2019	Poland	Cross- Sectional study	80	When indexed to body surface area, FM, and visceral adiposity, patients with AF possessed greater fat mass (FM), greater serum leptin levels, and lower levels of ADA, TNF-, and irisin. Hyperleptinemia increased the risk of AF slightly.
3	Larsen MA, *et al*.[51]	2018	Norway	Cross- sectional study	120	The L:A ratio proved capable to identify initial metabolic abnormalities in obese people, suggesting that it could be a useful clinical surrogate indicator of metabolic illnesses.
4	Zhao S,*et al*.[52]	2021		Cross- sectional study	100	Obesity-related hyperleptinemia and hypoadiponectinemia both constitute significant indicators for predicting cardiovascular consequences, implying that adiponectin and leptin play an important role in obesity-related cardiovascular disorders.
5	Lekwa T,*et al*.[53]	2015 5 year follow-up	Norway	Prospective-cohort study	300	Their findings indicate a high L/A ratio during pregnancy, especially in those with GDM, is associated with an undesirable CVD risk outline throughout follow-up.
6.	RahmaniA, *et al*.[54]	2021	Iran	Case-controlstudy	300	Although leptin levels and the L/A ratio were higher in patients compared to controls, adiponectin levels were far less in patients with CAD than in the controls.
7	KajikawaY, *et al*.[55]	2020	Japan	Cohort study	104	The research discovered variables linked to a rise in serum leptin and adiponectin levels. Serum leptin levels might be correlated positively with MetS, whilst adiponectin levels are negatively associated with MetS and CHD events, for patients with multiple coronary risk factors.
8.	Bidulesc u A, *et al*.[56]	2013 (6.2 years average offollow-up)	U.S.A	Cohort study	4,571	The results showed that adiponectin was significantly correlated with incident stroke in women, with an HR of 1.41 (1.04-1.91) per SD increase (p = 0.03), in contrast to men (p = 0.42). It was not linked with the occurrence of CHD in either men or women. Leptin was not linked to an increased risk of CHD or stroke.
9.	RostoffP, *et al*.[57]	2020		Cross- sectional study	68	Patients with a red blood cell distribution width RDW of 13.5% experienced a substantially greater median (interquartile range [IQR]) serum leptin-to-adiponectin ratio (1.7 [0.49-2.3] ng/g vs 0.66 [0.31-1.25] ng/g; P = 0.04) and median (IQR) tumor necrosis factor ranges (1.58 [1.42-1.97] pg/ml vs 1.39 [1.18- 1.

10.	Everson-Rose SA,*et al*.[58]	2021	Cross- sectional study	1399	Lower adiponectin levels were linked to greater carotid artery intima-media thickness, wider adventitial diameter, and faster baPWV; however, these associations were mitigated once cardiovascular disease risk factors were taken into account. Higher levels of leptin have been associated with greater carotid artery intima-media thickness and wider adventitial diameter, and, in contrast to standards, with slower baPWV, particularly among women with diabetes mellitus or obesity, in both minimally and fully adjusted models.
11.	Sawaguch T, *et al*.[59]	2019	Cross- sectional study	128	Adiponectin and brain natriuretic peptide (BNP), age, left atrial diameter (LAD), E/e' (early-diastolic left ventricular inflow velocity / early-diastolic mitral annular velocity), and left atrial volume index (LAVI) were found to have positive correlations. Leptin, on the other hand, correlated negatively with all of parameters. Adiponectin had a negative correlation and serum leptin had a positive correlation with BMI, estimated glomerular filtration rate (eGFR), triglyceride, hemoglobin, and albumin.
12.	ToulisKA, *et al*,[60]	2018	Cross- sectional study	698	Adiponectin levels in males were considerably lower in the IGT group corresponding to the non-IGT group (Whitney U test, p 10-4), while leptin levels in the IGT group were substantially elevated (p = 0.009). Adiponectin and leptin levels in females did not differ significantly between groups (Mann-Whitney U test, p = 0.073 and p = 0.08, respectively).
13.	Seven E,*et al*.[61]	2015	Prospectivestudy	6502	Neither adiponectin nor leptin were linked separately with CVD in the present investigation, promoting concerns regarding their significance in CVD.

arterial hypertension who alsohave this hormone can also be at increased risk for myocardial infarction. Leptin has been demonstrated to protect the cardiovascular, renal, and gastric systems from harm during ischemia/reperfusion injury, therefore, it is not entirely accurate to characterize it as a purely negative hormone. The argument that leptin-related injury to the cardiovascular system is caused by leptin's incapacity to exert its effects in obese people is that these people are resistant to leptin .[9]

According to studies, adiponectin prevents atherosclerosis, oxidative stress, and inflammation in the heart and blood arteries, maintaining normal heart physiology. Adiponectin has the potential to be a new pharmacological treatment for cardiovascular disease if more research on its advantageous effects is done.[9]

Additionally, in people without obvious cardiovascular disease (CVD), increased concentrations of circulating leptin and diminished adiponectin levels are linked to a variety of CVD risks, including lipid abnormalities. Dyslipidemia being a significant risk factor of CVD, and studies have shown that lipid ratios can predict CVD risk more accurately than single lipid measurements alone.[10]

Adipokines might be used in two clinical settings in the near future. First off, they might be a sign of a number of pathological ailments and illnesses linked to cardiovascular disease, metabolic syndrome, and obesity. Decreased serum levels of cardioprotective adipokines or higher levels of pro-inflammatory adipokines in the blood may serve as valuable biomarkers for cardiovascular disease that is imminent or has already manifested.[11]

CONCLUSION

Adipokines play a variety of roles and may impact a wide range of mechanisms, including energy and appetite regulation, lipid and glucose metabolism, insulin function, endothelial cell function, inflammation, blood pressure, homeostasis, atherosclerosis, metabolic syndrome, and so on. Comprehending the links between obesity, cardiometabolic condition, and CVDs, as well as the influenced adipokine secretion profile, is critical in establishing novel approaches for coping with obesity-associated consequences. This systematic review compiles scientific data from the past ten years and explores the obesity-cardiovascular-disease-cardiometabolic-disorder triangle and numerous adipokines concerned.

Limitations

There are several limitations to the present study.

- Despite the fact that many of the interactions found in our study were significant, we were unfit to forego drawbacks that perhaps weakened the validity of our findings.
- Second, substantial variation was discovered within the research projects.
- Race and CVD disease type differences (heart failure, coronary heart disease, myocardial infarction, and stroke) could account for some of the substantial disparities.

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