

An overview of the interaction between lipid profile and inflammation in obesity

Farwa Munir^{*1}, Zainab bintay Anis², Nida Islam², Shahzaib Naeem³, Shahrano², Atif Amin Baig¹

¹Faculty of Medicine, Universiti Sultan Zainal Abidin, Medical Campus, 20400 Kuala Terengganu, Terengganu, Malaysia

²University of Management and Technology, Pakistan

³Suriya Azeem Teaching Hospital, Pakistan.

farwamunir96@gmail.com

Abstract

Obesity is becoming a worldwide issue. It is a multifactorial health problem. One of the most highlighted factors is the extra fat storage in the body. There are multiple types of fats, divided into healthy and unhealthy fats. Serum lipid profile is one of the routine tests which measures triglycerides, total cholesterol, and lipoproteins in the body. It helps diagnose if an individual has specific high or low values to determine the link between weight and fat accumulation. There are possibilities that obesity is because of some other reason like genetic mutation or inflammation. The inflammatory mechanism of obesity is linked with the inflammation of adipose tissues leading to tissue hypoxia resulting in HIF-1 α and NF κ B activation. Many interleukins and cytokines are activated in response, causing inflammation in the body. The body's inflammatory response is also found to affect the lipid profile values. Researchers have found that inflammation and lipid profile are separate indicators but are linked, and one affects the other significantly. High saturated fatty acids, VLDLs, dietary fats, n6-fatty acids, and oxLDL increase inflammation in the body leading to obesity. On the other hand, unsaturated fatty acids, n3-fatty acids, and HDL decrease inflammation in the body. Inflammation also affects values, as in hypoxia, HIF-1 α is unregulated. It causes dyslipidemia, resulting in increased triglycerides and cholesterol in the body.

Keywords: Obesity, Lipid profile, HIF 1 α , NF κ B1, Inflammation, Dyslipidemia

Cite as: Farwa Munir, Zainab bintay A, Nida Islam, Shahzaib Naeem, Shahrano, Atif Amin B. (2022). An overview of the interaction between lipid profile and inflammation in obesity. Asian Journal of Medicine and Biomedicine, 6(1), 8-16.

DOI: <https://doi.org/10.37231/ajmb.2022.6.1.460>

Introduction

Fat is considered the most crucial component in our diet. It plays a vital role in the body. It is considered in diet that generally 30% portion should be from fat in a balanced diet. One gram of fat gives nine kilocalories to the body. Animal and plants that be eaten are the primary sources of fat. The fats commencing plant sources are liquid at room temperature and are widely known as oils, whereas those of animal basis are solid at room temperature. Carbon, hydrogen, and oxygen are the structural forms of fat. There are two types of saturated and unsaturated fats; saturated fat has all single bonds, whereas unsaturated fat has double or triple bonds^[1]. Excess fat causes many health problems. Excess fat is gathered around as visceral fat or subcutaneous fat, and when fat is accumulated in blood vessels, it causes coronary artery disease. High BMI and abdominal fat also cause insulin resistance and metabolic syndrome. The waist to hip ratio can calculate fat accumulation in the abdomen region. Studies have concluded that an increased waist to hip ratio increases the chances of CVD and diabetes mellitus two to three folds. To analyze fat content in an individual serum lipid profile, consider one of the general tests. The test measures triglycerides, cholesterol, LDL, HDL, and VLDL found in one's blood. A lipid profile test is also done for obese patients to categorize the level of dyslipidemia. Hypertriglyceridemia and low HDL levels contribute mainly to rising metabolic disorders such as diabetes, obesity, and CVD^[4].

The body's natural response to injury is an organ known as inflammation. Acute inflammation and chronic inflammation are two kinds of inflammation in acute inflammation. Five fundamental signs are categorized into heat, pain, redness, loss of function, and Chronic swelling inflammation is categorized by activating immunological components that are also different from those involved in an acute immune response. There is an essential connection between HIF-1 α and NKFB in the mechanism of inflammation. In case tissue is in a hypoxia state, then HIF-1 α and NKFS are activated, and this activation of H1F-1 α aid the adaptive response to the hypoxia state^[29].

On the other hand, NKFB function activation causes antiapoptotic and inflammatory mechanisms. There are two subunits of HIF, e.g., HIF Alpha and HIF beta, because of their alpha and beta subunits diners. Further, two main isoforms of HIF alpha are HIF-1 α and HIF-2 α , and both act differently on genes in the body. One isoform, HIF1 α , operates on erythropoietin (EPO), while the other isoform HIF2 α reacts to the heme regulating gene (hemopoietin genes). Inflammatory pathways are

activated by fatty acids, cholesterol, and modified lipids^[26]. These agents are directly related to inflammatory pathways within the body. Adipocytes, adipose tissue macrophages (ATMs), stromovascular cell fraction (SVF), natural killer (NK) cells, and T cells all contain adipose tissue. Leptin, vascular endothelial growth factor, and interleukin- 6 (IL-6) are considered upregulated genes, while adiponectin is considered downregulated genes. The inflammatory pathway in adipose tissue during hypoxia in the body is underlain by a reduction in PO₂ and expansion in tissue mass; as evident by recent research and studies, fats are energy-providing molecules and have other functions. Unsaturated fatty acids and omega 3 (n-3) fatty downregulate inflammation, and omega 6 (n-6) fatty acids are pro-inflammatory. Multiple environmental factors affect the body's normal functioning, leading to chronic inflammation. Mainly research is done on the inflammatory pathway and lipid profile studying cardiovascular issues or other diseases. Mainly there is a lack of studies connecting inflammation and dyslipidemia as co-existing factors of obesity.

Fats

Fats are one of the essential components of the human body. From lipid bilayer in the cell membrane to heat insulation and immunity of the body, fats play a significant role. Fats are among the three significant macronutrients consumed in the diet. A balanced diet has at least 30% fat, providing the most significant energy among all macronutrients. One gram of fat provides nine kcals¹. The fat consumed in meals can come from animal or plant sources. The fats from plant sources are liquid at room temperature and are widely known as oils, whereas those of animal origin are solid at room temperature^[2].

As per the structural formation of fats, they are made of carbon, hydrogen, and oxygen. Fats are classified into saturated and unsaturated fats based on carbon and hydrogen bonds. The saturated fats have all single bonds, whereas the unsaturated fats have double or triple bonds^[3]. As fats are hydrophobic, they are absorbed in the body in multiple forms. Sometimes, they form conjugate structures, such as; lipoproteins are divided into high-density, low-density, and very-low-density lipoproteins.

If it accumulates in the human body, extra fat causes many health problems; extra fat can either be gathered around vital organs known as visceral fat, or can gather under the skin known as subcutaneous fat. Fat in blood vessels can be accumulated which can cause coronary artery disease. Abdominal fat and higher BMI had been categorized as a cause of

insulin resistance and many metabolic syndromes^[4]. Multiple factors can cause obesity, and fat accumulation in the body is one of the most highlighted causes. The waist can calculate fat accumulation in the abdomen region to hip ratio. Increased waist circumference than hip circumference tells that fat has been accumulated around that person's viscera. Studies have concluded that an increased waist to hip ratio increase chances of CVD and diabetes mellitus by two to threefolds^[5]. BMI is the ratio of weight to height, and waist to hip ratio measures abdominal fat accumulation, but a serum lipid profile test is performed to study which type of fat is accumulated.

Lipid Profile

A serum lipid profile test is a general test performed to analyze the fat content of an individual's body. The test measures triglycerides, cholesterol, LDL, HDL, and VLDL found in one's blood^[6]. This test was primarily designed to measure cardiovascular risk, but now it is widely used as a parameter of general health^[7]. A blood sample for the respective test is drawn in the fasting state. It is recommended that the individual completely restrict diet and take only water or medication 12 to 14 hours before the test. A significant concern is that triglycerides remain elevated in the blood for several hours after the meal. Lipid profiling in non-fasting states is a long debate as it is hard for the patients to fast for 12 to 14 hours before lipid analysis^[8]. An advanced study that contrasted fasting and non-fasting values suggest that the non-fasting test has no significant impact on prognosis so it can be done at a random time of the day^[6]. Other than fasting or no fasting, there are multiple factors associated with cholesterol and triglyceride level variations in a lipid profile test such as the winter or summer season, supine or upright position, and prolonged tourniquet can alter the results by elevating or decreasing blood cholesterol or triglyceride levels^[9]. Diseased conditions also affect the lipid profile of a patient. Nephrotic syndromes increase LDL and VLDL in the blood whereas, infections and inflammation decrease blood LDL and VLDL values^[10].

Obesity is defined as an irregular and abnormal accumulation of fat in the body that alters normal health status. A lipid profile test is also done for obese patients to categorize the level of dyslipidemia. It is observed that obese individuals have abnormal lipoproteins that can cause cardiovascular diseases. An interventional study concluded that hypertriglyceridemia and low HDL levels contribute significantly to developing metabolic disorders such as diabetes, obesity, and CVD^[11].

Inflammation

For many years, inflammation has been characterized as the activation of immune and non-immune cells as the body's response to tissue injuries and infections. The combination of heat and redness, one of the primary indicators seen, gave rise to the word "inflammation," which is derived from the word "flame." As persons having acute inflammation, tumour (swelling), rubor (redness), dolor (pain), and calor (warmth) are all present^[12]. Inflammation usually results as a protection against infection to reduce its spread, accompanied by resolution, the return of damaged tissues back to their previous structure and functioning status^[13]. Inflammation refers to a broad range of physiological responses to a foreign entity, such as human bacteria, viruses, or dirt contaminants. Inflammations are classified as acute or chronic based on the processes involved in the inflammation and cellular mechanisms involved. According to recent research, inflammation is a crucial component in different chronic illnesses. Chronic diseases/disorders include diabetes, inflammatory bowel disease, eye disorders, cardiovascular disorders, obesity, cancer, autoimmune diseases, and arthritis are just a few of the diseases that people suffer from^[14].

The typical indicators of acute inflammation are calor, rubor, dolor, tumour, and a significant acute phase protein response. The primary objective of acute inflammation is to remove aggravating chemicals, restore tissue integrity, and remove necrotic tissue^[15]. Pattern recognition molecules promote acute inflammation through response to tissue injury and infection. On the other hand, low-grade inflammation is characterized by the absence of classic symptoms of inflammation and a moderate (at most) acute phase protein response. Sentinel cells, which assess dysfunction and tissue stress deviations from the normal homeostatic phase, induce low-grade inflammation^[16].

Chronic inflammation is characterized by activating immunological components that are also different from those involved in an acute immune response. Shifts in the inflammatory process from short- to long-term can compromise immunological resistance and produce severe changes in all organs and tissues, along with normal cellular physiology, raising the risk of non-communicable illnesses^[17].

Another type of inflammation, evident in auto-inflammatory conditions, is caused by genetic dysregulation of suppressing inflammatory reaction elements, resulting in unintentional inflammation.

External stressors are rarely the cause of acute flares of auto-inflammatory disorders. Autoimmune illnesses can be considered cellular damage where the stimulus lasts a long time ^[18].

In the mid-19th century, microscopy was brought into medicine, enabling inflammation to be identified histologically. In the early stages of acute inflammation, poly-morphonuclear leukocytes have been the most prevalent cells; however, cellular infiltrates consist chiefly of lymphocytes and monocytes/macrophages in chronic inflammation. The father of current pathology concluded that "inflammation" would not be a separate entity or rather a collection of inflammatory responses. He distinguished four types of inflammation. It includes exudative, infiltrative, parenchymatous, and proliferative, emphasizing the significance of the inflammatory stimuli ^[19].

Acute inflammation is a quick process that can last a few minutes to a few days. Its main characteristics are the leakage of plasma proteins or fluid and the transfer of leukocytes into the extravascular space. Chemical substances released by cells or plasma mediate these cellular and vascular processes involved in such fundamental pathological changes of inflammation as swollen, warmth, pain, redness, and impaired function. Although an inflammatory process can occur in response to any harmful stimuli, the reactivity of vascularized connective tissue is unique to this process. The acute inflammatory reaction has three primary steps: increased blood flow to the inflamed area, vasodilation and increased vascular permeability with plasma leakage from the microcirculation, and phagocytic leukocyte migration to the surrounding tissue ^[20].

Throughout the inflammatory process, sensors, mediators, and target tissues differ depending on the type of infection (bacteria, virus, parasite) ^[21]. Toll-like receptors (TLRs), which are expressed in tissue-resident macrophages and chemokine CXC motif ligand 8, chemokines (e.g., chemokine C-C motif ligand two and stimulate the production of inflammatory cytokines (e.g., TNF-, IL-6 and IL-1) and PGE2, for example, are used to recognize bacterial pathogens ^[15].

Such inflammatory products subsequently respond to target tissues such as local blood arteries, causing vasodilation, plasma leakage into the infectious area, and neutrophil extravasation (acute inflammation). These pathogens are then found and eliminated by neutrophils, mast cells, and tissue-resident macrophages—plasma components aid this process, which is started with antibodies and their components. The classic complement pathway

begins with C-reactive protein, natural antibodies, or serum amyloid protein generating antibodies ^[21]. Microbes, in essence, activate the traditional complement pathway. The elimination of infectious agents is achieved by a successful acute inflammatory response, which is proceeded by a repair and resolution phase driven by tissue-resident macrophages ^[15]. The transition from inflammation to resolution requires a shift in lipid markers from pro-inflammatory prostaglandins to anti-inflammatory lipoxins. Lipoxins reduce the involvement of neutrophils in this stage and, on the other hand, activate the role of monocytes, which remove dead cells and initiate tissue reconstruction. In contrast to TGF- β and other growth factors produced by protectins, resolvins and macrophages, which are another type of lipid marker, play an essential role in the inflammation resolution and the basis of tissue repairing ^[15].

A complicated biochemical process comprising numerous genes, peptides, genomic/ genetic polymorphisms, and many other substances is involved in acute and chronic inflammation ^[22].

An unbalance in natural antioxidants causes free radical generation from numerous environmental and biological sources, which results in several inflammatory illnesses ^[22]. Mast cells and Leukocytes are located in the damaged areas during an inflammatory response, causing a "respiratory burst" as just a response of increased oxygen absorption, which increases the generation and release of reactive oxygen species (ROS) just at the affected site ^[22]. On the other hand, inflammatory cells produce more soluble inflammatory mediators such cytokines, arachidonic acid, and chemokines that interact via active inflammatory cells near the infected site and produce additional reactive species. The oxidative/ inflammatory environment sets in motion an unfavorable cycle that can affect healthy stromal cells and adjacent epithelial cells, potentially leading to carcinogenesis over time ^[23].

Inflammatory mechanism

Inflammation is defined as the body's natural response to injury in any organ. It initiates the body's healing process by removing harmful agents and stimuli from the body ^[24]. However, diligent and unresolved inflammation in the body tends to be progressive for various diseases like type 2 diabetes or any neurodegenerative disease. The progressiveness of disease in metabolic tissues such as adipose, liver, pancreas, muscle, and brain have been reported ^[25]. There is such an example of obesity, which exhibits chronic inflammation in the body in response to increased immune cell infiltrates in the adipose tissue ^[26]. Another study has

supported increased HIF- α mRNA and protein in the body during obesity [26]. Adipose tissue during obesity secretes a variety of chemotactic factors that induce cell infiltrates into it. These could be macrophages, monocytes, or related immune cells. Immune cells, i.e. monocytes, migrate into the adipocytes, where they infiltrate the tissue through adhesion to endothelial cells. While on the other hand, the macrophages' function is to alternate inflammation through interaction with parenchymal adipocytes. When the saturated fatty acids are released from adipocytes during lipolysis, this process is instigated by tumor necrosis factor-alpha (TNF α) derived from macrophages. Moreover, the induction of saturated fatty acids results in inflammatory changes in macrophages. These cycles via TNF-R and TNF α receptors involving adipocytes and macrophages enhance adipose tissue inflammation [27].

In inflammatory mechanisms, the interaction between HIF-1 α and NF κ B is also significant.

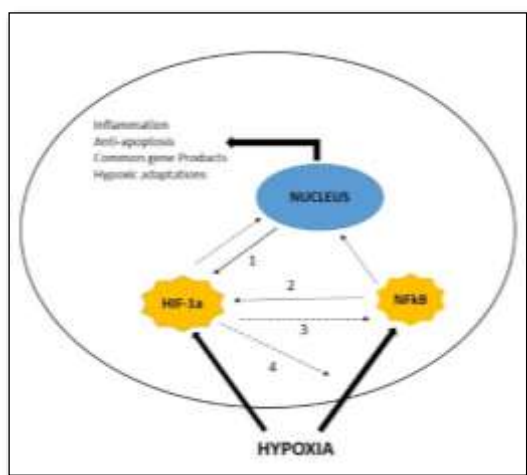


Figure 1. Interaction of HIF-1 α and NF κ B in the hypoxic state [28]

As shown in figure 1, if tissue is in a hypoxic state, it activates HIF-1 α and NF κ B. Activation of HIF-1 α helps the adaptive response to a hypoxic state, whereas activation of NF- κ B functions in the anti-apoptotic and inflammatory mechanism. In this interaction, basal levels of HIF-1 gene expression and upregulation of HIF-1 transcription occur by an NF- κ B-dependent regulatory mechanism (1 and 2). On the contrary, hypoxic induction of NF- κ B transcription is dependent on the presence of HIF-1 α [3]. HIF-1 α is directly linked with the regulating apoptosis mechanism through the modulation of NF- κ B signaling [4].

Hypoxia-inducible factor

Hypoxia-Inducible Factor (HIF) is a transcription factor that binds to specific nuclear cofactors and transactivates several of the genes, triggering a variety of adaptive responses to low oxygen levels in the body. HIF has two subunits, namely HIF α and HIF β , due to their alpha and beta subunit dimers. HIF- α exists in two main isoforms, HIF-1 α and HIF-2 α . Both of these isoforms, HIF-1 α and HIF-2 α , differently act on different genes in the body. These isoforms work in contrast to each other as they overlap in function with a tumor microenvironment in the body [31]. One of the isoforms, HIF1 α , operates on erythropoietin (EPO) while the other isoform HIF2 α reacts to the heme regulating gene (hemopoietin genes). When there is increased HIF signaling in the body, it can lead to inflammation and progressive tumorigenesis [32]. As HIF2 α plays a primary role in inflammation, activation of this inducible factor has been noted. It can lead to increased organ inflammation, as in the case of liver hypoxia. In liver hypoxia, activation is exhibited by steatosis and inflammation [29].

Hypoxia in adipose tissues

Adipose tissue contains adipocytes, stromovascular cell fraction (SVF), adipose tissue macrophages (ATMs), T cells, and natural killer (NK) cells. The stromovascular cell fraction plays a significant role in the inflammatory mechanism in adipose tissue [30]. In human adipocytes, the functionality of the cells in response to hypoxia changes the expression of thousands of genes. Some upregulated genes are leptin, vascular endothelial growth factor, and interleukin-6 (IL-6), while downregulated genes include adiponectin. Rather than just inflammatory genes, hypoxia also tends to inhibit the expression of genes that regulate the mechanism of oxidative metabolism in the body. However, it regulates the expression of genes that stimulate glycolysis. Studies have shown that hypoxia is related to a fall in insulin sensitivity as it stimulates the release of lactate while increasing the uptake of glucose by adipocytes in the body. Hypoxia relates to decreased insulin sensitivity and encourages the reaction of preadipocytes and macrophages [31]. The inflammatory pathway in adipose tissue during hypoxia in the body is underlain by a reduction in PO₂ and expansion in tissue mass, as evident by recent research and studies [32]. It has also been reported that hypoxia-induced inflammation in adipose and other tissues implicates activation of endoplasmic reticulum stress (ERS) and mitogen-

activated protein kinase (MAPK) signaling pathways. These pathways stimulate the role of HIF α in Inflammation in adipose tissue [34]. Chronic adipose tissue hypoxia has been proposed as one of the pathology mechanisms generating adipocyte malfunction. Hypoxia can cause oxidative stress in adipocytes in humans and animals and decrease the synthesis of beneficial adipokines like adiponectin. On the other hand, time-dose responses to hypoxia mitigate the consequences of hypoxic stress [33].

Impact on lipid profile

Inflammatory pathways are activated by fatty acids, cholesterol, and modified lipids. These agents are directly related to inflammatory pathways within the body. Furthermore, modified lipids and lipoproteins also regulate the activity of leukocytes [34]. Similarly, cytokines (pro-inflammatory signaling) also directly affect lipid profile. Whether diet-induced obesity or genetic-induced obesity in humans, oxidative stress and hypoxia are prevalent in adipose tissues. Whenever there is altered functionality of adipocytes or metabolic dysfunctionality in the body, hypoxia and oxidative stress are said to be related [33]. Lipoprotein aggregation, endothelial injury, leukocyte

recruitment, foam cell development, and inflammation are all caused by modified lipoproteins such as oxidized low-density lipoprotein (ox-LDL) and LDL interacting with proteoglycans of the extracellular matrix in the intima of blood vessels [35]. Lipoproteins and lipids such as chylomicrons, sphingolipids, ceramides, very-low-density lipoproteins (VLDL), cholesterol, apolipoproteins, including ApoB (apolipoprotein B), intermediate-density lipoproteins (IDL), and low-density lipoproteins (LDL) are all involved in lipid transit [36]. The synthesis of oxidized phospholipids (oxpls) is caused by oxidative lipoprotein modification by endothelial oxidizing agents, proteases, and lipases, which causes leukocyte recruitment, activation, LDL aggregation, and cholesterol crystal formation, and inflammation. Chronic intermittent hypoxia increased total cholesterol and triglyceride levels significantly. The levels of fasting triglycerides were approximately doubled, and the increases mainly were localized [37]. Another study shows that dyslipidemia was caused by transgenic overexpression of HIF-1 in adipose tissue [38]. Moreover, under O₂ deprivation, constitutive activation of growth-promoting pathways leads to a reliance on unsaturated fatty acids for life [39].

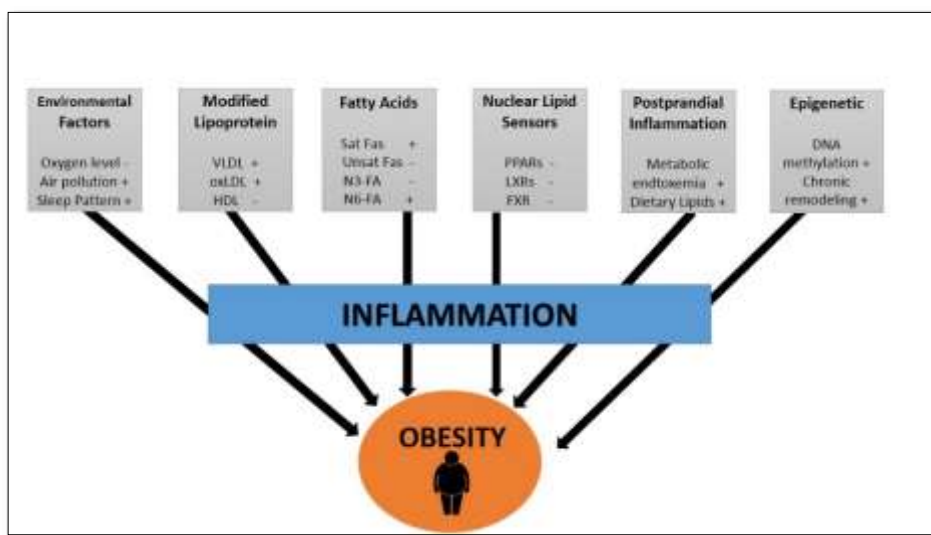


Figure 2. An overview of the impact of fats and epigenetic factors on inflammation leading to obesity [34],[40]

It has been summarized in figure 2 how the varying lipid values affect the inflammatory pathway. Sign + shows that the factor increases inflammation, whereas minus sign – shows that the factor has a negative association with inflammation and obesity.

Fats are not only energy-providing molecules but have other functions too. Saturated fatty acids are thought to be linked with inflammatory pathways such as that it increases intracellular levels of *NFκB* by TLR (a tool like a receptor) ^[41]. The inflammatory pathway can also be activated when fatty acids bind to G protein-coupled receptors in the immune response. Omega 6 (n-6) fatty acids are pro-inflammatory because it is the precursor of arachidonic acid, prostaglandins, and leukotrienes synthesis. The chain length and degree of saturation have a more significant role in the inflammatory pathway. Unsaturated fatty acids and omega 3 (n-3) fatty downregulate inflammation ^[42].

Dietary cholesterol causes less chronic systemic inflammation by elevating serum Alkaloids and CRP proteins ^[43]. A study conducted in hyper-lipidemic mice showed that high circulating VLDLs affect the liver and induce hepatic inflammation. Other than that, circulating lipoproteins cause vascular inflammation, and in such a way, it causes inflammatory obesity ^[44].

Environmental and Epigenetic Factors

Multiple environmental factors affect the body's normal functioning, leading to chronic inflammation. As summarized in figure 2, the oxygen level, air pollution, and sleeping pattern are significant contributors to inflammation that can further be linked with metabolic disorders such as obesity ^[40]. It is thought that prolonged exposure to polluted air results in overexpression of TNF- α , which reduces TNF- α gene methylation, especially in women resulting in inflammation. PM2.5 exposure leads to changes in the TLR2 gene, causing acute inflammation ^[45]. A study conducted in Italy concluded that the altered pattern of DNA methylation causes oxidative and inflammatory pathways, and air pollution plays a significant role ^[46].

A clinical study was conducted on mice experimenting with the effect of sleep deprivation. Results showed that the histone activity was reduced, and oxidative stress and inflammation were found in the hippocampus ^[47]. Another case study narrates that obstructive sleep apnea causes epigenetic modification, a prominent contributor to an inflammatory phenotype ^[48].

Mainly research is done on the inflammatory pathway and lipid profile studying cardiovascular issues or other diseases. Mainly there is a lack of studies connecting inflammation and dyslipidemia as co-existing factors of obesity. Studies should be done further to keep the obese individuals and normal understudy and link the role of *HIF-1 α* and *NFκB* with varying values of fatty acids and cases of obesity.

Objective

The purpose of this review article is to find the association between lipid profile of an individual with inflammation. As well as this article is intended to find gaps in current literature so help future researchers.

Conclusion

In human adipocytes, hypoxia causes overexpression of leptin, vascular endothelial growth factor, and interleukin-6 (IL-6) genes while downregulating adiponectin genes. Hypoxia, rather than only inflammatory genes, suppresses the expression of genes that control the body's oxidative metabolism system. Hypoxia-induced inflammation in adipose tissues is linked to the activation of signaling pathways that promote HIF α participation in inflammation. Further research has provided evidence on the impact of hypoxia-induced inflammation on lipid profile as modified lipoproteins such as oxidized low-density lipoprotein (ox-LDL) and LDL interact with proteoglycans of the extracellular matrix in the vascular endothelium of blood arteries, causing lipoprotein aggregation, endothelial damage, leukocyte recruitment, foam cell production, and inflammation. Several factors i.e. environmental factors (air pollution, sleep pattern), lipoproteins (VLDL, oxLDL), postprandial inflammatory factors (dietary lipids, metabolic endoxemia), and epigenetic factors (DNA methylation, chronic remodeling) induces an increase in inflammation while fatty acids (unsaturated fatty acids, omega-3 fatty acid) along with nuclear lipid sensors (PPARs, LXRs, FXR) dissuade inflammation process in human adipocytes.

However, further studies are necessary to better understand the function, regulation, and biological functions of cytokines in direct relation to obesity. This study domain might be valuable for establishing obesity-related food and health objectives, as well as dietary recommendations for individuals and demographic groups, and raising knowledge about several unnoticed obesity risk factors associated with dietary components.

References

1. Bockisch M. *Fats and oils handbook (Nahrungsfette und Öle)*. Elsevier; 2015.
2. Gunstone F. *The chemistry of oils and fats: sources, composition, properties, and uses*. John Wiley & Sons; 2009.
3. Vardon DR, Sharma BK, Jaramillo H, et al. Hydrothermal catalytic processing of saturated and unsaturated fatty acids to hydrocarbons with glycerol for in situ hydrogen production. *Green Chemistry*. 2014;16(3):1507-1520.
4. Smith U. Abdominal obesity: a marker of ectopic fat accumulation. *The Journal of clinical investigation*. 2015;125(5):1790-1792.
5. Hardy OT, Czech MP, Corvera S. What causes the insulin resistance underlying obesity? *Current opinion in endocrinology, diabetes, and obesity*. 2012;19(2):81.
6. Nigam P. Serum lipid profile: fasting or non-fasting? *Indian journal of clinical biochemistry*. 2011;26(1):96-97.
7. Campos H, Khoo C, Sacks FM. Diurnal and acute patterns of postprandial apolipoprotein B-48 in VLDL, IDL, and LDL from normolipidemic humans. *Atherosclerosis*. 2005;181(2):345-351.
8. Narayanan S. Pre and post analytical errors in lipid determination. *Indian Journal of Clinical Biochemistry*. 1996;11(1):12-16.
9. Cooper GR, Myers GL, Smith SJ, Schlant RC. Blood lipid measurements: variations and practical utility. *Jama*. 1992;267(12):1652-1660.
10. Alvarez C, Ramos A. Lipids, lipoproteins, and apoproteins in serum during infection. *Clinical chemistry*. 1986;32(1):142-145.
11. Nordestgaard BG. A test in context: lipid profile, fasting versus nonfasting. *Journal of the American College of Cardiology*. 2017;70(13):1637-1646.
12. Shahid SU, Sarwar S. The abnormal lipid profile in obesity and coronary heart disease (CHD) in Pakistani subjects. *Lipids in health and disease*. 2020;19(1):1-7.
13. Rasheed H, McKinney C, Stamp LK, et al. The toll-like receptor 4 (TLR4) variant rs2149356 and risk of gout in European and Polynesian sample sets. *PloS one*. 2016;11(1):e0147939.
14. Antonelli M, Kushner I. It's time to redefine inflammation. *The FASEB Journal*. 2017;31(5):1787-1791.
15. Arulselvan P, Fard MT, Tan WS, et al. Role of antioxidants and natural products in inflammation. *Oxidative medicine and cellular longevity*. 2016;2016.
16. Kotas ME, Medzhitov R. Homeostasis, inflammation, and disease susceptibility. *Cell*. 2015;160(5):816-827.
17. Straub RH. The brain and immune system prompt energy shortage in chronic inflammation and ageing. *Nature Reviews Rheumatology*. 2017;13(12):743-751.
18. Nathan C, Ding A. Nonresolving inflammation. *Cell*. 2010;140(6):871-882.
19. Heidland A, Klassen A, Rutkowski P, Bahner U. The contribution of Rudolf Virchow to the concept of inflammation: what is still of importance? *Journal of nephrology*. 2006;19:S102-9.
20. Kobayashi H, Higashiura Y, Shigetomi H, Kajihara H. Pathogenesis of endometriosis: the role of initial infection and subsequent sterile inflammation. *Molecular medicine reports*. 2014;9(1):9-15.
21. Medzhitov R. Inflammation 2010: new adventures of an old flame. *Cell*. 2010;140(6):771-776.
22. Kumar D. Molecular biology of acute and chronic inflammation. *Clinical Molecular Medicine*. Elsevier; 2020:389-402.
23. Tasneem S, Liu B, Li B, Choudhary MI, Wang W. Molecular pharmacology of inflammation: Medicinal plants as anti-inflammatory agents. *Pharmacological research*. 2019;139:126-140.
24. Chen L, Deng H, Cui H, et al. Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget*. 2018;9(6):7204.
25. Cildir G, Akincilar SC, Tergaonkar V. Chronic adipose tissue inflammation: all immune cells on the stage. *Trends in molecular medicine*. 2013;19(8):487-500.
26. Sun S, Ji Y, Kersten S, Qi L. Mechanisms of inflammatory responses in obese adipose tissue. *Annual review of nutrition*. 2012;32:261-286.
27. Itoh M, Suganami T, Hachiya R, Ogawa Y. Adipose tissue remodeling as homeostatic inflammation. *International journal of inflammation*. 2011;2011.
28. Garvey J, Taylor C, McNicholas W. Cardiovascular disease in obstructive sleep apnoea syndrome: the role of intermittent hypoxia and inflammation. *European Respiratory Journal*. 2009;33(5):1195-1205.
29. Qu A, Taylor M, Xue X, et al. Hypoxia-inducible transcription factor 2 α promotes steatohepatitis through augmenting lipid accumulation, inflammation, and fibrosis. *Hepatology*. 2011;54(2):472-483.
30. O'rourke R, White A, Metcalf M, et al. Hypoxia-induced inflammatory cytokine secretion in human adipose tissue stromovascular cells. *Diabetologia*. 2011;54(6):1480-1490.
31. Trayhurn P. Hypoxia and adipocyte physiology: implications for adipose tissue dysfunction in obesity. *Annual review of nutrition*. 2014;34:207-236.
32. Trayhurn P. Hypoxia and adipose tissue function and dysfunction in obesity. *Physiological reviews*. 2013;93(1):1-21.
33. Netzer N, Gatterer H, Faulhaber M, Bartscher M, Pramsöhler S, Pesta D. Hypoxia, oxidative

- stress and fat. *Biomolecules*. 2015;5(2):1143-1150.
34. van Diepen JA, Berbée JF, Havekes LM, Rensen PC. Interactions between inflammation and lipid metabolism: relevance for efficacy of anti-inflammatory drugs in the treatment of atherosclerosis. *Atherosclerosis*. 2013;228(2):306-315.
 35. Wong BW, Meredith A, Lin D, McManus BM. The biological role of inflammation in atherosclerosis. *Canadian Journal of Cardiology*. 2012;28(6):631-641.
 36. Buckley ML, Ramji DP. The influence of dysfunctional signaling and lipid homeostasis in mediating the inflammatory responses during atherosclerosis. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*. 2015;1852(7):1498-1510.
 37. Drager LF, Li J, Shin M-K, et al. Intermittent hypoxia inhibits clearance of triglyceride-rich lipoproteins and inactivates adipose lipoprotein lipase in a mouse model of sleep apnoea. *European heart journal*. 2012;33(6):783-790.
 38. Hauner H. 14 Obesity and Diabetes.
 39. Ackerman D, Simon MC. Hypoxia, lipids, and cancer: surviving the harsh tumor microenvironment. *Trends in cell biology*. 2014;24(8):472-478.
 40. Ramos-Lopez O, Milagro FI, Riezu-Boj JI, Martinez JA. Epigenetic signatures underlying inflammation: An interplay of nutrition, physical activity, metabolic diseases, and environmental factors for personalized nutrition. *Inflammation Research*. 2021;70(1):29-49.
 41. Shi H, Kokoeva MV, Inouye K, Tzameli I, Yin H, Flier JS. TLR4 links innate immunity and fatty acid-induced insulin resistance. *The Journal of clinical investigation*. 2006;116(11):3015-3025.
 42. Margioris AN. Fatty acids and postprandial inflammation. *Current opinion in clinical nutrition & metabolic care*. 2009;12(2):129-137.
 43. Tannock LR, O'Brien KD, Knopp RH, et al. Cholesterol feeding increases C-reactive protein and serum amyloid A levels in lean insulin-sensitive subjects. *Circulation*. 2005;111(23):3058-3062.
 44. Bieghs V, Wouters K, Van Gorp PJ, et al. Role of scavenger receptor A and CD36 in diet-induced nonalcoholic steatohepatitis in hyperlipidemic mice. *Gastroenterology*. 2010;138(7):2477-2486. e3.
 45. Zhong J, Colicino E, Lin X, et al. Cardiac autonomic dysfunction: particulate air pollution effects are modulated by epigenetic immunoregulation of toll-like receptor 2 and dietary flavonoid intake. *Journal of the American Heart Association*. 2015;4(1):e001423.
 46. Fiorito G, Vlaanderen J, Polidoro S, et al. Oxidative stress and inflammation mediate the effect of air pollution on cardio-and cerebrovascular disease: a prospective study in nonsmokers. *Environmental and molecular mutagenesis*. 2018;59(3):234-246.
 47. Andrabi M, Andrabi MM, Kunjinni R, et al. Lithium acts to modulate abnormalities at behavioral, cellular, and molecular levels in sleep deprivation-induced mania-like behavior. *Bipolar disorders*. 2020;22(3):266-280.
 48. Kim J, Bhattacharjee R, Khalyfa A, et al. DNA methylation in inflammatory genes among children with obstructive sleep apnea. *American journal of respiratory and critical care medicine*. 2012;185(3):330-338.