Relationship between obesity and chronic non-communicable and infectious diseases

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ABSTRACT

Introduction: Obesity increases the risk of chronic non-communicable diseases (NCDs) and affects the course of diseases of infectious origin. Objective: Reviewing the literature on how obesity influences the severity of the clinical picture of some of the non-communicable and communicable diseases of greatest impact in Peru. Methods: Documentary research, from studies developed in various contexts associated with the presence of obesity along with infections or NCDs. Results: The condition of obesity reached by bad consumption habits and low physical activity is the main responsible for the high rate of NCDs, consequently, mortality. Conclusions: Excess weight affects the immune system, contributing specifically to exacerbated phenomena of a systemic inflammatory response, determined by increased secretion of adipocytokines, which predisposes the body to develop and contract NCDs and infectious diseases.

Keywords: Obesity, Chronic diseases, Diabetes mellitus, Neoplasms, Fatty liver, Virus diseases; Coronavirus, Hepatitis, Aggressive periodontitis.
INTRODUCTION

Obesity, defined as an abnormal and excessive accumulation of fat in the body, is also recognized as a multifactorial disorder caused by an imbalance between calories consumed versus calories expended. This increases the risk of several debilitating and fatal diseases and thus affects the quality and duration of life. And it is estimated that by the year 2050, 50% of the world’s population will be obese, which implies an impact on the public health of populations in relation to the increase in the prevalence and control of noncommunicable and communicable diseases. Obesity, due to poor consumption habits and low physical activity, is mainly responsible for the high rate of these diseases and, consequently, of mortality rates.

In this sense, the increase in obesity rates in the population is considered a very important public health problem. Currently, it can be stated that there are about 1.6 billion overweight adults in the world. This phenomenon occurs in both developed and underdeveloped countries. It is worrying to note the high incidence of obesity in children since 20 million children under five years of age are overweight. The Organization for Economic Cooperation and Development (OECD) reports that in at least 13 countries of this organization, half of the adult population is overweight or clinically obese. In some countries, such as Japan, Korea, France, and Switzerland, these rates are lower, although these have recently increased.

Moreover, the WHO points out that obesity and overweight conditions are epidemically prevalent worldwide, causing the death of approximately 2.8 million people per year, which represents a public health problem. In most cases, apart from endocrine diseases, the problem of excess weight is due to dietary patterns characterized by high consumption of processed products, such as sweets and sodas with a high level of sugar, fast foods with a high level of salt and saturated fats, all with high caloric level and low nutritional value and low-fiber, and with physical inactivity, due to increased sedentary practices, both work (teleworking) and recreational (television and video games).

Several studies have demonstrated the relationship between obesity or excess weight and the increased risk of suffering from chronic noncommunicable diseases, as well as their influence on the course and effectiveness of treatment in diseases of infectious origin, such as influenza virus and hepatitis, among others. Chronic NonCommunicable Diseases (NCDs) refer to ailments or conditions of slow evolution, such as cardiovascular diseases (heart attacks, strokes), renal diseases, chronic respiratory diseases (obstructive, asthma), diabetes, cancer (endometrial, breast, ovarian, prostate, liver, etc.), diabetes and disorders of the locomotor system (such as osteoarthritis). Currently, worldwide, the prevalence and incidence of these diseases have been increasing, being recognized as serious public health problems, with a high impact on health costs associated with morbidity and mortality, as well as on the productive capacity of individuals and each country. For example, the WHO reports at least 41 million deaths due to NCDs in the world, with cardiovascular diseases causing the death of 17.9 million people per year, 9 million from cancer, 3.9 million from respiratory diseases, and 1.6 million from diabetes.

As for the most prevalent infections, there are viral infections such as flu, of which approximately 1 billion cases are recorded worldwide each year, of which around 5 million are serious and between 290,000 and 650,000 people die from respiratory causes related to influenza. Viral hepatitis, inflammation of the liver can have severe or chronic clinical symptoms, with a high probability of developing acute liver failure, cirrhosis, or cancer, caused by various types of viruses classified as hepatitis viruses: A, B, C, D, and E. The WHO estimates that in 2015 there were approximately 325 million people infected worldwide, 257 million with hepatitis B and 71 million with hepatitis C, and about 1.34 million deaths.

Indeed, if we take into consideration, data reported by the WHO that point out the increase in global prevalence by 300% between 1975 and 2016, where more than 650 million people are obese, 41 million children under five years of age were overweight or obese, more than 340 million children and teenagers (between 5 and 19 years of age) are overweight or obese, and the association that childhood obesity increases the probability of suffering from obesity and the risk of some disability in adulthood is worrying as this circumstance can influence the incidence of NCDs and infections.

In Peru, approximately 14 million people are reported to be overweight or obese, and around 240 thousand children under 5 years of age with excess weight problems, according to the results of...
the Demographic and Family Health Survey (ENDES, from its Spanish acronym) 2018. The Ministry of Health (MINSA, from its Spanish acronym) also points out that obesity is responsible for 43.6% of deaths due to hypertensive heart disease, 40.2% with diabetes mellitus type 2 (DM2), and 32.8% with chronic kidney disease (CKD), respectively. The Peruvian state has taken preventive measures, such as the decree of the “law of Promotion of healthy eating for children and teenagers” (law 30021 approved by Supreme Decree No. 017-2017-SA), which establishes protection and promotion of the right to health, implementing educational activities and encouraging physical activity, including among the actions the implementation of stores and healthy dining services in educational institutions, along with advertisements warning about excess consumption of sugars, sodium, and fats in processed products, to maintain or decrease the prevalence of obesity and overweight in the medium and long term.

Taking into account the above and understanding the relevance of the incidence of overweight and obesity in the country. The purpose of this study is to examine the literature on the influence of obesity on the clinical picture of some of the non-communicable and communicable diseases of greatest impact in the country, to make a warning call on the urgency of implementing effective strategies for prevention, control, and monitoring of compliance of it, with the purpose of contribute to the reduction of the incidence of related diseases.

METHODS

Documentary-type research is presented, in which a descriptive review of studies developed in various contexts associated with the presence of obesity along with infections or NCDs is performed. Information sources and search methods were used, such as Google Scholar, Crossref Metadata, Scielo, and PubMed between 2015 and 2020, in open access journals. In addition, key phrases such as obesity and acute infections; obesity and NCDs were used. The published information on the subject is compiled, analyzed, synthesized, and discussed, including a critical review of the state of knowledge reported in the scientific literature, published in medical journals in Spanish or English, they will complete the information on this topic in relation to the pathology of the clinical picture and the response to treatment. The product of integrating and summarizing the results of the studies included in this review is presented, as well as the Peruvian statistical data reflecting the prevalence of obesity, NCDs, and infectious diseases, which are published in public domain documents or web portals of the Ministry of Health.

RESULTS AND ARGUMENT

Excess weight consequences

Obesity is the excessive increase in fat accumulation and weight, or body fat, is due to the accumulation of triglycerides in the adipose tissue. This is a type of connective tissue, but free, formed by a group of cells known as adipocytes, which during this process begin to increase in volume, which can be hyperplastic (increase in the number of cells) or hypertrophic (increase in size).

According to clinical and experimental trials, both in humans and animals, it has been determined that these adipokines act mainly on the central nervous system, muscle, liver, bone, among others; thus actively influencing inflammatory processes and metabolic regulation of energy.

Adiponectin is an anti-inflammatory that acts at the level of monocytes inhibiting their adhesion to epithelial cells, which is why it is an endogenous modulator in obesity-related processes. However, in vitro studies, it was observed that IL-6 and TNF-α inhibit its expression, so it is very likely that it goes hand in hand with the processes of insulin resistance resulting from the inflammatory process in diabetes mellitus (DM with levels of IL-6 and TNF-α). Table 1 shows the mechanisms of metabolic and immunological functions, that detailed the correspondences between the analyzed variable.
Table 1 Mechanisms of metabolic and immunological functions.

<table>
<thead>
<tr>
<th>FACTORS</th>
<th>METABOLIC FUNCTION</th>
<th>IMMUNE FUNCTION</th>
<th>CHANGE IN OBESITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMMUNE FUNCTION</td>
<td>Regulation of appetite and energy expenditure. Regulation of insulin production expression</td>
<td>Neutrophil activation. The proliferation of T lymphocytes. Cytosine effector production. Regulation activation Monocytes-Macrophages. Wound healing</td>
<td>Increases (Reduced signing)</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>Decreased gluconeogenesis. Increased glucose consumption</td>
<td>Decreased response of T lymphocytes. Decreased lymphopoiesis B cells.</td>
<td>Increases</td>
</tr>
<tr>
<td>Resistin</td>
<td>Insulin resistance</td>
<td>Pro-inflammatory</td>
<td>Increases</td>
</tr>
<tr>
<td>Adipsin</td>
<td>Decreased GAD production.</td>
<td>Complement Activation</td>
<td>Increases</td>
</tr>
<tr>
<td>Visfatin</td>
<td>Increases insulin sensitivity</td>
<td>Pro-inflammatory</td>
<td>Decreases</td>
</tr>
<tr>
<td>Apelin</td>
<td>Insulin increases sensitivity and insulin decreases production.</td>
<td>Pro-inflammatory</td>
<td>Increases</td>
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<tr>
<td>Quinine</td>
<td>Adipocyte differentiation. -</td>
<td>Pro-inflammatory</td>
<td>Increases</td>
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<tr>
<td>MCPI</td>
<td></td>
<td>Chemoattractant</td>
<td>Increases</td>
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<tr>
<td>TNF -α</td>
<td>Insulin resistance, lipolysis, adipogenesis.</td>
<td>Pro-inflammatory</td>
<td>Increases</td>
</tr>
<tr>
<td>IL-6</td>
<td>Insulin resistance, lipolysis increase.</td>
<td>Pro-inflammatory</td>
<td>Increases</td>
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Moreover, the indicator that is frequently used to identify overweight and obesity conditions is the body mass index (BMI), which relates anthropometric measurements of weight and height, which according to the WHO establishes over 19 years of age, a condition of overweight if it is greater than 25 kg/m² and obesity if it is greater than 30 kg/m². In children and teenagers between 5 and 19 years of age, there are growth patterns adjusted for age and height, which in the case of overweight, the indicator is above the median with one standard deviation, and in obesity, if it is above two standard deviations.

Obesity and chronic noncommunicable diseases

Several studies have linked excess weight to a higher risk of NCDs, all of which have considerable relevance and impact on public health indicators. In Peru, the WHO in 2016 reported 69% of deaths due to NCDs, where 21% were cardiovascular diseases (which include vascular and structural diseases such as coronary artery disease, heart, atrial fibrillation, and ischemic and hemorrhagic disease), followed by cancer, chronic respiratory diseases and diabetes. In obesity, the increase in adipocytes contributes to a state of systemic inflammation that contributes to the development of these diseases, for example, it increases the size of the coronary artery, promoting atherosclerosis. Changes in the secretion of adipocytokines, as well as the structural change associated with the increase in body mass, affect blood flow, which generates arterial hypertension, which may increase risk of heart failure and atrial fibrillation. Obesity has been linked to an increased risk of developing cancers (esophageal, pancreatic, colon, rectal, breast, endometrial, kidney, thyroid, and gallbladder cancers). In these cases, it is associated with the excessive production of estrogens and breast and endometrial cancer. It has also been reported to be associated with the secretion of adipocytokines that in some way intervene in the stimulation of cell replication, as well as their
modulation in inflammation, also giving rise to altered immune responses and effects on the nuclear factor kappa β system and oxidative stress, all of which in some way affect the adequate cell turnover, influencing cell growth.\textsuperscript{13}

Obesity is associated with non-alcoholic fatty liver disease (NAFLD), a disease that can progress to non-alcoholic steatohepatitis (NASH), cirrhosis, and even liver cancer (hepatocellular carcinoma).\textsuperscript{17} It is estimated that obesity increases the risk of NAFLD by up to five times, associated with primary metabolic complications such as inflammation, negative regulation of adiponectin, dyslipidemia, and insulin resistance. When adipocytes concentrate viscerally, they release fatty acids that pass into the portal circulation and are then deposited in the liver, initiating hepatic steatosis.\textsuperscript{13} Another condition associated with insulin resistance is diabetes, a condition in which either no insulin is produced or the insulin that is produced is not as efficient in regulating blood sugar levels.\textsuperscript{14} In this regard, it is estimated that 80\% of people with DM2 are obese, and in these cases, it is explained by the increased size of adipocytes, which decrease the secretion of adiponectin along with the increased secretion of other cytokines that eventually contribute to the insulin-resistant condition, as well as the elevated levels of intracellular and extracellular lipids. At the hepatic level this insulin resistance causes elevated blood sugar levels, which in turn at the pancreatic level stimulates the β-cells to secrete more insulin, and this increased load on the pancreas in the long term, not only damages the pancreatic cells, but eventually decreases their ability to secrete more insulin, and again the body loses the ability to regulate blood glucose levels.\textsuperscript{13} This is why the body is predisposed to the development of diabetes.

Uncontrolled blood glucose can lead to renal disease, neuropathies, infections and amputations, retinopathy, gastroparesis, diabetic ketoacidosis, arterial hypertension, and stroke.\textsuperscript{13} In addition to the impact on inflammation, obesity can modify the pharmacokinetics of anti-TNF-α drugs. Recent pharmacokinetic studies have determined that obesity is a risk factor related to the increased elimination of anti-TNF drugs, which is why it has a reduced average half-life and low serum concentrations. This is related to the treatment of fatty liver disease and patients with rheumatoid arthritis.\textsuperscript{30}

Obesity, from the point of view of visceral adipose tissue, has also been associated with the development of chronic kidney disease (CKD), increasing 10 times the risk of suffering from glomerulopathies, nephrolithiasis, and renal cancer, and even increasing the mortality of patients with terminal CKD. Some studies indicate that the risk is associated with the ectopic accumulation of lipids, such as fatty deposits in the kidney, due to intraglomerular pressure and increased glomerular permeability, given by hyperfiltration that compensates the metabolic demand secondary to excess weight, which in the long term generates renal damage. Also, the action of adiponectin, leptin, and resistin, promoters of inflammation, and consequent insulin resistance directly impact the renal activity.\textsuperscript{31}

**Obesity and periodontal disease**

Oral diseases are mainly due to the consumption of alcohol, tobacco, and foods with high levels of sugar, hence about 530 million children have caries in primary teeth, as well as approximately 10\% of the world’s adult population suffer from periodontal diseases. Most of these disorders are preventable and treatable, but oral health care is very expensive, and most middle and low-income countries have no access to treatment and prevention services\textsuperscript{32}. In Peru, oral health is considered a public health problem, according to MINSA, in 2002, the prevalence of caries was around 90.4\%, and of periodontal diseases 85\%.\textsuperscript{13}

Periodontal disease includes infectious processes such as gingivitis and periodontitis, mainly caused by bacteria present in plaque and response to inflammation. In the case of periodontitis, it leads to the destruction of the soft tissue and alveolar bone supporting the teeth, which can lead to loosening or loss of the tooth. Various authors have related periodontitis to body weight, pointing to obesity as a possible risk factor for periodontitis.\textsuperscript{25,34} In this regard, there is evidence that in the gingival inflammatory process, collagen is lost and the periodontal attachment is destroyed, and cytokines such as TNF-α and IL-1 stimulate bone resorption...
and collagen destruction and stimulated fibroblasts to produce collagenases (proteolytic enzymes called metalloproteinases MMP-1, MMP-3, MMP-8, and MMP-V) that destroy the gingival connective tissue and in turn, osteoblasts activate osteoclasts in the resorption of periodontal bone.25

The treatment of periodontal disease includes the removal of plaque, scaling, root planing, local antibiotics and antioxidants, and even bone or gum grafts in severe cases. Zuniga et al34 reported that obese patients, as with other metabolic failure diseases, do not respond adequately to these types of therapies, the main culprit being the MMPs that are found in high levels in this type of diseases such as DM, arterial hypertension (AH), dyslipidemias and obesity. Likewise, this type of periodontal disease influences the alteration of fat metabolism and insulin resistance mechanisms, given in these diseases.35

**Obesity and viral infections**

Obesity contributes to systemic and intrinsic inflammation in B cells, and in relation to this, it has also been associated with a higher risk of contracting viral, bacterial and fungal infections. Among viral infections, acute respiratory infections are the most frequent, among the most common viruses: influenza A (H1N1) 2009, which caused the first pandemic of the 21st century, influenza B virus, respiratory syncytial virus (RSV), adenovirus, and parainfluenza virus (PIV). Currently, thanks to molecular biology, human metapneumovirus (HMPV), rhinovirus (RV), enterovirus, and new agents of the coronavirus (HCoV) family have been classified: HKU-1,10 NL-6311; and HCoV-SARS (agent of severe acute respiratory distress syndrome), bocavirus (HBoV) and 2019-nCov (SARS-Cov2), agent of COVID-19, the pandemic of 2020, which has the world population in an emergency.28,36

In Peru, as of 2018, MINSA reported 5290 cases of pneumonia in children under 5 years of age, with 54 deaths and 5366 in those over 60 years of age with 324 deaths, pointing to a total of 637 766 cases of acute respiratory infections in children under 5 years of age, equivalent to a cumulative incidence rate of 2263 per 10 000 <5 years.37 Influenza A is a potentially serious respiratory infection caused by the influenza virus, most human cases are caused by H1N1 and H3N2 strains. These infections are usually confined to the upper respiratory tract, including the nasal, tracheal, and bronchial epithelium. Severe cases are more frequent in overweight people and involve infections of the lower respiratory tract (the lungs), often requiring hospitalization, use of mechanical ventilators, may develop viral pneumonia and/or secondary bacterial infections, leading to acute lung injury (ALI), acute respiratory distress syndrome (ARDS), and eventually death.18

As a result of the 2009 influenza pandemic with the H1N1 virus, obesity was identified as a risk factor for the disease, as well as influencing the severity and mortality of infected individuals. Due to the chronic state of meta-inflammation that has systemic implications for immunity. Not only do obese people show delayed antiviral responses to influenza virus infection and experience slow recovery, but the efficacy of antivirals and vaccines is reduced18.

In this sense, both in humans and in obese murine models, high circulating leptin and low levels of adiponectin have been determined, showing systemic leptin resistance. And leptin is a modulator of B cells, at the level of their development, maturation, and activity38,39 which is why responses to vaccines decrease in obese individuals. When inoculation is performed, antibody titers are equal between obese and lean individuals; however, they then begin to decrease rapidly in obese individuals. Likewise, there is a higher production of specific IgG antibodies in lean individuals, while in obese individual IgM production prevails. 18

On the other hand, however, it is reported that obesity may influence the life cycle of the virus, thus, together with the low immune response leads to more severe pathogenesis. According to studies in alveolar epithelial cells from obese individuals, in vitro, a higher replication of H7N9 viral RNA was observed than the replication observed in cells from lean individuals. This difference in susceptibility of epithelial cells requires further study40,41.

Regarding the COVID-19 pandemic, the data reported so far suggest that obesity aggravates the severity of the disease. Zheng et al,26 found an association between the severity of COVID-19 and obesity, where higher the BMI, higher the proportion of severe patients, and they also indicate that obese patients who also have metabolic associated fatty
Liver disease (MAFLD) or non-alcoholic fatty liver disease have a six-fold increased risk of presenting severe COVID-19.

In COVID-19 complications, a systemic inflammatory response has been reported, promoted by the activation of CD14+ and CD16+ inflammatory monocytes stimulating an increased secretion of IL-6 and other pro-inflammatory factors, IL-6 is considered the main trigger of the inflammatory "storm" in patients. This situation is aggravated because IL-6 is also higher in obese patients in response to adipokines.

Another very prevalent viral infection is the hepatitis virus, of which five types A, B, C, D, and E are known and can be transmitted by consumption of contaminated food and water—in the case of type A—and by unprotected sexual intercourse, contact with contaminated blood through injections or body piercing (tattoos or piercing)—in the rest of cases. These infections lead to severe and chronic inflammation of the liver, which can lead to cirrhosis or cancer. For America, it is estimated that there are about 8 million cases of type B hepatitis, 11 million cases of type C hepatitis. These are the most serious, representing a serious public health problem, due to the high cost of treatment, as they often require liver transplants.

Worldwide, an estimated 291 million people are chronically infected with hepatitis B virus (HBV), one of the leading causes of cancer mortality. Likewise, it has been reported that obesity is associated with an increased risk of developing liver cancer in the general population and in patients with HBV. In this regard, increased liver cancer mortality is associated with increased liver cancer mortality in non-cirrhotic HBV patients with hypercholesterolemia or BMI ≥30 kg/m².

Good results have been reported in relation to the effect of statin treatment (3-hydroxy-3-methylglutaryl CoA reductase) on the liver condition, where a decrease in mortality is observed, regardless of cholesterol levels or BMI, i.e., in these cases, obesity does not interfere with the mechanism of action. On the other hand, alterations in pulmonary mechanics are usually common in obesity due to increased pressure caused by excess adipose tissue in the airways and respiratory muscles, altering the control of breathing and gas exchange. Susceptibility to and recurrence of acute respiratory infections has been associated with body mass index (BMI) in both children and adults, with the risk increasing up to twofold in those with obesity. Obese hospitalized patients are at high risk for pulmonary aspiration and community-associated respiratory tract infections.

Several studies have reported a direct association between BMI and increased risk of community-acquired pneumonia, especially in 6 women. In addition, it has been observed that obese patients on mechanical ventilation have higher mortality and higher risk of complications including sepsis, ventilator-associated pneumonia, and central venous catheter-related infections compared to normal-weight individuals. On the other hand, obesity has a strong association with the H1N1 influenza virus, affecting the course of the disease and increased mortality. Several studies have shown that subjects with obesity had a longer hospital stay and higher mortality and susceptibility to the development of other infections, mainly pneumonia. Increased production of proinflammatory cytokines, chemokines, and decreased NK cell activity are important determinants of the severity of this infection.

**CONCLUSIONS**

There is a very close relationship between obesity and chronic non-communicable and infectious diseases, since the condition of excess weight affects the immune system, contributing specifically to the exacerbated phenomena of systemic inflammatory response, determined by the increased secretion of adipocytokines, which not only predispose the organism to the risk of contracting diseases, but also affect the mechanisms of action of drugs, as well as the response to vaccines. Therefore, in a certain way, placing the population in a state of vulnerability to infections.

In this sense, the diseases aforementioned and obesity form a set or network of connections of risk factors, where biochemical reactions interact with the result of the individual’s lifestyle, at a nutritional level, dependent also on factors such as physical activity or harmful habits, such as alcohol, tobacco and drug consumption, making it difficult to control. Hence the importance of directing efforts to
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shape preventable factors such as promoting healthy lifestyles, educating the population, looking for tools and strategies to ensure good nutrition.

REFERENCES

7. Méndez A. La nutrición materna y la programación metabólica: el origen fetal de las enfermedades crónicas degenerativas en los adultos. CIENCIA ergo-sum. 2020; 27(3). DOI: https://doi.org/10.30878/ces.v27n3a7


