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Social inequalities and nutritional disparities: the link between obesity and COVID-19

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Abstract. – OBJECTIVE: Cohort studies, clinical audits of patients with COVID-19 in hospital and routine primary care records provided evidence-based insights on the relationship between excess weigh, obesity and COVID-19. The purpose of this umbrella review is to highlight the relationship between nutritional quality and social inequalities related to CDNCD, obesity and SARS-CoV-2 infection.

MATERIALS AND METHODS: Only articles published from 2008 to the present were included in the search to show an updated picture of the topic. The search for published studies was conducted in February 2021 in the scientific databases PubMed (MEDLINE). The terms used for the search were "COVID-19", "Obesity", "Disparities", "Nutritional inequalities", "Chronic degenerative non-communicable diseases" and "review" OR "systematic review" OR "meta-analysis" separated by the Boolean operator AND.

RESULTS: 1874 reviews were found, but only 99 met the objective. Obese or dysmetabolic patients are those who had a worse course of disease following COVID-19. This data was observed not only for Chinese and Caucasians, but also and above all among Africans, African Americans, Latinos and indigenous people. Plausible mechanisms to explain the association between obesity and COVID-19 outcomes, included the role of excess adipose tissue on respiratory function, metabolic dysfunction, the cardiovascular system, enhanced inflammatory response and impaired response to infection.

CONCLUSIONS: Today, chronic non-communicable degenerative diseases (CDNCDs) are responsible for 70% of public health expenditure, affecting 30% of the population (one or more chronic diseases). Unfortunately, given the health emergency due to SARS-CoV-2, infectious diseases are currently more at the center of attention. However, the spread of infectious communicable diseases and CDNCDs is facilitated in situations of social disparity. In fact, in the poorest countries there are the highest rates of malnutrition and there is a greater risk of contracting viral infections, as well as, paradoxically, a risk of comorbidity, due to access to cheaper food and qualitatively poor, with high caloric density.

Key Words:
Inequalities, COVID-19, Obesity, Communicable diseases, Chronic degenerative non-communicable diseases, Nutrition.

Introduction

Until the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, it was clear to everyone that the major challenge was the chronic degenerative non-communicable diseases (CDNCD). After the pandemic, they became the cause of the major complications of COVID-19 disease[1].

World Health Organization (WHO)'s definition of CDNCD, as a "health problem that requires continuous treatment over a period of time from years to decades", makes clear the reference to the commitment of resources, human, manage-

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rial and economic, in terms of both direct (hospitalization, drugs, medical assistance, etc.) and indirect (premature mortality, long-term disability, reduced quality of life, etc.) costs, necessary for their control[2].

CDNCDs, represented by obesity, heart disease, diabetes, neurodegenerative diseases, chronic respiratory diseases, cancer, have been up to now the most frequent causes of prolonged disability and death worldwide[3,4]. About 17 million people die prematurely each year from a chronic disease and the number is expected to grow.

It is estimated that around 70-80% of health resources worldwide are spent today on the management of chronic diseases; the data become even more worrying considering the most recent epidemiological projections, according to which in 2030 they will represent 80% of all diseases in the world[2].

In a global and national context in which the prevalence of CDNCDs reached increasingly relevant estimates, greater attention must be paid to prevention to reduce the global burden of the disease, which weighs heavily on the duration and quality of life of the population and on the resources of the National Health System (NHS).

Social inequality, which has its reflection on nutritional disparities, is the common basis of infectious diseases (IDs) and CDNCDs. The poorest societies that are also those with the highest rate of malnutrition are at high-risk of viral infections and paradoxically at risk of obesity-related metabolic diseases because it is allowed to buy cheap, but high-calorie and low nutritional quality food.

On the other hand, despite the economic and socio-cultural possibilities, the high-income populations suffer from obesity and cardiometabolic diseases, due to nutritional transition towards processed foods, with low health indexes[5], and lifestyle changes, which make them more susceptible to viral infections.

Following the current pandemic, the most severe clinical conditions in COVID-19 patients have been observed in patients suffering from obese, metabolic dysfunction, not only in the Chinese and Caucasian populations, but especially in Black, Latino and Native American[6].

The presence of multiple pathologies requires the intervention of different professional figures with the risk of aiming at the treatment of the single most serious disease rather than on the overall management of the patient, with possible diagnostic and therapeutic duplications that contribute to the increase in healthcare costs and make it difficult for the patient to participate in the treatment process.

In this historic moment, it is not possible to deny the relationship between CDNCDs and susceptibility to viral infection, between economic crisis and nutritional quality, increase in health expenditure and level of health care. Global responsibility, effective coordination and participatory management are needed for the current and future emergencies. To date, there are no data on the role of the link between obesity and COVID-19 pandemia to social inequalities and nutritional disparities.

This umbrella review seeks to answer the question of whether a healthy and sustainable diets, based on high quality nutritional approach can be used to invert the nutritional transition, in order to prevent and to block the dual pandemic of obesity and COVID-19.

The purpose of this umbrella review is to provide evidence-based insights on the relationship among nutritional quality and inequalities relating to CDNCDs, obesity and COVID-19.

Materials and Methods

The search for published studies was conducted in February 2021 in the scientific databases PubMed (MEDLINE). The terms used for the search were "COVID-19", "Obesity", "Disparities", "Nutritional inequalities", "Chronic degenerative non-communicable diseases" and "review OR systematic review OR meta-analysis" separated by the Boolean operator AND. Only articles published in from 2008 to present were included in the search to show an updated picture of the topic. 1874 review were found, but only 92 were selected because met inclusion criteria. We only included peer-reviewed studies meeting our inclusion criteria: (a) systematic and narrative reviews; (b) documenting any association between obesity and COVID-19; (c) documenting any association between poor nutrition and obesity; (d) focusing on any type of population and age; (d) written in English. We excluded: (a) meta-analysis; (b) original, primary studies. The search for published studies was independently performed by four authors (PG, MD, EC, FP).

Results

The initial search yielded to 1874 records. Following title and abstract screening, 99 were selected because met the objective, and were included in this umbrella review:

- 9 reviews dealt on epidemiological transition and demographic changes[7-15], presenting the historical passages from 10,000 years before Christ up to 2019, and describing the transition to agriculture, improved nutrition and lifestyle of the last century, the benefit of vaccines, and spread of chronic diseases;
- 4 reviews are focused on the effects of social inequalities and the role of prevention[16-19];
- 12 reviews highlighted the health costs of communicable and chronic non-communicable degenerative diseases: for many of low- and middle-income countries ID represent the 25% and mortality, and CDNCDs overlap these ID and increase the risk. Worldwide, 70% of public health resources are destined for CDNCDs[2,20-30];
- 9 reviews are focused on the health and social costs of obesity disease, underlining that overweight and obesity caused more deaths worldwide than underweight, with a increase of annual medical expenditure, according to BMI[12,31-38];
- 18 reviews reported information about the global economic impact of obesity[39-56];
- 18 reviews are about the quality of diet and its correlation with diseases[57-74];
- 29 reviews found the link among obesity, comorbidity and mortality for COVID-19[75-103];
- 15 reviews referred on food safety and food quality, as the main tools for the fight against obesity, the reduction of related diseases and the improvement of the quality of life[104-118].

Discussion

Epidemiological Transition and Demographic Changes

The epidemiological transition, that influence public health policies, highlighted a change in disease patterns and causes of death, since it gone from a high infant mortality rate and infectious epidemics typical of twentieth century to a pattern with high prevalence of chronic degenerative diseases[7].

The first epidemiological transition occurred with the transition to agriculture about 10,000 years before Christ, determining a model of infectious and nutritional diseases that still exist today[8].

The health achievements, development of improved nutrition and lifestyle of the last century have made possible to reduce morbidity and mortality, resulting in the second epidemiological transition[9]. The demographic changes related to the reduction in childhood mortality leads to an increase of population that can reach the adult age and can develop adult-related diseases. Over time, changes in risk factors have been observed, such as the prevalence, distribution and/or virulence of pathogenic organisms, environmental changes due to anthropogenic activities that could cause disease, social and cultural factors, such as lifestyle and diet. Thanks to the use of vaccines, some contagious diseases, such as smallpox, have been eradicated and every year 2 to 3 million deaths from other diseases, such as diphtheria, tetanus, pertussis, hepatitis and flu are prevented.

However, the end of the 20th century to the present, represents the third epidemiological transition[10], characterized by large population size, declining life expectancy and age of onset of chronic diseases in high-income countries, antibiotic resistance and rapid spread of novel infection.

Therefore, the mortality rate is not sufficient to measure the health of a population.

The DALY (DALY, Disability Adjusted Life Year) measures the gap between the real health situation and an ideal one, where everyone lives up to the age of the standard life expectancy in perfect health. The DALY combines in one index the time lived with disability and the time lost due to premature mortality[11].

The CDNCDs are included into the top 10 global causes increasing the DALYs in 2019. So, evaluating CDNCDs, it is very important to consider the number of healthy years lived as evidenced by the impact of years lost due to disability.

The most relevant diseases, in terms of epidemiology and health costs, are obesity, diabetes, ischemic heart disease and malignant tumors, which represent the main cause of mortality and years of life lost through disability, illness or premature death[2].

According to the Global Burden of Disease, the major determinants of CDNCDs in terms of DALY are mainly attributable to behavioral risk factors such as poor nutrition, reduced fruit and vegetable intake, high body mass index (BMI $\geq$ 25.0 Kg/m^2), cigarette smoking habit, high alcohol consumption, and low level of physical activity[12].

In elderly the obesity effect is much more complex compared to young people. In fact, the so called "obesity paradox" occurs: the body weight seems to be related to the maximal survival rate increasing with the age, with an increase of CVD risk, but a reduced mortality[13]. Although drug therapy, dietary intervention and surgical approaches

can reduce premature mortality and increase life expectancy, an increase in prolonged disability is observed, leading to serious socio-economic burdens. In addition, there is the burden of multimorbidity[14]. In fact, although life expectancy has almost doubled in the last 150 years, the incidence and prevalence of chronic diseases increased.

Worldwide, patients with one or more chronic diseases represent over 30% of the population and 70% of public health resources are destined for these diseases[15].

It is now well established that the challenge to chronic conditions is a "systemic challenge", which must overcome the limits of the institutions and the line between health and social services, promote integration between different professional skills, attribute an effective "centrality" to the person and his/her care and life project (patient-centered medicine).

Prevention and Social Inequalities

According to WHO "prevention is the card that offers the greatest potential for improvement" and "prevention at the population level is the most sustainable long-term strategy and allows you to tackle several chronic diseases and their respective risk factors simultaneously"[16].

Anyway, prevention must act simultaneously on the population and on the individual and on high-risk subjects, to enhance the impact on morbidity and mortality in the short and medium term.

As confirmed by the literature data, we are facing a real global food crisis and, worldwide, unhealthy diet become the one of the main causes of poor health[17].

The importance of nutrition education represents the first effective means of prevention in health protection. The adoption of correct eating habits as a health promotion action pushed the Governments to adopt strategies in this direction[18].

Moreover, to achieve a lasting result in changing food and dietary choices of vulnerable patients, it is essential to consider self-discipline, knowledge, managing daily stress, negotiating with family members and managing the social significance of food, together to a personalized approach[19].

Despite the observed global trends, the world's most vulnerable populations continue to die from infectious IDs, malnutrition and poverty. For many of low- and middle-income countries (LMICs) this means a double burden of disease, caused both by ID, high maternal and child mortality, but also by "emerging" health problems due to chronic diseases associated with a western lifestyle and the aging of the general population[19].

Deaths by ID were much higher among people living in the developing countries. Ironically, in the last years, the population has also been a victim of obesity, cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) in the lower-income countries[19].

In the meantime, although we are indeed experiencing an epidemiological transition to CD-NCDs, ID caused by emerging pathogens, such as SARS-CoV-2, and re-emerging pathogens, due to drug-resistant bacteria, represents a real and current threat globally.

Health Costs of Communicable and Chronic Non-Communicable Degenerative Diseases

ID occurs or emerges in cases where the immune system fails to eliminate infectious pathogens. Therefore, IDs represent a significant burden on public health and economic stability of societies around the world[20].

Yearly, worldwide at least 25% of deaths are related to ID[21]. They are represented in part by the neglected diseases (i.e., malaria, diarrheal diseases, tuberculosis, etc.)[20].

Paramyxovirus influenza is one of the largest ID in the world. The Spanish flu epidemic of 1918-1919, which killed more people than the World War I and more people than the human immunodeficiency Virus (HIV)/AIDS pandemic, is considered the most devastating in human history and a global disaster[22].

Seasonal influenza causes annual epidemics, representing a major public health and economic problem for our society[23]. Analyzing the direct (hospitalizations, visits, drug therapies) and indirect (loss of production and absence from work) costs in general population, on elderly patients and children, vaccination was found to be the most economical or profitable intervention[24].

IDs determine disability and death, especially in developing countries, costing billions of dollars year after year[25].

The increase in chronic diseases and the aging of the population are inevitably accompanied by multimorbidity, which obliges the Healthcare Systems to guarantee new assistance services and to pay more attention to primary and secondary prevention[2].

In Europe, it is estimated that chronic diseases are responsible for 86% of all deaths and an estimated health expenditure of around 700 billion euros per year[26].

CDNCDs are more frequent in the adult age groups: 53.0% already suffer in the 55-59 age group and among people over seventy-five the share reaches 85.3%. In the calculation of healthcare costs, deaths from communicable diseases must be added to deaths from CDNCDs. In 2016, 5,959,950 deaths from ID were counted. For the same year, however, there are 40,507,599 deaths from non-communicable diseases[27]. The projection to 2060 seems to maintain this trend: 7,805,122 deaths from ID, and 52,461,236 deaths from non-communicable diseases. Healthcare spending tends to grow exponentially with increasing age groups[28].

Considering that more than 859,000 Americans die of heart disease or stroke every year, the cost of healthcare system is around $199 billion per year and causing $131 billion in lost productivity on the job[28]. In 2017, the total estimated cost of diagnosed T2DM was $327 billion in medical costs and lost productivity[29] and the costs of treating Alzheimer's disease were estimated around $215 billion[30]. The total health expenditure is alarming.

Health and Social Costs of Obesity Disease

The most effective strategies in the fight against CDNCDs may start from the prevention of obesity, as well as by the early diagnosis of prediabetes, the main risk factors[12].

Obesity is a disease defined as excessive of body fat, presenting health risks because of adiposopathy, sustained by adipocyte hypertrophy, visceral adiposity and/or ectopic fat deposition and the secretion of a plethora of proinflammatory cytokines[31]. The adiposopathy determines the dysregulation of the metabolic pathways, leading to atherosclerosis, hypertension, dyslipidemia, T2DM, hyperandrogenemia in women and hypoandrogenemia/hyperestrogenemia in men[32].

Obesity and related diseases are associated with an annual social cost between 6 and 16 billion dollars (between 4 and 10% of public health expenditure). In addition, the data showed that the patient suffering from obesity costs 25% more to the National Health Service than a normal-weight patient and the cost increases with the increase in body weight: individuals with BMI between 35.0 and 40.0 kg/m^2 generate more than 50% of the expenditure of normal-weight people, while individuals with BMI greater than 40.0 kg/m2 double their spending (an increase of 100%)[33]. Considering an average life expectancy of about 83 years, the total cost of an obese individual is over 141,000 euros. Each increase in BMI of 1 point above 30.0 kg/m2 increases annual medical expenditure by 8%[33].

Obesity has become one of our major global health and economic problems[34]. Overweight and obesity are comparable to a global pandemic because, as estimated by the World Health Organization, the worldwide obesity prevalence of nearly tripled between 1975 and 2016. In fact, in 2016, more than 1.9 billion adults aged 18 years and older were overweight. Of these, over 650 million adults were obese and over 340 million children and adolescents aged 5-19 were overweight or obese. Obesity, strongly linked to child poverty, has its roots in a society characterized by gross inequalities[35]. The prevalence of overweight and obesity among children and adolescents aged 5-19 has risen dramatically from just 4% in 1975 to over 18% in 2016. In 2019, an estimated 38.2 million children under the age of 5 years were overweight or obese.

Overweight and obesity caused more deaths worldwide than underweight. Excess fat is no longer a problem exclusive of high-income countries, but is now on the rise in LMICs, particularly in urban settings. Globally, more people are obese than underweight, except in some regions of sub-Saharan Africa and Asia[36]. In Africa, the number of overweight children under five years has increased by nearly 24% since 2000. Almost half of the children under five years who were overweight or obese in 2019 lived in Asia[36]. By 2030, it was also predicted that 60% of the world's population, i.e., 3.3 billion people, could be overweight (2.2 billion) or obese (1.1 billion)[37].

In the light of the data above, obesity has important consequences for morbidity, disability and quality of life and lead to a higher risk of developing T2DM, CVDs including a higher prevalence of heart failure, hypertension and coronary heart disease, cancer, osteoarthritis, obstructive sleep apnea, symptoms of breathlessness and asthma, non-alcoholic fatty liver disease and its transition to non-alcoholic steatohepatitis[38]. Psychosocial and psychiatric consequences of obesity are also increasingly recognized[37]. In 2010, overweight and obesity were estimated to cause 3.4 million deaths, 4% of years of life lost, and 4% of DALYs[37].

The Global Economic Impact of Obesity

The global economic impact of obesity is approximately $2 trillion, or 2.8 percent of global Gross Domestic Product (GDP), reflecting the fact that obesity places a burden on both developed and developing economies[39].

The whole of Europe spends between 1.9% and 4.7% of the total annual healthcare costs and 2.8% of the annual hospital costs on the treatment of overweight or obese patients[40].

Indirect costs are attributed to the person's absence from work or the loss of productivity related to the disease. Intangible costs must be considered, such as the quality of life, including social life[41,42].

According to a study on the cost of four obese-related comorbidities, the direct medical costs due to obesity and related comorbidities (T2DM, hypertension, stroke and myocardial infarction) were €1343-2699 million, plus the costs due to comorbidities which amounted to €2701-5682 million[43].

In the US, the annual direct medical cost of overweight and obesity has been estimated to be approximately $266 and $1,723 higher, respectively, than that of normal-weight patients[44]. Moreover, American Diabetes Association estimated that the annual cost of diabetes in medical expenditures and lost productivity went from $132 billion in 2002 to $174 billion in 2007. The same trend was confirmed by the Centers for Disease Control and Prevention and the American Heart Association, which estimated the direct and indirect cost of CVD at $403.1 billion in 2006. Although some cost for overweight/obesity, diabetes, and heart disease may be overestimated, it is important to understand the magnitude of costs that could potentially be saved by better prevention and treatment of obesity[44].

In Latin America, as in other parts of the world, awareness of the economic and social impacts of obesity is low, although the costs are already high and rising. In Chile, the costs of obesity are estimated to account for 0.54% of GDP in 2016[45]. In Mexico, BMI-related diseases are estimated to have cost the Country US$ 806 million in 2010, rising to US$ 1.2 billion by 2017, for about 2.5% of GDP[46]. In Brazil, the healthcare costs associated with obesity are expected to double by 2050[47].

Increased prosperity and economic wellness in Asia and the Pacific lead to lifestyle changes with unexpected impacts in health and increased morbidity[48]. The Asian continent is still struggling against poverty with economic stagnation. While underweight is still a critical issue in some regions, the rate of overweight and obesity continue to rise in emerging countries. It is difficult to identify immediate nutritional interventions, although the importance of nutrition is well recognized for social and economic development. In recent years, attention to the economic evaluation of nutrition interventions has increased[49]. Over 80% of CVDs and T2DM burden are now found in low- and middle-income Asian countries[50]. Two in five adults, 1 billion people, are considered overweight or obese[51].

There is a relatively low prevalence rate of overweight and obesity in Japan and the Republic of Korea, although direct and total health costs are quite high. The same is true of the fast-growing economies of Southeast Asia, such as Singapore, where absolute direct costs are among the highest in the region. Indonesia, Thailand and the Philippines have comparable total direct costs, as do Central and Western Asia. South Asian countries, compared to other regions, have the lowest percentage of diret costs. Indirect costs are relatively similar to other countries and India has the highest absolute indirect costs[51].

Despite a high prevalence of infections on African continent, CDNCDs, particularly T2DM, contribute substantially to morbidity and mortality. In Africa, economic growth and subsequent rapid urbanization have led to a thriving, richer middle class, but with dramatic changes in diet and physical activity, contributing to the development of obesity[52]. Worldwide, diabetes and its complications involve catastrophic financial costs to the healthcare system. Future projections show that Africa will have the greatest increase in both diabetes burden and its complications but will contribute the least to global annual costs of diabetes care. In 2017, the International Diabetes Federation estimated the total healthcare expenditure due to diabetes at $3.3 billion. Specifically in Nigeria the costs have been estimated to be $1.639 billion per year. Surprisingly, in Sudan, the direct cost of T2DM control was $175 per year which included the cost of medications and outpatient care[53].

In Australia, studies confirmed that direct costs and government subsidies were higher for overweight and obesity compared to normal weight patients. Costs are likely to be much higher in those with known diabetes. It has been estimated that obesity cost the Australian economy $8.6 billion in 2011-12. It is also estimated that by 2024-25 a greater percentage of Australians will be obese class III (BMI of 40.0 kg/m^2 or more), with higher health risks and costs[54]. Due to the high immigration rate that characterized the Australian continent, there is evidence of ethnic differences in overweight and obesity[55].

Obesity costs are not expected to stabilize at any time in the near future. This ensures immediate and effective strategies to counteract the ever-increasing financial burden and decreasing quality of life[56].

Criticality of the Quality of the Diet as Cause or Prevention of Diseases

The impact on chronic diseases attributable to a potential improvement of the global food quality was analyzed only based on specific dietary factors (fruit, vegetables, legumes, cereals, etc.) but not compared to adherence to a "healthy" dietary model. Beyond the panorama of social costs, the effect of processed foods on food choice and self-control must be considered. Today, we must also deal with a new category of food, processed foods, also described as "junk-food," which is not only characterized by poor quality but is also addictive, leading to overeating, compulsions to eat and loss of control[57,58].

Afshin et al[59] underlined how global food consumption levels in relation to the main dietary factors associated with chronic diseases were suboptimal and that the main contributing factors to deaths were: a) reduced consumption of fruit (4.9 million attributable deaths/year), vegetables (1.8 million), nuts and seeds (2.5 million) and whole grains (1.7 million); b) high sodium consumption (3.1 million).

Wang et al[60] developed an alternative and complementary approach to assess the healthful effect of the diet on the prevention of chronic pathologies and explain the complex interrelationships between the individual dietary components and the chronic pathologies, calculating a score or index (AHEI, Alternate Healthy Eating Index), which summarizes individual adherence to different healthy dietary criteria based on scientific evidence.

A key point in the calculation of the disease load attributable to a dietary factor is the biological effect estimated as a relative risk of developing a pathology, adjusted for a specific dietary factor[61]. An 8.3-point increase in AHEI from 1999 to 2012 prevented 1.1 million premature deaths in the United States[62].

Biological effects can be generalized to a larger population. The quality of the global diet is slowly improving but remains far from optimal and varies from country to country. Improvements in diet quality have the potential to substantially reduce mortality rates.

The global average AHEI score increased modestly from 45.4 to 50.0, in the latest years. The quality of the diet varies substantially worldwide. The coastal countries of the Mediterranean, Caribbean and East Asia (except China and China Mongolia) have a higher AHEI score, while Central Asia, the South Pacific and Eastern and Northern Europe report lower scores.

Large inequalities in life expectancy exist not only based on sex, but also based on socioeconomic status, educational level, income, occupational group, and above all by eating habits and lifestyle.

The Joint Action on Nutrition and Physical Activity 2017 (JANPA) used the economic assessment of the obesity costs to encourage public action and to identify sectoral and lifetime approaches to prevent obesity, sedentary lifestyle and unhealthy nutrition[63].

Several behavioral and environmental factors have contributed to the long-term increase in obesity rates and related CDNCDs, including the widespread availability of high-energy foods, ultra-processed foods, and an increasingly sedentary lifestyle[64].

These factors have created obesogenic environments, putting people at greater risk, especially those belonging to socially disadvantaged groups. In particular, the obesogenic endocrine disruptors (obesogens) are chemicals potentially involved in weight gain by promoting adipogenesis and lipid accumulation and altering lipid homeostasis[65]. Unhealthy eating pattern, dietary intake of contaminated foods and water, and inhalation of airborne pollutants represent the major sources of human exposure to endocrine-disrupting chemicals. This is of particular concern given the potential impact of overweight and obesity on CDNCDs, such as CVDs, T2DM and cancers[66].

Many CDNCDs deaths could be prevented by addressing some of the major risk factors, as diet, smoking and physical activity. A growing number of countries have adopted policies to prevent and reverse the further spread of obesity[67].

Western diet represents the typical nutrient-poor food basket. They lack in micronutrients, antioxidants and polyphenols, while they are rich in highly processed and calorie-dense foods, environmental and process contaminants[32]. Moreover, these low-quality dietary patterns are poor in immunonutrients (Omega 3 Fatty Acids, Vitamin C, Arginine, Glutamine, Selenium, Zinc, Vitamin, E and Vitamin D), which can play a key role in improving immune responses against viral infections[68]. Although there are conflicting evidences, dietary supplementation with some nutrients, such as vitamin D and zinc, may modulate immune function[68,69].

Interestingly, recent findings underlined the potential regulatory mechanism of Vitamin D in suppressing cytokine storm and reducing viral load in SARS-CoV-2 infection[70-72]. Immune system dysfunction is considered to increase the risk of viral infections, such as SARS-CoV-2, especially in patients with obesity[73].

Therefore, a dietary quality shift towards the optimal healthy reference diet could prevent million premature deaths[74].

Role of Obesity and Comorbidity in Different Population Risk Categories and Mortality for COVID-19

The overfed malnourished as well as the undernourished malnourished patient have the same risk of impaired immune system[75].

Chronic diseases, such as obesity, have been recognized as predisposing factors to a worse outcome of severe COVID-19 disease[76-78]. CD-NCDs are usually coupled to protein-energy malnutrition, which is demonstrated to impair immune cell activation. This allows longer viral persistence and increased dealing of pro-inflammatory factors[77].

COVID-19 symptoms range from asymptomatic to death[79], across a broad clinical spectrum, from fever, cough, myalgia, fatigue, dyspnea, progressive respiratory failure, intestinal symptoms, pneumonia, acute respiratory distress syndrome (ARDS) myocarditis, and organ insufficiency, until death[80]. The presence of one or more comorbidities, such as hypertension, obesity, chronic lung disease, T2DM, kidney disease and CVDs, makes the course of COVID-19 more aggravating[81]. Moreover, some COVID-19 patients develop interstitial pneumonia that can evolve into ARDS[82].

The most critical conditions that led to hospitalization in the intensive care unit (ICU), with the need for mechanical ventilation, were observed in those patients with inspired oxygen fraction (FiO2) lower than 60%[83]. Dramatically, over 50% of COVID-19 patients needed respiratory support.

At the base of the critical conditions in patients with COVID-19 there is an excessive pro-inflammatory response, with a massive release of interleukins (IL) IL-1β, IL-6 and tumor necrosis factor (TNF)-α and various chemokines[84], such as CXCL-10, RANTES/CCL-5, MCP-1 and similar[85], in conjunction with a release of anti-inflammatory cytokines[80].

Patients affected by COVID-19 showed a markedly higher level of specific agents such as IL-1ß, IFN-γ, IP-10 and as well for the monocyte chemoattractant protein-1, that are involved in triggering an immune response, together with a series of inflammatory markers[85-86].

COVID-19 patients with obesity and comorbidities were more exposed to an evolution in ARDS, requiring mechanical ventilation and ICU hospitalization[83].

Finally, obesity is characterized by a low-grade inflammation with increased leptin level and reduced adiponectin; in this context, the SARS-CoV-2 virus is more prone to be internalized into adipocytes and enhance the "cytokine storm", typical characterization of COVID-19 disease[87-89].

Hussein et al[90] described some mortality COVID-19 risk factors such as an age over 70 and BMI greater than 25.0 kg/m^2. Moreover, patients with obesity need an advanced respiratory support respect to normal weight[91-92].

Of interest, OSAS can also potentially exacerbate inflammation in COVID-19-related sepsis or ARDS. For these patients it would be useful to apply a Non-Invasive Ventilation (NIV) that helps them to contrast the respiratory syndrome linked to SARS-CoV-2 infection. NIV, however, generates aerosol droplets that increase viral transmission risk[93].

Several studies about COVID-19 reports and diagnosis demonstrated that SARS-CoV-2 has a disproportionate impact on different population groups, like people living in poor world areas, which are also affected by different obesity phenotypes[35].

Europe is the continent most affected by CD-NCDs-related morbidity and mortality[27].

Restrictive measures during the COVID-19 lockdown caused a reduction in accessing healthy food and maintaining appropriate levels of physical activity[94]. Furthermore, quarantine was associated also to a worsening of sleep quality and to an increase in BMI values[95]. This leads to increased risk of obesity, T2DM and relative CVDs. In particular, Italy was the second most affected Country in the world by the COVID-19 pandemic in March 2020 and a recent report revealed that most of patients (96.2%) who died in hospital due to COVID-19 had comorbidities, mainly CD-NCDs[96].

The African American population has a higher COVID-19 mortality, considering the incidence of other comorbidities. Social factors contribute to increase the risk of coronavirus exposure, due also to live in densely populated areas, with limited compliance with COVID-19 rules[97].

The different burden of COVID-19 on certain groups overlaps with variations in the prevalence of obesity. For example, black women are most affected compared to white and Asian women[98].

In the United States, the first cause of death is a poor diet and an unhealthy lifestyle. Nutritional disparities all over the country are driven by socioeconomic, educational, and environ-

mental disadvantages that have affected vulnerable communities in the past and persist even today. People experiencing food insecurity have mainly access to low-cost and energy-dense ultra-processed food[6].

Obesity and nutritional health disparities are closely correlated with the alarming ethnic disparities related to COVID-19[6]. Historically, ethnic minority groups had not equal opportunities for economic, physical and mental health, and these inequities increased the risk of being unhealthy and/or dying from severe infections such as COVID-19 (Figure 1).

Many of these factors are contributing to the higher level of obesity in some racial and ethnic minority groups[99].

In particular, Black, Latin and Native Americans are among the most affected by SARS-CoV-2 infection and high mortality. Compared to White Americans, hospitalization rates for COVID-19 among Native Americans and Black Americans are approximately five and four and a half times higher respectively, while Latin Americans have been hospitalized about four times higher. Black adults, Hispanic and non-Hispanic, have a higher prevalence of obesity and are more prone to suffer from worse COVID-19 symptoms[6].

Another important example should be found in Indian population. India is the second country in the world for infected people. In this Country comorbid conditions play a key role in COVID-19 infection, linked to malnutrition. Also, viral infections, such as HIV, and malaria-related deaths could contribute to worsen Indian health scenario, because people with COVID-19 and these diseases interrupt suddenly therapies and expose more to Coronavirus infection[100].

In China, older SARS-CoV-2 patients had a more severe course in the presence of comorbidities. Among these, CVD and T2DM are the main causes of mortality, followed by chronic respiratory diseases, hypertension and cancer[101].

Information about COVID-19 Russia's situation is lacking. Published data focuses only on the importance of psychiatric service during the growing fear in lockdown. Psychological and psychotherapeutic support to the most vulnerable groups and the management of the mentally ill with severe acute respiratory syndrome has been one of the most followed practices in SARS-CoV-2 comorbidities[102].

Concluding the world panorama, in Australia, the death rate and the proportion of cases requiring hospitalization remained below the

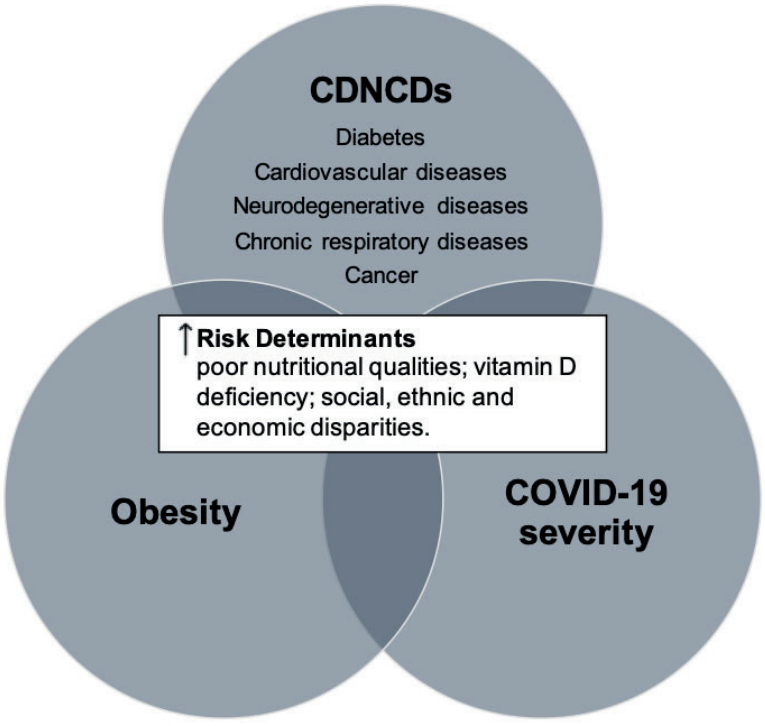

Figure 1. The relationship between nutritional and socio-economic inequalities in CDNCDs, obesity, and COVID-19. CDNCDs: Chronic Degenerative Non-Communicable Diseases.

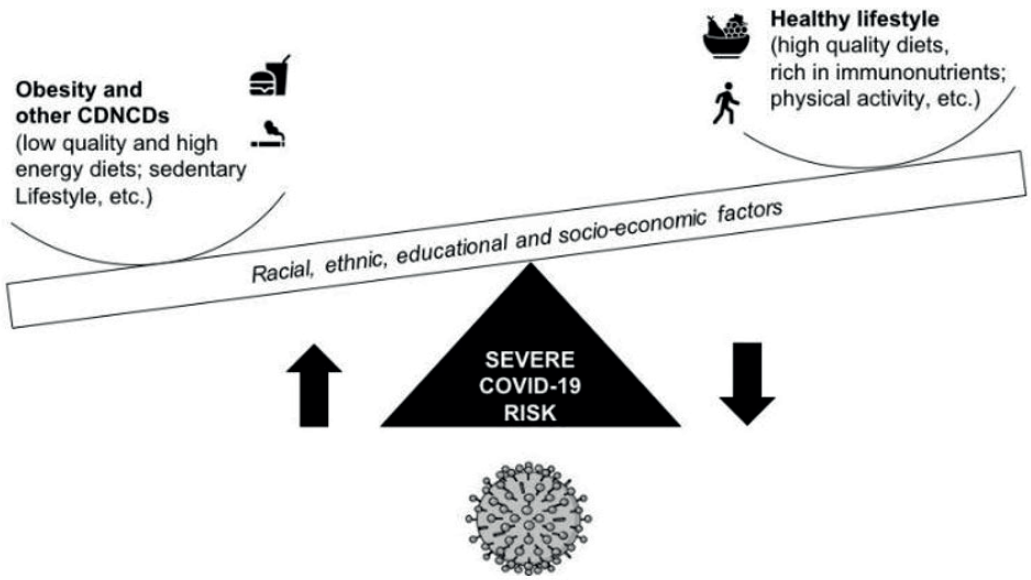

Figure 2. The role of obesity and CDNCDs comorbidities in the risk of developing severe COVID-19.

corresponding values reported by other comparable high-income Countries. The most reported comorbidities among hospitalization cases were CVD (19%), T2DM (18%) and chronic respiratory conditions (13%) and the comorbidities conditions among COVID-19 cases admitted to the ICU were T2DM (26%) and CVD (21%), both conditions related to obesity[103].

Many studies have been published about relationships between obesity in different people groups and COVID-19 infection worsening (Figure 2). However, there are several limitations in the current evidence for a link between Coronavirus and obesity, as strategies are different, COVID-19 exposure is unequal and sample size is often small. This important aspect needs to be investigated further.

In Table I and Table II literature findings are summarized to highlighted the health and social costs of obesity disease and the role of obesity and comorbidity in different population risk categories and mortality for COVID-19.

Food Safety and Food Quality

The topic of food is relevant within contemporary societies for many reasons, including the social and environmental effects of food.

Consumption patterns and their consequences are a function of both income and lifestyle. Currently, the World is grappling with significant burdens of malnutrition, overweight and obesity[104]. Nutritional transitions represent both an opportunity and a threat to the health and wellbeing of populations worldwide. Low-quality but high-energy diets contribute to the increase of diet-related obesity and CDNCDs[105].

Unhealthy diets are usually in conflict with the four principles of a healthy diet, with nutrient-poor foods replacing nutrient-rich foods[106]. Characterized by low consumption of fruits, vegetables, whole grains, nuts and seeds, milk and seafood, unhealthy diets lack the necessary micro- and macronutrients for the protection against obesity and related-CNCDs. These diets might also contain highly processed foods, high content of trans-fats, sodium and added sugars, as well as red meat, processed meats and sugar-sweetened beverages (SSBs)[107].

Obesity depends on wrong food choices and on a progressive process of deconstructing and individualizing meals[108]. Moreover, the social repercussions of eating disorders concern life expectancy and diseases that affect the health care systems. Nutritional education is the privileged tool to tackle the problem.

For lifestyle and food changes promotion, operators are required communication and persuasion skills, such as to overcome food convictions[109].

Moreover, the role of health education programs in increasing knowledge and improving attitudes to inadequate diet and physical activity is demonstrated[110]. New approaches in self-initiated care in the CDNCDs prevention are successful in promoting community health, leading to the strengthening of positive health approaches.

Table I. Health and social costs of obesity disease.

Title	Nation/Country	Aim	References
Why primary obesity is a disease?	/	Revision of the literature aiming to define obesity as diseases and highlight the limits and the inaccuracy of common tools used for the diagnosis of obesity.	De Lorenzo et al (2019)[31]
Obesity: A preventable, treatable, but relapsing disease	USA	Discussion over the criteria for defining primary obesity as a disease.	De Lorenzo et al (2020)[32]
Excess body weight increases the burden of age-associated chronic diseases and their associated health care expenditures	Italy	Determine the net health costs of excessive adiposity and associated age-related chronic diseases.	Atella et al (2015)[33]
The Obesity Crisis, How to fight a Scourge as damaging to the Global Economy as War	/	Analysis of the impact of obesity on the quality of life, and development of a comprehensive catalog of interventions that could be used to reduce its prevalence.	Dobbs et al (2015)[34]
Tackling poverty, treating obesity: a 'whole system' approach	UK	Statistical analysis of data supporting the link between poverty and obesity	Hayre et al (2020)[35]
World Health Organization Obesity and overweight	/	General overview on obesity and overweight: definition, causes, consequences and strategies to reduce its burden.	WHO (2020)[36]
European Guidelines for Obesity Management in Adults	/	General overview on obesity with focus on the best strategies to tackle this disease	Yumuk et al (2015)[37]
The importance of a correct diagnosis of obesity	/	Importance of identify the specific sub-group of obesity to better manage the patients	Gualtieri et al (2020)[38]
Economic burden of obesity: A systematic literature review	/	To assess the economic burden of obesity and to identify, measure and describe the different obesity-related diseases included in the selected studies	Tremmel et al (2017)[39]
Economic costs of adult obesity: A review of recent European studies with a focus on subgroup-specific costs	Europe	Update on economic costs of obesity in Europe, with a focus on variables such as sex, age, socio-economic status, and morbidity factors.	Von Lengerke et al (2011)[40]
Economic costs of overweight and obesity	/	Brief overview of selected economic consequences associated with excess of weight.	Lehnert et al (2013)[41]
Obesity Epidemiology: From Aetiology to Public Health	/	Scholarly text providing a general overview of obesity: prevalence and trends; health, social, and economic consequences; the underlying causes of the obesity epidemic, the existing evidence regarding strategies to prevent it.	Crawford et al (2010)[42]
Economic burden of obesity and its complications in Germany	Germany	To estimate the burden of obesity and selected comorbidities in terms of health outcome and costs to society in Germany.	Sander et al (2003)[43]
The direct and indirect costs of both overweight and obesity: A systematic review	Irish	Analysis of studies that focus on the economic burden of obesity and the lack of homogeneity in their structure	Dee et al (2014)[44]
Diagnóstico del estado nutricional de mesnores de 6 años, gestantes, nodrizas y adultos mayores, bajo control en el Sistema público de salud	Chile	Report providing systematized information on the nutritional status of the population under control in the public health system in 2013 in the different regions and Health Services of the country.	Chile Ministry of Health, G. of C. (2013)[45]
Obesity prevalence in Mexico: impact on health and economic burden	Mexico	Overview of the impact of public health policies at both national and regional levels based on Mexican Health and Nutrition Surveys 1999 and 2000, and Mexican National Health and Nutrition Survey 2006.	Rtveladze et al (2014)[46]
Health and Economic Burden of Obesity in Brazil	Brazil	To measure the future consequences of the obesity epidemic on the health care costs.	Rtveladze et al (2013)[47]
Fiscal policies for diet and the prevention of noncommunicable diseases	/	Report of the Geneva technical meeting of global experts in fiscal policies. The objectives of the meeting were to review evidence and existing guidance, discuss country case studies and provide considerations with regards to the scope, design and implementation of effective fiscal policies on diet.	World Health Organization. (2015)[48]
Health economics of nutrition intervention in Asia: Cost of malnutrition	Asia	Review of the economic impact of nutrition problems and interventions aimed at their resolution in Asia.	Mizumoto et al (2015)[49]
Cost-effectiveness of interventions to control cardiovascular diseases and diabetes mellitus in South Asia: A systematic review	Asia	Systematic review on the cost-effectiveness of individual-, group- and population-level interventions to control cardiovascular disease and diabetes in South Asia.	Singh et al (2018)[50]
Wealthy But Unhealthy: Overweight and Obesity in Asia and the Pacific: Trends, Costs, and Policies for Better Health	Asia	Book examining the trends and prevalence and economic costs of obesity and overweight, as well as policy recommendations.	Helble et al (2018)[51]
Trends in obesity and diabetes across Africa from 1980 to 2014: An analysis of pooled population-based studies	Africa	To estimate trends from 1980 to 2014 in age-standardized mean body mass index (BMI) and diabetes prevalence in Africa, in order to assess the co-progression and assist policy formulation.	NCD Risk Factor Collaboration (NCD-RisC) – Africa Working Group. (2017)52
Economic Impact of Diabetes in Africa	Africa	To assess the economic burden of diabetes in Africa, and to describe the way forward in tackling the epidemic of this disease.	Mapa-Tassou et al (2019)[53]
Weighing the cost of obesity: A case for action	Australia	Study on the additional costs of obesity and benefits of intervention in Australia	PwC Australia. (2015)[54]
Ethnic differences in overweight and obesity and the influence of acculturation on immigrant bodyweight: Evidence from a national sample of Australian adults	Australia	To examine ethnic differences in body mass index (BMI) and overweight/obesity in Australia, and the influence of acculturation on bodyweight among Australian immigrants.	Menigoz et al (2016)[55]
Getting to grips with the obesity epidemic in Europe	Europe	Review of the literature regarding obesity and its impact on the economy	Cuschieri et al (2016)[56]

Table II. Role of obesity comorbidity or risk factors on infectious diseases.

Comorbidity/Risk Factor	Nation	Aim	References
Malnutrition	International	Literature review focusing on the link between deficient nutrition, immunodeficiency, and susceptibility to infectious diseases.	Katona et al (2008)[75]
Obesity	International	Literature review analysing obesity-related factors that can contribute to the development of COVID-19-related illnesses.	Alberca et al (2020)[76]
Obesity	USA	Analysis of estimates costs of obesity for the United States in separate categories for inpatient, non-inpatient, and prescription drug spending.	Finkelstein et al (2009)[77]
Diabetes	France	Multicentre observational study in people with diabetes hospitalised for COVID-19 in 53 French centres.	Cariou et al (2020)[78]
Hypertension; diabetes; cardiovascular disease; cerebrovascular disease	China	Analysis of epidemiological, demographic, clinical, laboratory, radiological, and treatment data of 138 consecutive hospitalized patients with confirmed novel coronavirus-infected pneumoniae.	Wang et al (2020)[79]
Diabetes; hypertension; cardiovascular disease	China	Epidemiological, clinical, laboratory, radiological characteristics and treatment and clinical outcomes of 41 patients with laboratory-confirmed 2019-nCoV infection.	Huang et al (2020)[80]
Hypertension; obesity; chronic lung disease; diabetes; cardiovascular disease	USA	Report presenting age-stratified COVID-19-associated hospitalization rates and clinical data for patients admitted in March 2020.	Garg et al (2020)[81]
Hypertension; diabetes	China	Retrospective cohort study describing the clinical characteristics and outcomes in 201 patients with COVID-19 pneumonia who developed acute respiratory distress syndrome (ARDS) or died.	Wu et al (2020)[82]
Diabetes	Canada	Retrospective case series of 38 adult patients with SARS-related critical illness admitted to 13 intensive care units (ICUs) in the Toronto area.	Fowler et al (2003)[83]
Obesity; diabetes; hypertension	/	Analysis of the link between obesity and severe COVID disease	Sattar et al (2020)87
Diabetes; hypertension; cardiovascular disease; obesity	/	Systematic assessment of potential prognostic factors in patients with diabetes with COVID-19.	Apicella et al (2020)[88]
Obesity	France	Retrospective cohort study including 124 patients admitted in the intensive care unit of a single French center for SARS-CoV-2.	Muscogiuri et al (2020)[89]
Obesity; diabetes	/	Overview of the current evidence on the link between OSA, obesity, and disturbed glucose homeostasis.	Pugliese et al (2020)[91]
Obesity	/	Analysis of the possible pathophysiological mechanisms (hormonal and metabolic) that link obesity and sleep disturbances.	Muscogiuri et al (2019)[92]
Obesity; obstructive sleep apnea	/	Analysis of the possible link between obstructive sleep apnea and COVID-19 disease severity.	Suen et al (2020)[93]
Obesity	Italy	Analysis of the impact of the COVID-19 pandemic on eating habits and lifestyle changes among the Italian population aged ≥ 12 years.	Di Renzo et al (2020)[94]
Obesity	Italy	Investigation on the effect of quarantine on sleep quality and body mass index (BMI).	Barrea et al (2020)[95]
Hypertension, diabetes	USA	Review of the literature ragarding hypertension, African Americans and COVID-19	Ferdinand et al (2020)[97]
Obesity	/	Evidence-based insights on the relationship between excess weight and COVID-19	Public Health England (2020)[98]
Obesity	/	Obesity as a negative prognostic factor in COVID-19 disease	Centre for disease control and prevention (2020)[99]
Diabetes; hypertension; cardiovascular disease	India	Discussion over the socio-economic, health and National healthcare challenges following lockdown, with focus on population belonging to low socio-economic stratum.	Gopalan et al (2020)[100]
Obesity; cardiovascular disease; diabetes mellitus; fchronic respiratory diseases; hypertension; cancer	/	Discussion over the prognostic importance of anthropometric and metabolic parameters in COVID-19 disease	Stefan et al (2020)[101]
Diabetes	Australia	Report on the measures taken by the Australian government to contain the COVID-19 pandemic, and their effect on the national health care system, with particular focus on the impact on diabetes care	Andrikopoulos et al (2020)[103]

Food quality and quantity are essential to improve health, nutrition and food security[111]. A sufficient food quantity refers to the ability to consume enough calories to support life, allow physical activity and maintain a healthy body weight[112].

Attaining enough food is a challenge in LMICs, where food insecurity, food deserts and undernutrition is widespread. While undernutrition occurs due to a lower-than-average calorie intake, moderate food insecurity is characterized by both reduced food quality and quantity[113]. In high-income areas where there is a large supply of food, the challenge is to limit excess caloric intake to reduce overweight, obesity and diet-related diseases[64]. However, an increasing trend in low-income communities, located within high-income Countries, is food insecurity and micronutrient deficiencies: individuals may consume enough calories (high quantity), but not enough essential nutrients (low quality). While it is still debating on which food should be classified as "healthy" and "unhealthy", many argue that diets should be evaluated holistically, through dietary patterns[114] or the nutrient density of foods[115]. Food safety describes the impact and potential hazards that food may cause for human health[116]. Safe foods are those that are free from pathogens, chemicals or contamination. In turn, food safety regulations and controls ensure that a food product's nutrient density remains intact upon consumption[117].

Fung et al[118] evaluated that dietary quality, defined by healthy diet indices (e.g. Mediterranean Diet, AHEI and Dietary Approaches to Stop Hypertension diet), was associated to lower weight gain in 4 years, with greater benefits observed in overweight women. These healthy dietary patterns are characterized by a high consumption of plant food (whole grains, fruits, vegetables, legumes, seeds, oil and nuts), moderate consumption of dairy products and seafood, and low intake of meat and processed food[117].

A healthy diet is perceived as one that effectively prevents the onset of obesity, and malnutrition in all its forms (i.e., underweight, overweight/obesity and micronutrient deficiencies), even in emergency situations, such as the COVID-19 pandemic.

Conclusions

A lot of studies had been published about correlations between obesity in different people groups and COVID-19 infection worsening[119]. What emerges from this global scenario is the social inequality accentuated by the COVID-19 pandemic. In particular, social determinants of health (e.g., ethnic discrimination, access to healthcare and healthy food, socioeconomic status and education), obesity, chronic diseases and severe COVID-19 outcomes are all interrelated. Therefore, it is not possible to deny the relationship between CDNCDs and viral infection susceptibility, between economic crisis and nutritional quality, increase in health expenditure and level of health care.In the light of all the health expenditures that each Continent deals with, it would be fundamental to formulate a multidisciplinary strategy to fight the depletion of the individual health status and the predisposition to viral infection and other exogenous risk factors[119-120].

It is evident that social inequality implies a different access to food and a different household expense for food. In low-income Countries, in turn, access to cheap, high-calorie, low-quality junk food is growing, with an increase in obesity. In these same Countries, however, the risk of spreading viral diseases is higher, which is not followed by proper and equitable health care.

Considering this scenario, policy actions will be necessary to improve access to quality food, so as to fight and prevent obesity and malnutrition in general. Furthermore, health inequalities in Europe affect the average life expectancy of around 5 years, when considering a state of good health[120].

In conclusion, the goals are to make all Countries less vulnerable to CDNCDs, which facilitate the spread and virulence of viruses and that Health Systems realize an implementation plan to reduce the burden of health expenditure and social costs and safeguard the population vulnerability.

Conflict of Interests

The authors declare that they have no conflict of interests.

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