REVIEW ARTICLE

To Study the Evidence of Linking Adipokines (Adiponectin, Leptin) with Metabolic Syndrome: A Systematic Review

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ABSTRACT

Background: A growing body of world health has shown that there is a correlation between derangement of adipokines section and metabolic syndrome, but a small number of studies also refused the data. Considering these aspects, this study is intense in pursuing precise knowledge regarding the same and the conclusion.

Aim and Objective: This study investigates the connection between markers of metabolic syndrome and adipokines, particularly leptin and adiponectin.

Methods: PubMed, Scopus, and Web of Science databases were used for a thorough literature review. From 2013 to 2023, the terms "adipokines and metabolic syndrome", "adiponectin and metabolic syndrome", and "leptin and metabolic syndrome" were searched. This review made use of the preferred reporting items for systematic review and meta.

Results: About 3448 previous studies were searched, of which 85 studies fulfilled the inclusion and exclusion criteria. A total of 85 papers comprised this systematic review, and we examined 60 of them. An overvalue of most studies showed that decreased adiponectin levels are linked with a higher risk of metabolic syndrome. However, patients with metabolic syndrome had higher risk levels of both leptin and the leptin-adiponectin ratio.

Conclusions: Obesity affects the generation of adipokines, which regulates the many factors of the metabolic syndrome, through unique and linked pathways. Therefore, we conclude that obesity resulting from a high-fat, high-sugar, high-lipid diet may affect various organs, increasing the risk of metabolic diseases and the underlying causes of insulin resistance and triggering an inflammatory response.

Keywords: Adipokines, Adiponectin, Diabetes mellitus, Leptin, Metabolic syndrome.

Highlights

- *The key objective of this comprehensive investigation is to investigate real data regarding the connection between imbalanced and metabolic syndrome.*
- *This review indicates that reduced levels of adiponectin are linked to a higher risk of metabolic syndrome.*
- *Research findings indicated that individuals with metabolic syndrome exhibited elevated levels of leptin and the leptin-adiponectin ratio.*

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INTRODUCTION

These metabolic and clinical risk factors, which include obesity, dyslipidemia, hypertension, and type 2 diabetes mellitus, are together referred to as the "metabolic syndrome", or "Met. S".[1] Met. S has a major independent effect on the onset of coronary heart disease and type 2 diabetes.[2] Globalization raises the possibility of developing metabolic syndrome by increasing the prevalence of central obesity, particularly in developing countries.[3]

It implies that insulin resistance and metabolic syndrome are significantly influenced by central obesity. The mechanism by which adipocytes produce specific cytokines known as

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"adipokines formation" may point to a connection between obesity and insulin resistance metabolic syndrome in the central nervous system.[4] Therefore, the international diabetes federation (IDF) believes that central obesity is the main cause of metabolic syndrome.[5]

Adipose tissue secretes several adipokines that influence the regulation of metabolic processes, as it is an active endocrine organ. The two main hormones adipocytes produce leptin and adiponectin, which are essential for platelet function, insulin sensitivity, glucose homeostasis, and lipid metabolism, are released by adipose tissue.[6] Polypeptide hormones known as adipokines affect many aspects of life, but primarily the pancreas, the liver, fat and carbohydrate metabolism, and the restoration of insulin sensitivity are affected.[7]

The adipocyte-produced adipokine adiponectin has an anti-inflammatory effect on the cellular component of the arterial walls.[8] As an endogenous insulin sensitizer, adiponectin regulates fat and carbohydrate metabolism in insulin-sensitive tissues.[9] Type 2 diabetes, insulin resistance, obesity, and atherosclerosis are all caused by low adiponectin levels. Furthermore, a recent study discovered an inverse link between elevated serum adiponectin and the risk of developing metabolic syndrome.[10] Adiponectin also reduces hepatic glucose synthesis while increasing muscular glucose absorption and oxidation of fatty acids.[10]

Adipose tissue contains the adipokines leptin, which is involved in energy expenditure, glucose and lipid metabolism, and the regulation of pro-inflammatory T cells.[11] It acts on the hypothalamus to control appetite and increase energy levels, which in turn regulates body weight.[12] It also helps immune cells produce anti-inflammatory cytokines. Furthermore, Janus kinase (JAK)2 is activated upon leptin binding to its receptor. Consequently, this promotes the activation of insulin receptor substrate (IRS), mitogen-activated protein kinase (MAPK), and signal transducer and activator of transcription (STAT).[12] Suppressors of cytokine sign signaling (SOCS3) can be activated by these pathways and inflammatory chemicals. This anti-inflammatory cytokine acts as an inhibitory feedback loop to leptin and insulin signaling, limiting cellular responses to inflammatory cytokines.[13] It has been suggested that excessive weight gain and glucose intolerance may result from the co-development of insulin resistance and leptin resistance *via* SOCS3.[13] Despite some evidence indicating that obese people had greater leptin levels than normal people, another study found no differences in leptin levels between obese patients with and without type 2 diabetes mellitus. Mature people with type 2 diabetes have been found to have reduced leptin concentrations.[14]

Because adipocytes are key players in the development of vascular disease and metabolic syndrome, they must produce adipocytokines and other bioactive substances. Adipocytes are cells that store energy and release a range of bioactive chemicals such as growth factors, cytokines, hormones, and others. Adipocytes are cells that not only store energy but also release a range of hormones, cytokines, growth factors, and other bioactive substances, according to recent research on the biology of these cells.[14] Numerous physiological benefits, such as anti-inflammatory, anti-diabetic, and anti-atherosclerotic qualities, have been associated with adipocytokines. Elevated adiponectin plasma levels are linked with the development of visceral adipose tissue. Recent studies have shown a strong relationship between high levels of leptin and obesity. Insulin sensitivity and lipid metabolism may be impacted by leptin. If we understand how leptin works, it may be easier to develop novel therapeutic approaches for metabolic diseases like diabetes and obesity.[15] The current investigation searches for proof of a connection between the metabolic syndrome and adipokines such as leptin and adiponectin.

MATERIALS AND METHODS

A systematic review search covering the period from January 1, 2013 to March 2023 was conducted using the PubMed, Scopus, and Web of Science databases. "Adipokines and metabolic syndrome", "Adiponectin and metabolic syndrome", and "Leptin and metabolic syndrome" are all mentioned in the database. Following their examination of the full-text publications and individual assessments of the abstracts and citations the two reviewers searched for a consensus as to which research should be included. Numerous more works were discovered after a review of the references. The PRISMA principles were carried out in the systematic review.

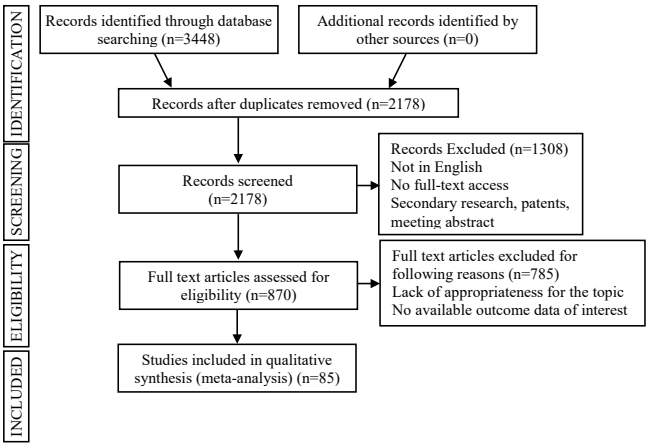

Figure 1: An illustration showing the steps involved in including an article in this systematic review

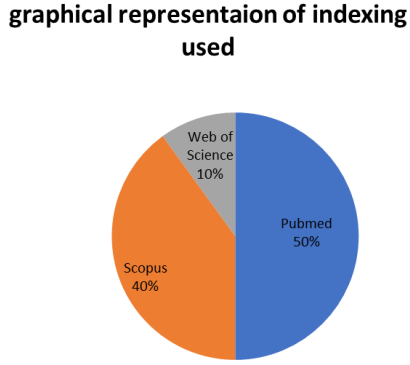

Figure 2: Graphical representation of articles indexing

Table 1: Showing the studies of levels of Adipokines (Adiponectin &Leptin) in metabolic syndrome

S. No	*References*	*Publication year*	*Study design*	*Source of article*	*Outcomes*
1.	Idalia CE *et al.*	2023	Cross-sectional study	PubMed	Children with normal body weight had considerably lower leptin levels.[16]
2.	Xiaosi H *et al.*	2023	Cross-sectional study	PubMed	Diabetes and pre-diabetes were found to be significantly correlated with low levels of adiponectin in a community.[17]
3.	Tuppad S *et al.*	2022	Case-control Study	Scopus	Adiponectin levels were significantly lower in type 2 diabetes mellitus than in healthy controls.[18]
4.	Lee K W *et al.*	2022	Cohort study	PubMed	Greater levels of adiponectin were linked to a lower risk of Metabolic syndrome, whereas greater levels of leptin and the LA ratio were linked to a higher incidence of the conditions in Korean men and women.[19]
5.	Singhal A *et al.*	2022	Cross-sectional study	Web of Science	The concentration of serum adiponectin was significantly inversely correlated with BMI, systolic blood pressure, total cholesterol, and low-density lipoprotein.[20]
6.	Ahmad K *et al.*	2022	Cross-sectional study	Scopus	TG: HDL-C ratio was a more reliable predictor of insulin resistance in metabolic syndrome structures than basting blood glucose (FBG).[21]
7.	Zhao Y *et al.*	2022	Case-control study	PubMed	Individuals with metabolic syndrome had significantly higher serum insulin and leptin levels.[22]
8.	Sigit L *et al.*	2021	Cohort study	Scopus	Adiponectin levels were decreased in patients with metabolic syndrome.[23]
9.	Gezira K B *et al.*	2021	Cross-sectional study	Scopus	A significant ($p < 0.01$) association was found between gender, leptin level, glycosylated hemoglobin fasting blood glucose.[24]
10.	Olesia M B *et al.*	2021	Case-control study	PubMed	Children who were overweight had significantly higher total leptin levels than the normal group ($p < 0.01$).[25]
11.	TALAT A M *et al.*	2021	Cross-sectional study	PubMed	Patients with obesity had a higher ratio of leptin to adiponectin than participants in excellent health.[26]
12.	Lee *et al.*	2020	Cohort study	Scopus	A correlation was found between a lower incidence of metabolic syndrome and higher adiponectin levels.[27]
13.	Wattanapol P *et al.*	2020	Case-control study	Web of Science	Compared to healthy individuals' women with metabolic syndrome reported significantly decreased serum adiponectin levels.[28]
14.	Khaldoon A *et al.*	2020	Case-control study	PubMed	Type 2 diabetes mellitus groups, showed significantly higher levels of LAR and leptin and significantly lower levels of adiponectin compared to healthy persons.[29]
15.	Atarod Z *et al.*	2020	Case-control study	Scopus	Compared to the non-diabetic group, the diabetes group's serum adiponectin levels were considerably lower.[30]
16.	Kalyani RS *et al.*	2020	Case-control study	PubMed	The mean serum (16.93 ± 3.86) and salivary (24.96 ± 8.21) adiponectin levels were significantly substantially lower in the group (diabetic persons) compared to group 2 (normal patients).[31]
17.	Tullaya S *et al.*	2020	Cross-sectional study	Scopus	Higher fasting blood glucose and HbA1c levels were associated with a higher incidence of type 2 diabetes mellitus in the Thai IFC group.[32]
18.	Zaha C D *et al.*	2020	Cross-sectional study	PubMed	The levels of leptin and adiponectin were considerably ($p < 0.01$) lower in the obese participants. Moreover, a significant ($p < 0.01$) correlation was found between metabolic syndrome and the ratio of leptin to adiponectin.[33]
19.	Zahary S *et al.*	2019	Cross-sectional study	Scopus	Individuals with metabolic syndrome had considerably lower serum adiponectin levels than individuals without the disorder.[34]
20.	Behiry EG *et al.*	2019	Cross-sectional study	PubMed	A positive statistical correlation between the TG/HDL ratio and the homeostatic model assessment of insulin resistance, or HOMA-IR[35]
21.	Adejumo N E *et al.*	2019	Case-control study	Web of Science	LAR was linked to a better metabolic syndrome outcome in both males and females than adiponectin and leptin alone.[36]

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22.	Karen S *et al.*	2019	Cross-sectional study	PubMed	Higher levels of adiponectin were adversely correlated with the risk of metabolic syndrome in Brazilian teenagers.[37]
23.	Jamal L *et al.*	2019	Case-control study	Scopus	Children with metabolic syndrome had significantly higher leptin levels ($p < 0.001$) than children in the healthy group.[38]
24.	Shameela Majeed *et al.*	2019	Case-control study	PubMed	People with metabolic syndrome had higher leptin levels than normal people ($p < 0.001$).[39]
25.	Nabila A *et al.*	2018	Cross sectional study	PubMed	Those with diabetes and insulin resistance had significantly lower levels of adiponectin than people without the condition.[40]
26.	Zhengtao Liu *et al.*	2018	Cross-sectional study	PubMed	Decreased adiponectin levels have been linked to an increased risk of metabolic syndrome.[41]
27.	Chen CV *et al.*	2018	Cross-sectional study	Scopus	The L/A (leptin/adiponectin) ratio may be a more positive indicator of metabolic syndrome in a person with schizophrenia than leptin or adiponectin alone.[42]
28.	Gupta V *et al.*	2018	Case-control study	PubMed	In postmenopausal women, high L:A ratios are a robust predictor of metabolic syndrome[43]
29.	Demir S *et al.*	2018	Case-control study	Scopus	Higher levels of leptin were found in individuals with metabolic syndrome compared to healthy ones.[44]
30.	Hiba S *et al.*	2017	Case-control study	Scopus	Leptin and metabolic syndrome are clearly and plausibly correlated.[45]
31.	Tseng P et. al	2017	Case-control study	PubMed	Metabolic syndrome has a positive correlation with serum leptin in comparison to normal patients.[46]
32.	Kumar A *et al.*	2017	Case-control study	Web of Science	The healthy group's serum adiponectin was significantly lower when comparing cases of metabolic syndrome to controls.[47]
33.	Kang RD *et al.*	2017	Cross-sectional study	PubMed	For both men and women ($p = 0.024$ and $p = 0.019$), the L/A ratio is a better predictor of the regression of metabolic syndrome than serum adiponectin.[48]
34.	Clarisse N A *et al.*	2017	Cross-sectional study	Scopus	It was found that in metabolic syndrome, LAR was significantly associated with higher levels of leptin and lower levels of adiponectin.[49]
35.	Madeira I *et al.*	2017	Case-control study	PubMed	Individuals with metabolic syndrome exhibited significantly higher leptin levels than those without the illness.[50]
36.	Wang L H *et al.*	2017	Cross-sectional study	Web of Science	Reduced adiponectin levels and metabolic syndrome were positively correlated.[51]
37.	Jain V *et al.*	2017	Cross-sectional study	PubMed	Blood glucose BMI and IL-6 were positively correlated, but adiponectin and waist circumference were negatively correlated.[52]
38.	Nappo A *et al.*	2017	Cohort study	Scopus	Children from Europe with higher leptin concentrations are more likely to develop metabolic syndrome, even after controlling for body mass index.[53]
39.	Gee L *et al.*	2017	Cohort study	Web of Science	Elevated L/A levels, which indicate an imbalance between the two hormones, were a more accurate marker of metabolic syndrome than leptin or adiponectin alone.[54]
40.	ALNOR Y *et al.*	2016	Case-control study	Scopus	Serum leptin levels were found to be higher in the metabolic syndrome group than in the non-metabolic syndrome group.[55]
41.	Agathi N *et al.*	2016	Cross-sectional study	PubMed	An inverse correlation was found between adiponectin and metabolic syndrome.[56]
42.	Eslamian M *et al.*	2016	Cross-sectional study	PubMed	A considerable positive connection between adiponectin and metabolic syndrome in the lipid profile.[57]
43.	Silva GM *et al.*	2016	Cross-sectional study	Scopus	Patients' serum adiponectin was greater, and their levels of leptin were lower.[58]
44.	Farooq R *et al.*	2016	Case-control study	PubMed	Patients with type 2 diabetes mellitus showed significantly lower adiponectin levels and significantly higher leptin levels compared to controls.[59]
45.	Shafiee G *et al.*	2015	Case-control study	PubMed	It was found that Mets supporters had significantly lower levels of adiponectin than normal subjects.[60]
46.	Ding S Y *et al.*	2015	Cohort study	Scopus	An inverse connection between adiponectin and other components of the metabolic syndrome.[61]

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47.	Jimenez SG *et al.*	2015	Cross-sectional study	PubMed	Individuals with metabolic syndrome had greater levels of leptin (26.7 ±13.7) compared to those without it (20.1 ± 13.9; $p < 0.001$).[62]
48.	Jimenez G S *et al.*	2014	Case-control study	Scopus	People with metabolic syndrome had higher leptin levels than people with normal.[63]
49.	Mohamed A *et al.*	2014	Cross-sectional study	PubMed	Leptin had a significant positive association ($p < 0.05$) with developing components of metabolic syndrome, while adiponectin exhibited a negative correlation ($p < 0.0001$) with the same components.[64]
50.	Bălăşoiu M *et al.*	2014	Case-control study	PubMed	Patients with type 2 diabetes mellitus had significantly larger proportions of adipocytokines than the control group.[65]
51.	Hamodi Z A *et al.*	2014	Case-control study	PubMed	Compared to normal individuals, type 2 diabetes and obese patients had lower levels of adiponectin, but higher levels of leptin and LAR.[66]
52.	Timar R *et al.*	2014	Cross-sectional study	Scopus	People with metabolic syndrome had higher levels of leptin and lower levels of adiponectin than people without the condition.[67]
53.	Jialal I *et al.*	2014	Cross sectional study	PubMed	A considerably greater RBP4/adiponectin ratio was linked to metabolic syndrome.[68]
54.	Beverley A *et al.*	2014	Case-control study	PubMed	Those with metabolic syndrome had higher adiponectin levels than controls.[69]
55.	Diana A *et al.*	2013	Cross-sectional study	Scopus	Individuals with metabolic syndrome, leptin, and somatic depression symptoms have different connections.[70]
56.	Sandip Z *et al.*	2013	Cross-sectional study	PubMed	Adiponectin levels had a positive link with insulin sensitivity index and a negative correlation with metabolic syndrome.[71]
57.	Vega G L *et al.*	2013	Cross-sectional study	Scopus	Men with higher adiponectin/leptin ratios had better lipid profiles and insulin sensitivity than women.[72]
58.	Kim YJ *et al.*	2013	Cohort study	Scopus	Elevated adiponectin is a clear protective factor against incident metabolic syndrome in both men and women.[73]
59.	Kuppan G *et al.*	2013	Cross-sectional study	PubMed	Adiponectin levels were higher in type 1 diabetes mellitus and in type 2 diabetes mellitus as compared to the NGT (normal glucose tolerance) group.[74]
60.	Shah A *et al.*	2012	Cross-sectional study	Scopus	There is a significant link between leptin and obesity however, there is less of a correlation between adiponectin and obesity because of metabolic factors.[75]

Inclusion Criteria

- Cross-sectional, case-control, and cohort studies were used for this review.
- Research conducted after 2013 was assembled.
- Studies where metabolic syndrome and its association with adipokines (adiponectin, leptin) levels are studied

Exclusion Criteria

- Other systematic reviews were excluded
- Non-English papers were excluded because of the structural language barrier
- All studies in which metabolic syndrome has been studied in conjunction with some other disorder (a metabolic syndrome in myocardial infarction patients, metabolic syndrome in cancer patients, etc) have the potential to alter the findings and have been excluded.
- Studies, where the full text was not available were excluded.

Study selection

Research examining potential links between adipokines and metabolic disorders was included in the evaluation. Two distinct, independent evaluations were carried out for each featured article at different periods. If disputes should emerge amongst the reviewers, a third reviewer provided feedback on the content. The reviewers confirmed every highlighted paper's eligibility.

Analytic process

The literature that was acquired was examined using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) standards as the analytical technique. The terminology employed in this work is consistent with the statement made by ICS. Criteria established by the Standards for the Reporting of Diagnostic Accuracy (STARD) and the Consolidated Standards of Reporting Trials (CONSORT) were used to evaluate the caliber of the included literature and reduce selection bias.

Literature search

Figure 1 summarizes the steps involved in conducting a literature search. The comprehensive online literature search from PubMed, Scopus, and Web of Science databases revealed 3448 records. Among these records, 785 were excluded and 85 were selected and retrieved in full-text versions.

Figure 2 Summarizes the graphical representation of the article's indexing. The comprehensive online literature search depicts 50%PubMed, 40%Scopus, and 10%Web of Science studies that were included in this systematic review.

RESULT

The table includes a review of the main results from the included studies.

Table 1 shows the impact of adipokines, including adiponectin and leptin, on several components of the metabolic syndrome by aggregating 60 articles from 85 research that satisfy the inclusion and exclusion. Of the 33 papers that address adiponectin, 25 (75.7%) indicate a correlation between lower adiponectin levels and metabolic syndrome, whereas the remaining 8 (24.2%) indicate higher adiponectin levels. Low blood adiponectin levels and elevated serum leptin levels are linked to obesity, dyslipidemia, hypertension, and diabetes mellitus. Of the 28 research on leptin that we could find, two (7.14%) suggested that the hormones were reduced in metabolic syndrome, whereas 26 (92.8%) showed an increased level of leptin in metabolic syndrome. 13 (100%) of the studies that looked at people with metabolic syndrome were shown to have a leptin/adiponectin ratio (LAR) and higher values of the ratio. This implies that LAR, as opposed to leptin and adiponectin alone, is a more reliable marker of metabolic syndrome.

DISCUSSION

India has contributed significantly to the increase in metabolic syndrome cases worldwide. A group of physiological and biochemical conditions known as metabolic syndrome include high triglyceride levels, aberrant cholesterol, hypertension, excessive fasting glucose, and central obesity. Reasons indicate that individuals with metabolic syndrome are twice as likely to have cardiovascular disease and five times as likely to develop type 2 diabetes. Two adipokines that have been connected to inflammatory diseases and metabolic syndrome comorbidities are leptin and adiponectin.[2]

It has been demonstrated by earlier research that adipose tissue is necessary for energy metabolism. It has been demonstrated that adipose tissue secretes a range of hormones referred to as "adipokines", which may act as a mediating factor between metabolic syndrome risk factors and obesity. It is commonly known that adipokines have a significant role in the development and advancement of the metabolic syndrome.[7] The activation of pro-inflammatory cytokines called adipokines is one of the main ways that an excess of adipose tissue causes damage.[15] A growing amount of evidence suggests that elevated adipokines synthesis and release from adipocytes, particularly adiponectin, and leptin, may be associated with obesity-related health issues such as dyslipidemia, insulin resistance, and atherosclerosis.[76]

Apart from its primary actions on improving insulin sensitivity and demonstrating anti-inflammatory properties, adiponectin influences multiple other metabolic pathways. Metabolic disorders and cardiovascular illnesses, such as lipodystrophy, essential hypertension, non-alcoholic hepatic steatosis, type 2 Diabetes Mellitus, and coronary artery disease, have been linked to hypoadiponectinemia. Adiponectin may be suppressed by testosterone, which is one of the many reasons why women may have higher levels of the hormone than men.[77]

Adipocytes produce the 16-KDa adipokine leptin, which is synthesized by the obesity (Ob) gene. The production of oxygen radicals, phagocytosis, chemotaxis, chemotaxis, neutrophil growth, and the activation of macrophages/monocytes and natural killer cells are among the activities that leptin impacts.[78] Studies have indicated a relationship between its levels and measurements of glucose, insulin, insulin resistance, and obesity. Decreased leptin transport across the endoplasmic reticulum and blood-brain barrier, which prevents leptin from signaling, can also lead to leptin resistance.[79,80] Leptin signaling protects beta-cells against the negative effects of obesity, such as cholesterol accumulation, when body weight increases.[81] One of the main risk factors for obesity is leptin resistance which can be brought on by compromised leptin transport and signaling.[82] There is a variation in leptin levels between the genders because women produce more leptin per unit of adipose tissue than men. Hiba S *et al.* discovered a positive correlation between leptin, cholesterol, and blood glucose levels in a distinct study.[82]

High levels of LAR and leptin were associated with greater blood pressure, cholesterol, and fasting plasma glucose, according to a study conducted in Yemen and Sub-Saharan Africa.[83] Esther *et al.* discovered that the connections between leptin, LAR, and the elements of the metabolic syndrome were unstable and variable.[84] Numerous investigations found no statistically significant difference in serum levels of adiponectin and leptin between persons with type 2 diabetes, metabolic syndrome, and controls. However, a few studies have discovered a link between blood adiponectin levels and obesity.[85]

LIMITATION

- We found very few prospective and follow-up studies in this systemic review.
- Single-center studies formed most of the research in this review. Hence, high-quality prospective multi-centric studies need to be evaluated further.
- Studies only from the last 10 years online based.
- Research that was not completely available online was excluded from our study.
- No unpublished study was uncovered.

CONCLUSION

Information gathered from many sources in the literature suggests a connection between obesity, metabolic syndrome, and adipokine levels. According to the review's findings, adipokines play a significant part in the emergence of metabolic syndrome. Adipocytes create large amounts of adiponectin, a special and necessary adipocytokine that is continuously present in the plasma at significantly high concentrations. Adiponectin slows the onset of vascular alterations and controls the metabolism of fat and glucose in healthy people. The

onset of metabolic syndrome is inversely linked with elevated levels of adiponectin. Elevated leptin from hypertrophied adipose tissues and low levels of circulating adiponectin have been related to detrimental effects on other organs and may contribute to the development of metabolic and cardiac disease. Measuring leptin levels can help determine who is more likely to experience cardiometabolic problems. In both men and women, elevated leptin levels have been linked to an increased risk of metabolic syndrome. A novel approach to treating metabolic syndrome might involve adjusting this adipokine ratio. Poor adiponectin/leptin ratio, a sign of malfunctioning adipose tissue may be connected to elevated inflammation a feature of the metabolic syndrome. This review examines the connection between inflammatory pathways, adipokines, and the emergence of insulin resistance. Though adiposity caused by overnutrition, lipids, and glucose can affect different tissues to mediate an aberrant inflammatory response and advance the pathogenesis of insulin resistance and metabolic disease.

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