



## **Relationship between Obesity-Related Hypertension: A Narrative Review**

**Behdad Dehbandi<sup>1</sup>, Hafiz Fahad Ullah Saeed<sup>2</sup>, Muhammad Furqan<sup>2</sup>,  
Ubaid Khan<sup>2\*</sup>, Muhammad Farhan Akhtar<sup>2</sup>  
and Hafiz Muhammad Waqas Siddque<sup>2</sup>**

<sup>1</sup>*Abiproddmedical Center, Latvia.*

<sup>2</sup>*Department of Medicine, King Edward Medical University Lahore, Pakistan.*

### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JAMMR/2021/v33i2131150

#### Editor(s):

(1) Ashish Anand, GV Montgomery Veteran Affairs Medical Center, University of Mississippi Medical Center, Jackson and William Carey School of Osteopathic Medicine, USA.

#### Reviewers:

(1) Premkumar Daivasikamani, AIMST University, MALAYSIA.

(2) Edy Noverly, Mohammad Hoesin General Hospital and Universitas Sriwijaya, Indonesia.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/76236>

**Received 24 August 2021**

**Accepted 28 October 2021**

**Published 06 November 2021**

**Review Article**

### **ABSTRACT**

The main cause of obesity is an imbalance in consumption and caloric intake. Obesity is described as an excessive and abnormal accumulation of more than 20 percent of body fat in an individual's average body weight. The average body weight refers to an "individual's maximum healthy weight," which is determined primarily by their height, age, and muscular growth. Obesity, however, is diagnosed by calculating the BMI which is a measure of individual's body weight and height. Additionally, according to the National Institutes of Health, a person with a maximum limit of BMI of 30 kg/m<sup>2</sup> is declared obese. Moreover, despite World Health Organization concerns, the prevalence of obesity is increasing among children and adults worldwide. Excessive overweight continues to be the most underestimated public health problems on a global scale, including the fact that obesity is linked with an increased risk of sickness, disability, and death. Cardiovascular disorders, especially diabetes and hypertension have become a leading cause of death globally and these are the primary illnesses linked with obesity. However, the mechanisms behind obesity-related hypertension and other metabolic disorders remain little understood. In this present review, we discussed the correlation between cardiovascular disease and obesity, focusing on the biological processes underlying the relationship between hypertension and obesity.

\*Corresponding author: E-mail: [ubaidkhanafri@yahoo.com](mailto:ubaidkhanafri@yahoo.com);

*Keywords: Obesity; hypertension; mortality.*

## 1. INTRODUCTION

Obesity has been defined “as a weight that is 20% greater than the average weight,” that correlates to the mortality rate for individuals of a particular age, height, and gender [1]. Obesity guidelines and recommendations have introduced the BMI scale, which is measured by “multiplying an individual's weight by 703 and dividing by twice their height in inches”. Currently, BMI is now used to diagnose the level of obesity or overweight [2-13]. Therefore, an individual with a BMI of “25.9–29 is considered an overweight person,” while a person BMI of “greater than 30 is considered to be obese” [14]. In 2005, World Health Organization declared 1.6 billion people over the age of 15 an overweight individual [15].

Moreover, approximately 20 million children of less than five years old and 400 million adults were classified as overweight. WHO defined 'globesity' as a “global phenomenon of obesity that is now on the rise.” The condition is crucial because obesity-related diseases are becoming common, especially cardiovascular diseases, which are currently the leading cause of mortality worldwide [16].

Studies showed that obesity can cause several severe health complications, including type II diabetes mellitus, hyperlipidemia, hypertension, an elevated risk of cardiovascular disease, unexplained heart failure, miscarriage, and a rising prevalence of bowel, prostate, breast, and endometrial cancer [17]. Although the connection between hypertension and obesity among children and adults is well-known, the process by which obesity induces hypertension is still being investigated [18].

Sodium retention with an upsurge in renal reabsorption, the sympathetic nervous system activation, renin-angiotensin system and the amount of intravascular and intra-abdominal fat, are all thought to play a role in the pathogenesis of obesity-related hypertension. Obesity-related hypertension is a medical condition in which blood pressure is consistently at or over 140/90 mmHg far from the normal level which is 120/90 mmHg [19].

The current study investigated the processes by which obesity may trigger elevated arterial blood pressure, as well as how obesity management

may be used as a preventive strategy to treat hypertension.

## 2. OBESITY AND HYPERTENSION

Obesity is associated with multiple etiologies which include ethnicity, socioeconomic wellbeing, and lifestyle [20]. Obesity results when caloric intake is more than its expenditure [21]. The exact cause of obesity is unknown, but it arises from the combination of several factors such as the genetic makeup of an individual which regulates appetite and body metabolism [22]. Excessive weight only occurs when there is an excess of calories available to the tissues.

The total amount of fat in one's diet may have a large effect on weight than the total number of calories. Fat calories are instantly stored in adipocytes, which leads to obesity as their number increases by multiplication [23]. Fatty diets also raise cholesterol levels in the blood [24].

Carbohydrates and alcohol raise blood triglycerides levels, which is another etiological factor for atherosclerosis. Fat accumulation in vessels in form of plaques leads to narrowing and obstruction of vessel wall which leads to organ ischemia and eventually death [25]. High fat diet raises norepinephrine in the blood leading to activation of alpha and beta receptors which ultimately leads to hypertension [26]. Fat cells, particularly of the abdomen, release a large amount of signaling factors that ultimately affect end organs, for example, leading to glomerulopathy [27].

Free-fatty acids have a direct action on ion channels of smooth muscles' cell membrane, and activate phosphorylation of calcium-independent isoenzyme of Protein Kinase C. Pro-inflammatory cytokines reduce the formation of nitric oxide by endothelial cells which leads to increased vascular resistance and hence to hypertension (Bolsani-Lopse et al., 2015).

Angiotensinogen derived from adipocytes leads to the formation of Ang I and Ang II which results in increased vascular resistance (due to direct action of Ang II on vessels), and ultimately it leads to sodium and water retention through aldosterone production by the adrenal cortex [28]. Hypertensive patients also have increased

sodium in urine due to pressure natriuresis effect owing to fluid overload [29].

Free- fatty acids also increase alpha-adrenergic sensitivity leading to vasoconstriction. Another mechanism of hypertension also includes inhibitory action of free fatty acids on Sodium Potassium ATPase pumps, which raises resting smooth muscle tone and overall resistance [28].

### **3. MECHANISM OF PATHOPHYSIOLOGY OF HTN AND OBESITY**

Various factors play role in development of hypertension which include genetic, dietary, and environmental factors. Changes in function of adipocytes in obese people lead to SANS and RAAS dysfunction leading to alterations in the body handling of fluids. Kidneys also respond differently in obesity by increasing production of angiotensin II. Studies also suggest that uric acid may also influence hypertension by deteriorating functions of blood vessels and kidneys (Fig. 1). DNA methylation and histone modifications are some of the epigenetic changes which play role in development of hypertension in obese people [30] (Table 1).

#### **3.1 Vascular Injury**

One of the earliest manifestations in obesity related vascular dysfunction is arterial stiffness and endothelial injury. Arterial stiffness results from alterations in extracellular matrix and dysfunctions of smooth muscles in blood vessels. Other studies also suggest that vascular stiffness due to endothelial injury is highly associated with insulin resistance. In hypertensive rats, altered vascular response to insulin is observed [31]. Due to insulin resistance, there are changes in signaling mechanisms in blood vessels which leads to decreased production of NO, so the relaxation is impaired. Further, there is enhancement of ET-1 pathway which leads to vascular contraction. In obese people, there is alterations in the secretions of signaling molecules and hormones such as leptin, adiponectin, tumor necrosis factor and IL-6 which contribute to hypertension. Adiponectin has main role in insulin resistance [37].

#### **3.2 Renal Injury**

Renal dysfunction also causes hypertension in obese individuals. Due to increase in tubular reabsorption of sodium, the blood pressure curve is shifted to the higher levels. Also there is

hyperinsulinemia and abnormal Renin-Angiotensin- Aldosterone System and sympathetic nervous system activation which leads to enhanced sodium reabsorption. Proinflammatory immune cells and increased oxidative stress causes tubulointerstitial inflammation which contributes to chronic renal disease [32].

#### **3.3 SNS Over Activation**

In obese individuals there is aberrant activation of sympathetic nervous system in various organs including muscles, heart and kidneys and baroreceptor dysfunction leading to hypertension. Dysfunctional adipocytes cause increased leptin secretion which also enhances sympathetic nervous system activity [19]. Changes in STAT3 (signal transducer and activator of transcription) signaling in arcuate nucleus may also lead to obesity. Obesity, obstructive sleep apnea (OSA) and hypertension are closely related to each other. In OSA, there is hyperactivity of sympathetic nervous system which leads to increased vascular resistance and is a major factor leading to hypertension in obese individuals. Treatment with continuous positive airway pressure (CPAP) is the mainstay therapy in obese individuals with OSA [31].

#### **3.4 RAAS**

Ang II directly regulates endothelial and renal function. There is also modulation in ET-1 signaling. Increased aldosterone levels are also present in obese individuals which is responsible for hypertension. Aldosterone enhances activity of NADPH which increases oxidative stress in body and decreases Nitrous Oxide (NO) pool. Spironolactone can be used to decrease blood pressure in these individuals owing to its mechanism being aldosterone antagonist, but insulin resistance does not change (Kang et al., 2013).

#### **3.5 Immune and Inflammatory Mechanisms**

Studies suggest that there is imbalance and aberration in adaptive and innate immune system in obese individuals which directly affects various organs of body including kidney, CNS, and perivascular tissue contributing of hypertension. Studies indicated that pro-inflammatory cytokines such as tumor necrosis factor (TNF) and IL-6, released by macrophages leads to insulin resistance by changing activity of IRS and

contribute to impaired insulin signaling. Evidences suggest that T-cells dysfunction and dysregulation is involves in pro-inflammatory responses which are involves in hypertension [33]. These responses cause infiltration of macrophages into vascular and adipose tissues. On the other hand, T regulatory cells decrease

inflammation and have anti-inflammatory effect by promoting formation of M2 macrophages. Furthermore, in patients with Type 2 DM, imbalance in T-cells ratio (i-e, decrease levels of T regulatory cells and increased levels of TH17 cells) adds to the vascular dysfunction leading to HTN [38].

**Table 1. Factors affecting the pathophysiology of obesity and HTN**

<b>Sr.No.</b>	<b>Factor</b>	<b>Reasons</b>	<b>Affect</b>	<b>References</b>
1.	<b>Vascular Injury</b>	Alterations in extracellular matrix, Dysfunctions of smooth muscles, Alterations in the secretions of signaling molecules and hormones (leptin, adiponectin, tumor necrosis factor and IL-6)	Insulin Resistance, Decreased production of NO, Hypertension	[31]
2.	<b>Renal Injury</b>	Hyperinsulinemia, Abnormal Renin- Angiotensin- Aldosterone System and sympathetic nervous system activation, Proinflammatory immune cells and increased oxidative stress	Increase in tubular reabsorption of sodium, Tubulointerstitial inflammation, Chronic renal diseases	[32]
3.	<b>SNS Over activation</b>	Aberrant activation of sympathetic nervous system, Increased leptin secretion, Changes in STAT3	Enhanced sympathetic nervous system activity, Obesity, Obstructive sleep apnea(OSA) and Hypertension	[31]
4.	<b>RAAS</b>	Increased aldosterone levels, Enhanced activity of NADPH	Increases oxidative stress, Decreases Nitrous Oxide (NO) Hypertension	(Kang et al., 2013)
5.	<b>Immune and Inflammatory Factor</b>	Release of pro-inflammatory cytokines (TNF, IL-6), T-cells dysfunction and dysregulation	Vascular dysfunction leading to HTN, Insulin resistance, Pro-inflammatory responses	[33]
6.	<b>Incretins and DDP</b>	DPP-4 increased production in T cells and kidneys, Decrease accumulation of M1 macrophages and increase amount of M2 macrophages in fat tissue/vascular atherosclerotic lesions.	Hypertension	[34]
7.	<b>Estrogen</b>	Decreased estrogen level, Increased BMI	Hypertension	[35]
8.	<b>Nutritional Factors</b>	Diets rich in fructose contributing to more lipid production, Increased lipid and cholesterol in blood, High salt intake	Hypertension	[36]
9.	<b>Intestinal microbes</b>	Changes in gut flora leads to changes in IR, T2DM, and HTN	Serious metabolic disorders	[36]

### 3.6 Incretins and DPP

Human gut produces some hormones including “Glucagon like peptide (GLP-1) and Glucose dependent insulintropic peptide” which enhance glucose mediated release of insulin and contribute to glucose-insulin homeostasis. DPP-4 is largely produced in T cells and kidneys, and can decrease accumulation of M1 macrophages and increase amount of M2 macrophages in fat tissues or vascular atherosclerotic lesions. So, studies suggest that inhibition of DPP-4 can be used to treat immune related hypertension on obese individuals [34].

### 3.7 Estrogen

In premenopausal women, estrogens decrease risk of cardiovascular diseases but this effect is lost in premenopausal women who have DM and BMI > 25. Estrogen also modulates Ang II signaling by decreasing AT1R expression. There are two aspects of the severity of this combination. It is associated with high mortality and morbidity which results from their consequences including, heart failure, cardiac death, kidney disease and stroke. Also, Increased BMI causes hypertension which is difficult to be treated even with multiple

medications and invasive measures need to be taken to treat such hypertension e.g., sympathetic denervation of kidney [35].

### 3.8 Nutritional Factors

Diets rich in fructose contribute more to lipid production than other carbohydrates and increase lipids and cholesterol in blood. High fructose corn syrup (HFCS) is a classic example. Fructose also raises uric acid levels. This ultimately leads to hypertension. High salt intake is one of the main contributors to hypertension. Studies on salt intake and hypertension suggests that after removing salt from diet, hypertension resolves too much extent. Beet root juice can also help in controlling blood pressure [36].

### 3.9 Intestinal Microbes’ Relation with Hypertension and Obesity

Several studies suggested that changes in gut flora can lead to serious metabolic disorders and hence IR, T2DM, and HTN. LPS (lipopolysaccharides) derived from gut microbes regulate various hormones in fat tissue that change body’s response to glucose and inflammation [36].

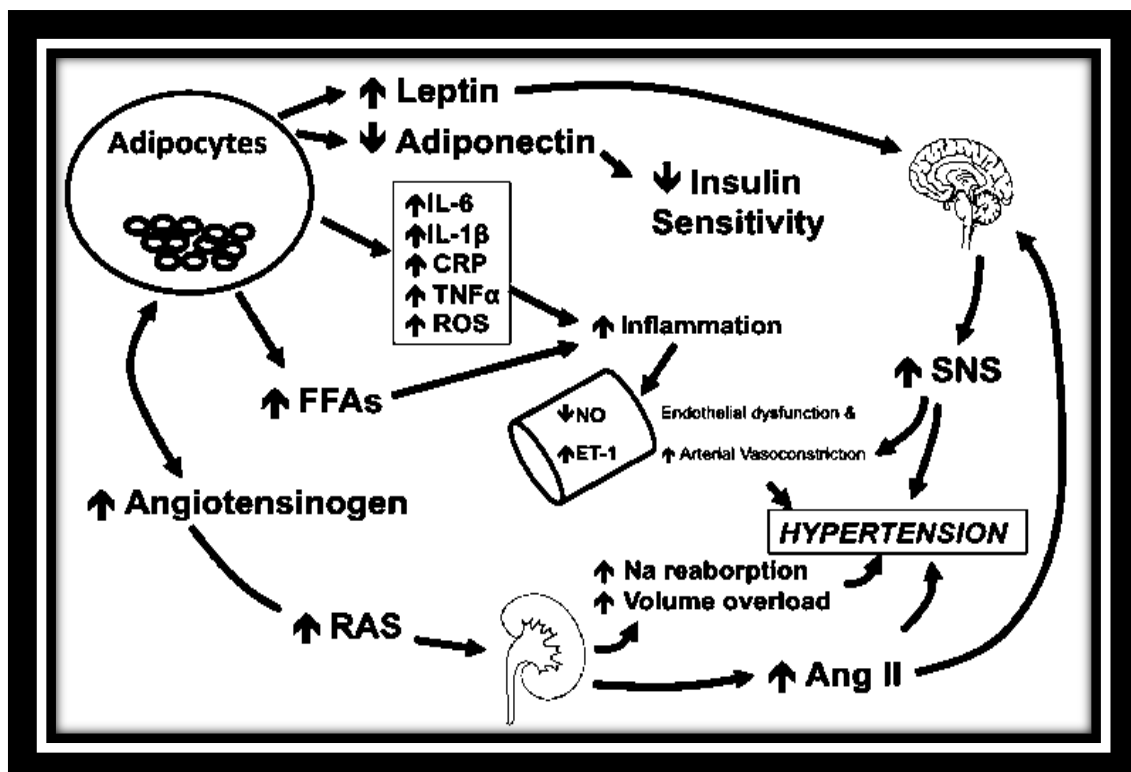


Fig. 1. Schematic representation of pathophysiology of HTN and obesity

## 4. MANAGEMENT OF OBESITY-RELATED HYPERTENSION

Various antihypertensive agents such as diuretics, beta-blockers, RAAS blockers and calcium channel blockers can be used to treat hypertension but they are associated with significant side effects which include hyperglycemia, hyperlipidemia, hyperuricemia, sexual dysfunction etc. That is why, it is advised to cope with obesity which is the main cause of hypertension [39]. Low calorie diet with a total of 500-1500 calories and 500-1200 calories for men and women respectively is suggested for this purpose. Diet should include restricted salt intake and lower amount of cholesterol and saturated fatty acids along with increased number of fish, raw vegetables, lean meats, fruits, whole grain. Moderate and constant exercise and adequate night sleep is also advised to counter obesity. The main objective is to increase lean body mass as compared to fat mass [40].

### 4.1 TREATMENT

The main approach to treat hypertension caused by obesity is weight loss because weight loss causes reversal of the pathophysiological mechanism of hypertension in obesity. Weight loss is first tried by non-pharmacological means such as lifestyle modifications. If weight loss is not possible or it does not lead to required decrease in blood pressure then pharmacotherapy is adopted. Metabolic surgery can also be done to control BP in obese patients [41].

#### 4.1.1 Lifestyle modification

Lifestyle modification such as "caloric restriction and increased physical activity" is the mainstay of treatment of obesity. Low calorie diet with a total of 500-1500 calories and 500-1200 calories for men and women respectively is suggested for this purpose. Diet should include restricted salt intake and lower amount of cholesterol and saturated fatty acids along with increased amount of fish, raw vegetables, lean meats, fruits, whole grain. Moderate and constant exercise and adequate night sleep is also advised to counter obesity [42]. The main objective is to increase lean body mass as compared to fat mass. It also includes cessation of smoking and alcohol consumption. Many patients try to adopt these lifestyle modifications but the rate of drop-out from this modification is high unfortunately. This drop-out cannot be

solely attributed to loss of motivation, but changes in counter-regulatory hormones which maintain the weight at a specific range can also exist and lead to failure of lifestyle modification [43].

#### 4.1.2 Pharmacological therapy for hypertension in obesity

Obese people are at increased risk of treatment-resistant hypertension. Most hypertension guidelines and recommendations do not address specific antihypertensive agents for obese people, however there are some recommendations for optimal choice of anti-hypertensive agents. There is a strong evidence for considering "ACEIs and ARBs as first-line because of the role of RAAS in pathogenesis of obesity-related hypertension." Studies showed that these drugs have potential benefit of increasing insulin sensitivity in patients of diabetes mellitus [44]. As SNS activation has also been observed in hypertensive obese individuals, beta-blockers can also be used for hypertension but they are associated with decreased insulin sensitivity and weight gain. That is why these drugs should be limited in patients with comorbid post-myocardial infarction or heart failure. In addition, carvedilol and nebivolol are associated with decreased risk of weight gain and less metabolic side effects as compared to older beta-blockers. Studies indicated that these calcium channel blockers are used as second line treatment with ACEIs/ARBs [45].

#### 4.1.3 Effect of metabolic (bariatric) Surgery in the treatment of obesity-related hypertension

Bariatric surgery is one of the latest and advanced gastrointestinal procedures globally. Different types of bariatric surgery include: "Sleeve Gastrectomy, Roux-en-Y Gastric Bypass, Duodenal Jejunal Bypass with Sleeve Gastrectomy, Duodenal Switch, Revisional Surgery, Laproscopic Adjustable Gastric Banding."

In one study, it is estimated that >680,000 metabolic procedures were done in 2016 according to obesity and metabolic disorders survey. Bariatric surgery has become the most useful and successful strategy for attaining a pronounced and durable weight loss in obese patients according to the pooled analyses of

many randomized control trials and observational studies [19].

There is also evidence that bariatric surgery is also helpful in treating type 2 diabetes mellitus. Many individuals who have undergone these procedures achieved complete remission of diabetes mellitus with blood glucose level below diagnostic criteria of diabetes mellitus in the absence of other pharmacological therapies. Inclusion of bariatric surgery in treatment algorithms for T2DM proposed by "International Diabetes Organization" represents success of bariatric surgery in treating T2DM [46].

## 5. CONCLUSION

Conclusively, obesity is considered a major risk factor for hypertension, type-2 diabetes and other problems such as kidney disease due to its increasingly tubular reabsorption that impairs the pressure natriuresis and ultimately causes expansion of volume through the activation of RAS and SNS. In addition, obesity also causes cardiovascular complications via several mechanisms including inflammation, hypertension, hyperglycemia, atherosclerosis, and dyslipidemia, these disorders co-exist especially in the presence of "excess visceral fat" in order to cause metabolic syndrome, in consequence, and it causes disturbances in fat metabolism via lipid accumulation. For the treatment purpose, pharmacological treatment and lifestyle modifications are recommended by the medical community, consumption of fruits and vegetables, animal proteins, less sugar and fat, fiber, omega-3 fatty acids, vitamins, and proper exercise is considered vital approach to combat obesity related hypertension.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Nuttall FQ. Body mass index: obesity, BMI, and health: a critical review. *Nutrition Today*. 2015;50(3):117.
2. Aronow WS. Association of obesity with hypertension. *Annals of Translational Medicine*. 2017;5(17).
3. Bell BB, Rahmouni K. Leptin as a mediator of obesity-induced hypertension. *Current Obesity Reports*. 2016;5(4):397-404.
4. Bolsoni-Lopes A, Alonso-Vale MIC. Lipolysis and lipases in white adipose tissue—An update. *Archives of Endocrinology and Metabolism*. 2015;59: 335-342.
5. Frohlich ED. Clinical management of the obese hypertensive patient. *Cardiology in Review*. 2002;10(3):127-138.
6. Hall JE, Crook ED, Jones DW, Wofford MR, Dubbert PM. Mechanisms of obesity-associated cardiovascular and renal disease. *The American Journal of the Medical Sciences*. 2002;324(3):127-137.
7. Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G. Mechanisms of obesity-induced hypertension. *Hypertension Research*. 2010;33(5):386-393.
8. Leggio M, Lombardi M, Caldaroni E, Severi P, D'emidio S, Armeni M, et al. The relationship between obesity and hypertension: An updated comprehensive overview on vicious twins. *Hypertension Research*. 2017;40(12):947-963.
9. Lotfy M, Singh J, Kalász H, Tekes K, Adeghate E. Suppl 2: Medicinal chemistry and applications of incretins and dpp-4 inhibitors in the treatment of type 2 diabetes mellitus. *The Open Medicinal Chemistry Journal*. 2011;5:82.
10. Seravalle G, Grassi G. Obesity and hypertension. *Pharmacological Research*. 2017;122:1-7.
11. Strumpf E. The obesity epidemic in the United States: Causes and extent, risks and solutions. *Issue Brief (Commonw Fund)*. 2004;(713):1-6.
12. Jiang SZ, Lu W, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. *Experimental and Therapeutic Medicine*. 2016;12(4): 2395-2399.
13. Portela DS, Vieira TO, Matos SM, de Oliveira NF, Vieira GOJB, Childbirth. Maternal obesity, environmental factors, cesarean delivery and breastfeeding as determinants of overweight and obesity in

- children: Results from a Cohort. 2015; 15(1):1-10.
14. Kitahara CM, Flint AJ, Berrington de Gonzalez A, Bernstein L, Brotzman M, MacInnis RJ, et al. Association between class III obesity (BMI of 40–59 kg/m<sup>2</sup>) and mortality: A pooled analysis of 20 prospective studies. *PLoS medicine*. 2014;11(7):e1001673.
  15. Najafipour H, Yousefzadeh G, Forood A, Karamouzian M, Shadkam M, Mirzazadeh A. Overweight and obesity prevalence and its predictors in a general population: A community-based study in Kerman, Iran (Kerman coronary artery diseases risk factors studies). *ARYA Atherosclerosis*. 2016;12(1):18.
  16. Mc Namara K, Alzubaidi H, Jackson JK. Cardiovascular disease as a leading cause of death: How are pharmacists getting involved? *Integrated Pharmacy Research & Practice*. 2019;8(1).
  17. Fruh SM. Obesity: Risk factors, complications, and strategies for sustainable long-term weight management. *Journal of the American Association of Nurse Practitioners*. 2017;29(S1):S3-S14.
  18. Jiang SZ, Lu W, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. *Exp Ther Med*. 2016;12(4):2395–9.
  19. Shariq OA, McKenzie TJ. Obesity-related hypertension: A review of pathophysiology, management, and the role of metabolic surgery. *Gland Surgery*. 2020;9(1):80.
  20. Portela DS, Vieira TO, Matos SM, de Oliveira NF, Vieira GO. Maternal obesity, environmental factors, cesarean delivery and breastfeeding as determinants of overweight and obesity in children: Results from a cohort. *BMC Pregnancy and Childbirth*. 2015;15(1):1-10.
  21. Rosenbaum M, Leibel RLJP. The physiology of body weight regulation: Relevance to the Etiology of Obesity in Children. 1998;101(Supplement 2):525-539.
  22. Guyenet SJ, Schwartz MWJTJCE, Metabolism. Regulation of food intake, energy balance, and body fat mass: Implications for the Pathogenesis and Treatment of Obesity. 2012;97(3):745-755.
  23. Life JS. *The Life Plan Diet: How Losing Belly Fat is the Key to Gaining a Stronger, Sexier, Healthier Body*. Simon and Schuster; 2014.
  24. Huff T, Boyd B, Jialal I. Physiology, cholesterol. *StatPearls [Internet]*; 2020.
  25. Kawarazaki W, Fujita T. The role of aldosterone in obesity-related hypertension. *American Journal of Hypertension*. 2016;29(4):415-423.
  26. Kim M, Bae S, Lim KM. Impact of high fat diet-induced obesity on the plasma levels of monoamine neurotransmitters in C57BL/6 mice. *Biomolecules & Therapeutics*. 2013;21(6):476.
  27. Okabayashi Y, Tsuboi N, Sasaki T, Haruhara K, Kanzaki G, Koike K, et al. Glomerulopathy associated with moderate obesity. *Kidney International Reports*, 2016;1(4):250-255.
  28. Gluck ME, Viswanath P, Stinson EJ. Obesity, appetite, and the prefrontal cortex. *Current Obesity Reports*. 2017;6(4):380-388.
  29. Ajayi S, Adebisi A, Kadiri S. Increased urinary sodium excretion is associated with systolic blood pressure in first degree relatives of hypertensive patients in Ibadan, Southwestern Nigeria. *Pan African Medical Journal*. 2018;31(1).
  30. González H. Pathophysiology of Obesity. In *Managing Patients with Obesity*. Adis, Cham. 2016;5-21.
  31. DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. *Nature Reviews Endocrinology*. 2014;10(6):364-376.
  32. Van Rooy MJ, Pretorius E. Obesity, hypertension and hypercholesterolemia as risk factors for atherosclerosis leading to ischemic events. *Current Medicinal Chemistry*. 2014;21(19):2121-2129.
  33. Saltiel AR, Olefsky JM. Inflammatory mechanisms linking obesity and metabolic disease. *The Journal of Clinical Investigation*. 2017;127(1):1-4.
  34. Zhang J, Chen Q, Zhong J, Liu C, Zheng B, Gong Q. DPP-4 inhibitors as potential candidates for antihypertensive therapy: Improving vascular inflammation and assisting the action of traditional antihypertensive drugs. *Frontiers in Immunology*. 2019;10:1050.
  35. Srivaratharajah K, Abramson BL. Hypertension in menopausal women: The effect and role of estrogen. *Menopause*. 2019;26(4):428-430.
  36. Petriz BA, Castro AP, Almeida JA, Gomes CP, Fernandes GR, Kruger RH, et al. Exercise induction of gut microbiota modifications in obese, non-obese and hypertensive rats. *BMC Genomics*. 2014; 15(1):1-13.



37. Maziarz MP, Preisendanz S, Juma S, Imrhan V, Prasad C, Vijayagopal P. Resistant starch lowers postprandial glucose and leptin in overweight adults consuming a moderate-to-high-fat diet: A randomized-controlled trial. *Nutrition Journal*. 2017;16(1):1-10.
38. Lastra G, Syed S, Kurukulasuriya LR, Manrique C, Sowers JR. Type 2 diabetes mellitus and hypertension: An update. *Endocrinology and Metabolism Clinics*. 2014;43(1):103-122.
39. Landsberg L, Aronne LJ, Beilin LJ, Burke V, Igel LI, Lloyd-Jones D, et al. Obesity-related hypertension: Pathogenesis, cardiovascular risk, and treatment—A position paper of the The Obesity Society and the American Society of Hypertension. *Obesity*. 2013; 21(1):8-24.
40. Brady TM. Obesity-related hypertension in children. *Frontiers in Pediatrics*. 2017;5:197.
41. Foulds HJ, Bredin SS, Warburton DE. The relationship between hypertension and obesity across different ethnicities. *Journal of hypertension*. 2012;30(2):359-367.
42. Dorresteijn JAN, Visseren FLJ, Spiering W. Mechanisms linking obesity to hypertension. *Obesity Reviews*. 2012;13(1):17-26.
43. Wadden TA, Webb VL, Moran CH, Bailer BA. Lifestyle modification for obesity: New developments in diet, physical activity, and behavior therapy. *Circulation*. 2012;125(9):1157-1170.
44. Becton LJ, Shatat IF, Flynn JT. Hypertension and obesity: Epidemiology, mechanisms and clinical approach. *The Indian Journal of Pediatrics*. 2012;79(8):1056-1061.
45. Apovian CM, Aronne LJ, Bessesen DH, McDonnell, ME, Murad MH, Pagotto U, et al. Pharmacological management of obesity: An Endocrine Society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2015; 100(2):342-362.
46. Chrysant SG. Pathophysiology and treatment of obesity-related hypertension. *The Journal of Clinical Hypertension*. 2019; 21(5):555-559.

© 2021 Dehbandi et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*  
<https://www.sdiarticle4.com/review-history/76236>