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CHEMERIN-ADIPONECTIN AXIS IN HYPOTHYROIDISM

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Hypothyroidism disrupts energy and metabolism due to insufficient thyroid hormones production, leading to metabolic disorders such as insulin resistance and dyslipidemia. Recent studies have demonstrated the impact of adipokines, chemerin and adiponectin on thyroid function. This review analyzes the involvement of these hormones in the metabolic and inflammatory complications of hypothyroidism, their effects and interactions through complex signaling pathways, as well as their possible contribution to the etiology and treatment of hypothyroidism, considering the importance of integrating biomarker data.

K e y w o r d s: chemerin, adiponectin, hypothyroidism, hormonal interactions, biomarker data.

Hypothyroidism, characterized by insufficient production of thyroid hormones (THs), disrupts energy balance and metabolic homeostasis [1]. Thyroxine (T4) and triiodothyronine (T3), two thyroid hormones, are important modulators of metabolic rate that affect the metabolism of proteins, fats, and carbohydrates [2, 3]. Weight gain, insulin resistance, and dyslipidemia are just a few of the metabolic disorders that can result from thyroid hormone dysregulation [4]. Adipose tissue secretes several adipokines, among them chemerin and adiponectin, which are important for hormonal and metabolic control [5, 6]. While adiponectin has anti-inflammatory, anti-atherogenic, and insulin-sensitizing qualities [1, 5], chemerin is implicated in immunological responses, cell proliferation, and tissue remodeling [7]. There is more to hypothyroidism than a thyroid hormone imbalance. Two hormones that control inflammation and metabolism are chemerin and adiponectin. The activity of these hormones is significantly influenced by thyroid hormone levels. This connection contributes to the explanation of why untreated hypothyroidism results in serious health issues such metabolic disorders and cardiovascular disease. The impact of these hormones on thyroid function has been demonstrated by recent research. These findings offer valuable insights into the underlying mechanisms of hypothyroidism and highlight potential avenues for improved therapeutic interventions. The objective of this review explores how chemerin and adiponectin contribute to the metabolic and inflammatory complications observed in hypothyroidism. We hypothesize that dysregulation of the chemerin-adiponectin axis underpins metabolic complications in hypothyroidism. Pro-inflammatory chemerin (elevated in hypothyroidism) and dysregulated adiponectin (variably reported) interact antagonistically via TNF-α, creating a self-amplifying cycle of metabolic dysfunction (Figure).

Methodology

To gather relevant papers on chemerin and adiponectin in hypothyroidism, this review used a carefully planned approach. A thorough literature search (January 2010 - March 2025) was carried out using Google Scholar, PubMed, and Scopus, utilizing keywords such as “Chemerin”, “Adiponectin”, and “Hypothyroidism” combined with Boolean operators. The inclusion criteria ruled out research that were restricted to *in vitro* experiments or animal models and instead focused on studies that provided quantitative data on blood levels or gene expression in humans. Two stages of screening were used in the

selection process: first, titles and abstracts were reviewed for relevance, and then full-text publications were evaluated for methodological quality using the Newcastle-Ottawa Scale for observational studies. The final selection prioritized high-quality studies providing clinically relevant quantitative data on serum levels or gene expression in human hypothyroidism.

Biological functions of chemerin and adiponectin

Adipose tissue is the primary source of the adipokine chemerin. Chemerin modulates immune responses, adipogenesis, and energy metabolism via CMKLR1/NF-κB signaling [8, 9]. According to Yang et al., metabolic diseases such as obesity and insulin resistance frequently cause changes in its levels [9]. Chemerin signals via CMKLR1-dependent NF-κB and MAPK cascades [8]. White adipose tissue is the primary source of adiponectin, the most prevalent adipokine in the bloodstream . In contrast to chemerin, adiponectin exerts anti-inflammatory effects via AMPK/PPAR-α pathways [5].

Adiponectin is essential for inflammation, lipid metabolism, and glucose homeostasis [1, 5]. Adiponectin activates AdipoR1/R2-mediated AMPK phosphorylation, these receptors are expressed in a variety of organs, such as the liver, muscle, and hypothalamus and through which, adiponectin produces its effects [5]. These receptors' activation generates off downstream signaling cascades that improve lipid profiles, lower inflammation, and increase insulin sensitivity. Obesity and insulin resistance are frequently inversely connected with circulating adiponectin levels [1, 5]. More research is necessary to fully understand the intricate regulatory processes controlling the production of adiponectin and how it interacts with other hormones and signaling pathways [10].

Overview of chemerin

Chemerin is a adipokine that has become a molecule of great interest because of its involvement in a variety of physiological processes, such as inflammation, adipogenesis, and energy metabolism [11]. Although its role in a number of metabolic disorders, such as obesity and type 2 diabetes, is fairly well-established [12], its potential involvement in thyroid dysfunction, particularly hypothyroidism, is still being investigated and debated. Chemerin is primarily produced in the liver and adipose tissue as an inactive precursor, prochemerin [13]. Prochemerin undergoes proteolytic cleavage by various serine proteases, producing several active isoforms that may have opposing biological functions [13, 14].

The inactive form of chemerin, chemerin-S163, is released into extracellular spaces or the circulatory system after prochemerin is truncated at its N-terminal by a 20-amino acid signal peptide. In the extracellular environment, chemerin is further cleaved at the C-terminus by enzymes like plasmin, elastase, and cathepsin G, resulting in chemerin-K158, -S157, and -F156, each of which has a different affinity for the receptor CMKLR1; further chymase cleaves the bioactive chemerin to produce chemerin-F154, which ceases its activity [15]. The primary active isoform, chemerin-156, binds to G protein-coupled receptors (GPCRs), including chemokine-like receptor 1 (CMKLR1), G protein-coupled receptor 1 (GPR1), and C-C motif chemokine receptor-like 2 (CCRL2) [16]. GPR1 can also bind chemerin, but it has a weaker signaling capacity and may function as a decoy receptor [17].CMKLR1 is primarily expressed on immune cells, including dendritic cells and macrophages, mediating chemotaxis and influencing inflammatory responses [18]. C-C motif chemokine receptor-like 2CCRL2, a non-signaling receptor, is expressed in barrier cells and may control leukocyte migration [18].

Role of chemerin in inflammation

Chemerin is an important mediator of inflammation that was first discovered in skin cultures treated with tazarotene. Depending on the circumstances, it can either promote or resolve inflammation. During inflammatory responses, polymorphonuclear cells release elastase and cathepsin G, which transform chemerin into active forms (chemerin-157 and chemerin-156) that start a variety of inflammatory processes, including vascular endothelial dysfunction, angiogenesis, the recruitment of antigen-presenting cells, and enhanced immune cell chemotaxis [19]. Chemerin's signaling mechanisms include binding to ChemR23/CMKLR1, a G protein-coupled receptor present in immune cells, which triggers the NF-kB pathway, which in turn releases inflammatory mediators and matrix-degrading enzymes [18]. Among the molecular processes that are triggered by this binding are interactions with the TLR4 receptor, which triggers the NF-kB pathway. When this pathway is activated, matrix-degrading enzymes [20], and inflammatory mediators are re-

leased. Phosphorylated AKT and p65 levels rise in response to chemerin stimulation, while total AKT and p65 levels stay constant [20]. The following is the order in which the signaling cascade occurs: The TLR4 receptor is bound by chemerin, 2) CMKLR1 phosphorylates AKT, 3) NF-kB pathway activation triggers inflammatory reactions, and 4) cytokines (IL-1β, IL-6, and TNF-α) are produced. Through proteolytic processing, chemerin can also have anti-inflammatory properties. Serine proteases can transform chemerin into chemerin-158 and chemerin-155. Additionally, mast cell chymase changes active chemerin-157 into inactive chemerin-154, thus promoting anti-inflammatory responses [21].

According to Li et al., timing and enzymatic processing are necessary for this signaling duality [21]. Additionally, chemerin promotes dendritic cell migration to lymph nodes and promotes blood vessel formation via pathways such as MAPK and Akt [21]. Proteases transform chemerin into anti-inflammatory peptides (chemerin-155 and chemerin-154) as inflammation subsides, which stimulate IL-10 production and macrophage activation. As reported by Zhao et al., elevated chemerin concentrations are found in the synovial fluid of arthritis patients [22], and its chemotactic actions on macrophages and immature dendritic cells have been highlighted by the discovery that CMKLR1 is a chemerin receptor on these immune cells [19].Chemerin can be activated by a number of inflammatory proteases, such as tryptase, elastase, and cathepsin G, which strengthens its pro-inflammatory function [23].

Furthermore, CCRL2 contributes to the actions of chemerin; when TNF-α, lipopolysaccharide (LPS), and interferon-gamma (IFN-γ) activate endothelial cells, its expression rises, suggesting that it is involved in inflammatory responses associated to chemerin [24]. Elevated levels of plasma chemerin have been associated with rheumatoid arthritis disease activity, indicating that it may be a biomarker [25]. According to some research, chemerin levels and BMI are negatively correlated, which suggests that systemic inflammation associated with obesity – rather than an increase in adipose tissue – may be the cause of elevated chemerin levels [25]. Nevertheless, other studies revealed a relationship between chemerin and disease activity, which is consistent with previous findings, but no correlation between serum chemerin and BMI. Interestingly, chemerin levels and disease activity, as well as other inflammatory indicators including C-reactive protein (CRP) and IL-6, decreased following 16 weeks of adalimumab treatment (a TNF-α antibody) [26].

An important part of the pathophysiology of hypothyroidism is inflammation and metabolic syndrome, both of which are influenced by the multifunctional adipokine chemerin. Chemerin, which is mostly produced by adipose tissue, affects a number of physiological functions, such as energy metabolism and immunological responses. As a chemoattractant, it alters the activity of immune cells that are vital to the body's inflammatory response, including dendritic cells and macrophages [27, 28].

By direct these immune cells to areas of inflammation or damage, chemerin's position enables it to make a substantial contribution to the body's defense mechanisms [11]. Chemerin is essential for metabolic regulation in besides its function in inflammation. It has a major impact on how fats and carbohydrates are metabolized, and it frequently correlates with elements of the metabolic syndrome such visceral obesity, insulin resistance, and dyslipidemia. Individuals with obesity and associated metabolic disorders have been found to have elevated levels of chemerin, indicating that it may play a role in the genesis of these illnesses [11, 29]. Numerous inflammatory disorders have been shown to contain immunoreactive chemerin, according to clinical research. For instance, fibroblasts, mast cells, and endothelial cells have increased chemerin levels in the early phases of inflammation-related clinical alterations. The rate of synthesis of some homologous peptides from chemerin determines its dual function as a pro-inflammatory and anti-inflammatory mediator [21]. This adipokine is strongly associated with the metabolic dysfunctions that are characteristic of hypothyroidism because it may influence adipocyte differentiation and alter metabolic pathways. Understanding chemerin's function in these interconnected networks offers important insights into possible treatment targets for controlling metabolic irregularities, as hypothyroidism frequently manifests as metabolic syndrome symptoms.

Chemerin in hypothyroidism

Chemerin's role in hypothyroidism is emerging as a critical link to metabolic dysfunction. Studies have shown that people with thyroid dysfunction exhibit different patterns in their blood levels of chemerin, with hypothyroidism patients showing higher amounts of chemerin [30]. Elevated chemerin in hypothyroidism correlates strongly with TSH

and metabolic markers. There are multiple important links between chemerin and thyroid function: 1) an inverse relationship with HDL cholesterol [30]; 2) a positive correlation with TSH levels [30]; 3) a direct correlation with BMI and triglycerides [31] and 4) a negative correlation with T3 and T4 levels [30]. According to studies, obese people in the upper TSH tertile had higher levels of chemerin than people in the lower tertile [31]. This rise is linked to lower thyroid hormone levels, which impair the lipoprotein lipase enzyme's activity and raise triglyceride levels [30]. These correlations are further supported by studies on animals, which shows that rats given methimazole had far higher levels of chemerin than they did at baseline [31]. Since chemerin also impacts insulin sensitivity and glucose metabolism in hypothyroidism, these effects go beyond straightforward hormonal interactions. In 2019, Al Doghaither et al. this suggests that thyroid hormones, chemerin, and the regulation of metabolism have a complicated interaction that could contribute to the overall pathophysiology of hypothyroidism [32]. When L-thyroxine was administered to subclinical hypothyroid rats, Gong et al. found that the rats' elevated chemerin levels were reversed [33]. Chemerin may be responding to the inflammatory state brought on by hypothyroidism, according to this. Ozdemir et al., on the other hand, have found no apparent difference in chemerin concentrations between hypothyroid and euthyroid people [4]. Differences in study populations, methods, or the degree and course of hypothyroidism could be the cause of these disparities. Given the contradictory findings in the literature, more research is also necessary to determine how levothyroxine replacement affects chemerin concentrations [33, 34]. Furthermore, little is known about the clinical relevance of changed chemerin levels in hypothyroidism. Although chemerin has been connected to metabolic diseases [11], more research is necessary to determine its precise function in the etiology of hypothyroidism and its related consequences. Reduced thyroid hormone levels in individuals with hypothyroidism can cause metabolic abnormalities and impaired energy homeostasis, which may be impacted by variations in chemerin levels [35]. Thyroid tissue exhibits unique chemerin expression patterns, as revealed by RNA sequencing data analysis. Normal thyroid samples have high amounts of both chemerin and chemerin-1, while thyroid cancer samples have much lower levels of these proteins [36]. Chemerin is found in human biological fluids in a number of active forms, such as chemerin-156, chemerin-157, and chemerin-158. In thyroid tissue, chemerin-2 and CCRL2 expression is lower, with only minor differences observed between normal and cancerous samples [36]. This difference is particularly significant because thyroid cancer makes up approximately 1% of all tumors, with papillary carcinoma accounting for 80% of those cases [37]. Additionally, chemerin expression is correlated with thyroid-stimulating hormone (TSH) levels, as studies show that patients with thyroid cancer have higher levels of both chemerin and TSH than control groups [37]. This correlation has been used to distinguish between benign thyroid lesions and thyroid cancer, highlighting chemerin's potential diagnostic utility. While chemerin appears elevated and pro-inflammatory in hypothyroidism, the role of the protective adipokine adiponectin is more complex, as explored below.

Overview of adiponectin

Within the adipokine family, adiponectin is a unique hormone that promotes insulin sensitivity and metabolic health [38]. This substance affects the liver, skeletal muscle, and pancreas, among other organs, and coordinates a number of vital energy metabolism processes [39]. There are two receptor-mediated mechanisms by which adiponectin affects metabolism. According to Yamauchi and Kadowaki, it increases peroxisome proliferator-activated receptor alpha signaling through AdipoR2 and activates AMP kinase via AdipoR1 [40]. Through AMPK activation, adiponectin improves insulin-stimulated glucose transport as well as basal glucose absorption in skeletal muscle [38]. In the liver, it enhances glucose transport while lowering gluconeogenesis, hence raising metabolic efficiency. Clinical research suggests that adiponectin is essential for preserving energy balance in addition to controlling glucose [38]. The main biological roles of adiponectin are closely related to its capacity to improve insulin sensitivity and have anti-inflammatory [41], and anti-atherogenic [42] properties. Adiponectin's anti-inflammatory properties are essential for its defense against cardiovascular and metabolic disorders. A crucial stage in the development of atherosclerosis, it decreases the adherence of monocytes to vascular endothelial cells by inhibiting the production of endothelial adhesion molecules [43, 44]. Additionally, adiponectin reduces inflammation in adipose regions via modifying macrophage activity by lowering their

polarization toward an anti-inflammatory phenotype [45, 46]. Adiponectin slows the evolution of metabolic problems and cardiovascular diseases through these methods. Furthermore, adiponectin influences a wide range of physiological processes beyond glucose and lipid metabolism, including cell proliferation and angiogenesis, via interacting with several cell signaling pathways and interacting with other hormonal systems. Despite its positive effects, obesity, type 2 diabetes, and coronary artery disease are associated with lower levels of adiponectin, creating a paradox whereby adiposity causes a decline in this important adipokine [47].

Structure and production

Adiponectin is a 244-amino acid protein with unique structural domains that make up its molecular structure. This hormone has 15 collagenous repeats, a hyper variable domain, an N-terminal sequence, and a C-terminal region that resembles complement factor C1q [39]. Low molecular weight (LMW) trimers, medium molecular weight (MMW) hexamers, and high molecular weight (HMW) multimers greater than 400 kD are the three main types of adiponectin that are present in serum [48]. The form with the highest molecular weight is thought to be the most physiologically active of these [49]. The most prevalent peptide hormone made from fat tissue is adiponectin, which is produced and released by white adipocytes [39]. The process of production requires intricate post-translational changes that need for certain chaperone proteins, including ER oxidoreductase 1-LA and endoplasmic reticulum resident protein 44 [39].

Role of adiponectin in metabolic regulation and disease

An important adipokine released by adipose tissue, adiponectin influences the pathophysiology of several metabolic disorders and is involved in metabolic control. Its major purpose is to increase insulin sensitivity, which is essential for preserving glucose homeostasis [47]. This adipokine inhibits hepatic gluconeogenesis while simultaneously boosting glucose absorption and fatty acid oxidation in skeletal muscles through its effects on many metabolic pathways [50]. Adiponectin is a crucial regulator in the prevention and management of insulin resistance and type 2 diabetes because of these combined effects on blood glucose levels and lipid profiles [51]. Adiponectin has anti-inflammatory qualities in addition to its insulin-sensitizing actions [45], which emphasizes its preventive function against metabolic disorders [52]. Chronic low-grade inflammation, a frequent characteristic of obesity and associated illnesses, is reduced by adiponectin's inhibition of pro-inflammatory cytotoxins. Because low levels of adiponectin can cause endothelial dysfunction and atherosclerosis, they are frequently linked to increased risk factors for cardiovascular illnesses [43, 47]. On the other hand, adiponectin may have a function in protecting the arteries because it is associated with a reduced likelihood of cardiovascular problems [53]. Adiponectin is a key mediator in the delicate balance of metabolic processes overall, and its dysregulation is closely associated with the onset and progression of metabolic disorders as show in Figure, suggesting that it may be a promising therapeutic target for the treatment of these conditions [54]. The promise of adiponectin as a treatment requires more research.

Adiponectin in hypothyroidism

Adiponectin levels in individuals with hypothyroidism demonstrate diverse patterns, as seen in clinical research. Median values for adiponectin in hypothyroid patients are reported to be around 12.5 μg/ml, which is significantly higher than the levels observed in euthyroid patients, typically around 6.26 μg/ml [55]. Several factors link thyroid function to adiponectin levels. Notably, there is a positive correlation between adiponectin and high-density lipoprotein (HDL) cholesterol, while a negative correlation exists with body mass index (BMI) and plasma triglycerides [56]. Additionally, strong correlations have been noted between adiponectin and indicators of insulin resistance [57], as well as distinct behaviors related to thyroid-stimulating hormone [55]. Importantly, when hypothyroid individuals achieve euthyroidism, a dramatic decrease in adiponectin levels occurs, with statistical significance ($P = 0.047$). This decrease in adiponectin is particularly relevant to glucose metabolism during thyroid dysfunction [57]. According to research, adiponectin resistance can arise in hypothyroid conditions as a compensatory mechanism, which explains why thyroid insufficiency is associated with higher adiponectin levels ,as show in the Table [55]. This resistance emphasizes the intricate connection between thyroid function and adipose tissue control, especially with regard to lipid metabolism and glucose balance. These discoveries advance our knowledge of the

T a b l e. Clinical studies on chemerin/adiponectin in thyroid dysfunction

Population	Key Findings	Limitations	References
Hypothyroid patients	↑ Chemerin correlates with ↑ TSH, ↓ T3/T4, ↑ triglycerides, ↓ HDL.	Small sample size; no follow-up post-therapy	[30]
Obese hypothyroid	Adiponectin ↑ in hypothyroidism; ↓ after levothyroxine (*P* = 0.047).	Did not measure HMW adiponectin isoforms	[55]
Euthyroid vs. hypo	No chemerin difference; *adiponectin ↑ in hypothyroidism linked to insulin resistance	Confounding by BMI variability	[4]
Subclinical hypo rats	Levothyroxine ↓ chemerin; reverses metabolic inflammation	Animal model; human relevance unclear	[33]
Hypothyroid + neuropathy	↓ Adiponectin in neuropathy subgroup; suggests neuroprotective role	Cross-sectional; causality not established	[58]

Note. ↑ – Increase; ↓ – decrease; HDL – high density lipoprotein; T_4 – thyroxine; T_3 – triiodothyronine; BMI – body mass index

larger pathophysiology of hypothyroidism. Nonetheless, a number of studies have consistently found that hypothyroid individuals had lower serum adiponectin levels than euthyroid controls. Rashad et al., for example, observed that hypothyroid individuals, particularly those with peripheral neuropathy, had noticeably reduced levels of adiponectin [58]. This difference highlights the complex mechanisms behind thyroid dysfunction and its effects on metabolism. According to some research, thyroid hormones may have a direct impact on the expression and secretion of the adiponectin gene [33, 59]. However, other research suggests that a secondary effect of variables including insulin resistance and obesity [55]. Additionally, there are contradictory findings about how levothyroxine replacement treatment affects adiponectin levels. According to some research, adiponectin levels rise after therapy [33], but other studies reveal no discernible change or even a drop [4, 60]. Differences in patient groups, methods of therapy, and research designs might be the cause of these discrepancies. The exact mechanics and therapeutic implications of these discoveries require more investigation. Further research is also necessary to determine the function of adiponectin as a biomarker for hypothyroidism, since other variables like body mass index may restrict its diagnostic potential [61].

Interaction between chemerin and adiponectin in thyroid dysfunction

The interaction between chemerin and adiponectin in thyroid dysfunction is characterized by a negative correlation [62], that exacerbates metabolic complications in hypothyroidism, forming the core of our central hypothesis. influences metabolic dysregulation, mediated partly by TNF-α. *In vitro* studies confirm TNF-α increases chemerin mRNA expression and secretion while suppressing adiponectin transcription in adipocytes [62], disrupting the balance between pro- and anti-inflammatory signals.

Molecular pathways

Chemerin Signaling mediated by Binds CMKLR1 [63], which activating two pathways, MAPK pathway is rapid phosphorylation of ERK-1/2 and p38 (peak activation at 30 min) [64]. While NF-κB pathway is delayed p65 phosphorylation (peak at 60 min) [64]. Inhibits insulin sensitivity via ERK-dependent IRS-1 phosphorylation [64]. Adiponectin Signaling Activates AMPK via AdipoR1 and PPAR-α via AdipoR2 respectively [65].

Thyroid-specific modulation

Thyroid hormones (T3) regulate gene expression via nuclear receptor complexes involving

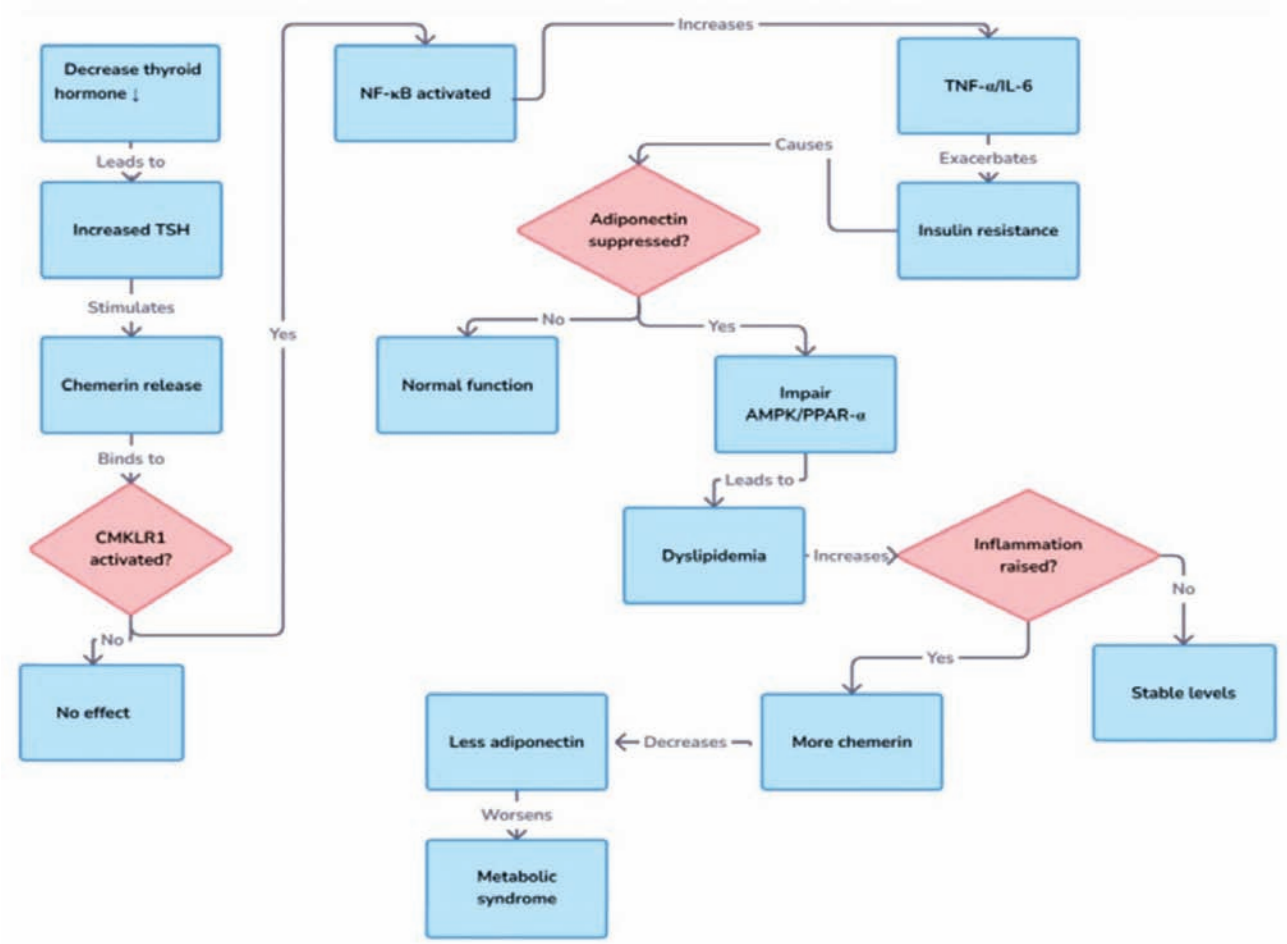

Figure. Chemerin-adiponectin-thyroid axis in hypothyroidism. 1 – ↑ TSH → Chemerin release: TSH stimulates chemerin secretion from adipocytes [36]. 2 – Chemerin → NF-κB → TNF-α/IL-6: CMKLR1 activation drives inflammation and insulin resistance [18, 64, 71]. 3. – Adiponectin ↓ → AMPK/PPAR-α ↓: TNF-α suppresses adiponectin, worsening dyslipidemia [62]. 4 – Feedback Loop: Inflammation amplifies chemerin and suppresses adiponectin, perpetuating metabolic syndrome [71]

coactivators/corepressors, impacting mRNA stability and translation [65]. Emerging evidence suggests that TSH directly modulates chemerin secretion via TSHR signaling in adipocytes, independent of T3/T4 [36]. Elevated TSH in hypothyroidism activates cAMP-PKA signaling, increasing *RARRES2* (chemerin) transcription in adipocytes [36] and exacerbating CMKLR1-mediated inflammation. Conversely, adiponectin resistance in hypothyroidism may arise from ER stress-induced ubiquitination of AdipoR1, impairing AMPK activation despite elevated circulating levels [55].

Clinical implications in hypothyroidism

The reciprocal imbalance as in Figure, (↑ chemerin, ↓ adiponectin) independently predicts metabolic syndrome risk, [62] exacerbating insulin resistance and dyslipidemia [66, 67], inflammation and oxidative stress [68, 69]. This imbalance underlies cardiovascular complications in thyroid disorders [69], highlighting chemerin-adiponectin crosstalk as a therapeutic target [70, 71].

Limitations and future directions

There is a crucial knowledge gap regarding metabolic-endocrine interactions since the molecular processes underlying the relationship between adipokines and thyroid hormones are yet unknown. Targeting thyroid-stimulating hormone (TSH) receptors has been the focus of recent advances in the treatment of hypothyroidism, especially by researchers at Mount Sinai. This has opened up new possibilities for novel therapeutic approaches. Pharmaceutical developments are also looking at tissue-specific

improvement of triiodothyronine (T3) signaling and slow-release liothyronine (LT3) formulations to overcome therapy limitations [72].

Priorities for future study include:

• Noninvasive hormone monitoring devices to enhance personalized nature of treatment.

• Thyroid tissue engineering using advanced regenerative medicine techniques.

• precise diagnostics powered by artificial intelligence to improve illness management and categorization.

• combining biomarker data with patient-reported outcomes to connect clinical and life experiences.

Notably, 10–20% of patients continue to experience persistent symptoms (e.g., fatigue, cognitive dysfunction) despite achieving normalized free thyroxine (T4) and TSH levels, underscoring the need for deeper mechanistic insights and patient-centered therapeutic approaches [72]. Investigations into genetic factors are also underway to identify additional markers for more precise diagnoses and personalized treatment options, *RARRES2* rs17173608 variants correlate with chemerin levels in autoimmune hypothyroidism [73]. In thyroid diagnostics are expected through enhanced imaging technology and point-of-care testing tools that provide quick and accurate results, particularly in resource-limited areas. AI artificial intelligence systems utilizing large datasets can identify subtle patterns in genetic, clinical, and imaging data that traditional analyses may overlook [73]. Additionally, research is ongoing into chemerin as a potential marker for body composition, with a focus on understanding its production by organs like the liver and lungs and its role in metabolic control and balance [64].

Conclusion. The chemerin-adiponectin axis imbalance is central to the metabolic pathophysiology of hypothyroidism, offering a promising target for novel therapies. Hypothyroidism's metabolic and inflammatory consequences are intricately linked to adipokines chemerin and adiponectin, which modulate insulin sensitivity, lipid metabolism, and immune responses. While chemerin promotes inflammation and correlates with thyroid dysfunction, adiponectin's anti-inflammatory role is paradoxically disrupted in hypothyroidism. Their interaction highlights a therapeutic target for mitigating metabolic syndrome in thyroid patients. Persistent symptoms despite normalized hormone levels demand innovative approaches, including precision diagnostics, AI integration, and regenerative medicine. Addressing these gaps requires elucidating molecular mechanisms and prioritizing patient-centered strategies. Advancing research on adipokine-thyroid crosstalk promises to transform hypothyroidism management, improving outcomes for those resistant to conventional therapies.

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ВІСЬ ХЕМЕРИН-АДИПОНЕКТИН ЗА ГІПОТИРЕОЗУ

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Гіпотиреоз спричиняє порушення енергетичного обміну та метаболізму через недостатнє продукування гормонів щитоподібної залози, що призводить до таких патологічних станів, як інсулінорезистентність і дисліпідемія. Останні дослідження продемонстрували вплив адипокінів хемерину та адипонектину на функцію щитоподібної залози. У цьому огляді проаналізовано їхню роль у метаболічних та запальних ускладненнях гіпотиреозу, розглянуто вплив та взаємодію через сигнальні шляхи, а також можливий внесок у патогенез та терапію гіпотиреозу з огляду на важливість інтеграції даних біомаркерів.

Ключові слова: хемерин, адипонектин, гіпотиреоз, гормональні взаємодії, дані біомаркерів.

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