EDITORIAL

OBESITY: THE COVERED RISK OF CANCER

Almost all developed and developing nations now experience a sharp increase in the incidence of overweight and obesity, which affects 60-70% of the adult population in industrialized nations and is more common in females and metropolitan regions (1). Overweight and obesity are now more common over the world than ever before-in adults, by 27%, and in children, by 47% (2). When a person's caloric intake exceeds their metabolic and physical activity-related energy expenditure, obesity results. Fat is deposited and accumulates as ectopic fat tissue, increasing the risk for several disease entities as a result of excessive or aberrant fat tissue formation that surpasses genetically and epigenetically established adipose tissue stores (3). The World Health Organization defines obesity as having a body mass index (BMI) ≥30 kg/m^2 (≥30 kg/m^2 as grade 1, ≥35 kg/m^2 as grade 2, and ≥40 kg/m^2 as grade 3), with normal values being between 18.5 to 24.9 kg/m^2 and overweight being intermediate values of 25 to 29.9 kg/m^2 respectively (4). According to these criteria, roughly 35% of adults in the USA over the age of 20 are already overweight, and the prevalence of obesity is expected to rise to 42% in persons over the age of 18 by 2030 (5).

With an estimated 14.1 million incident cases and 8.2 million fatalities per year, cancer ranks as the second largest cause of death globally (6). Obesity is a recognized risk factor for a number of cancers, in addition to the well-established cancer risks factors such as genetic predisposition, ionizing radiation, nicotine use, infections, unhealthy diet, alcohol intake, sedentary lifestyle, and other environmental exposures (7). Due to the rising prevalence of risk factors, particularly obesity and metabolic syndrome, cancer incidence will continue to rise (8).

According to global estimates, obesity and overweight were linked to 5.5% of cancer cases in the UK, while others asserted that the relative risk of cancer death linked to obesity was roughly 14.2% in men and 19.8% in women (9). The link between obesity and cancer is fairly strong, particularly when it comes to gastrointestinal (GI) tract tumors, where being overweight increases the risk of cancer by 1.5-2.4-fold. The types of cancer that are most strongly linked to obesity have been defined by several studies to include breast cancer in postmenopausal women, colorectal cancer (particularly in men), hepatocellular carcinoma, endometrial cancer, ovarian cancer, esophageal adenocarcinoma, gastric cancer, pancreatic cancer, gall bladder cancer, thyroid, kidney cancer, multiple myeloma and meningioma (10).

Numerous theories have been put out to explain how obesity may raise the risk of some malignancies. As a result of the release of mitogenic signals, the local microenvironment that supports tumor growth also drives cell survival mechanisms and the development of tolerance in cytotoxic host T cells (11). The overproduction of estrogen by fat tissue, also known as adipose tissue, has been linked to an increased

risk of developing breast, endometrial, ovarian, and other cancers. Increased blood levels of insulin and insulin-like growth factor-1 are common in obese people (IGF-1). Insulin resistance causes high insulin levels, or hyperinsulinemia, which precedes the onset of type 2 diabetes, another proven cancer risk factor. Increased insulin and IGF-1 levels have been linked to an increased risk of endometrial, renal, prostate, and colon cancers (12, 13).

Chronic inflammatory diseases like gallstones or non-alcoholic fatty liver disease are frequently seen in obese people. These circumstances can result in oxidative stress, which damages DNA and raises the risk of developing biliary tract and other malignancies (14). Adipokines, which are produced by fat cells, are hormones that can either promote or inhibit cell growth. For instance, as body fat accumulates, the blood level of an adipokine called leptin rises as well. Leptin levels above a certain point can encourage the development of abnormal cells. Adiponectin, another adipokine, may have antiproliferative properties that inhibit the development of tumors but is less prevalent in obese individuals than in individuals with a healthy weight. Mammalian targets of rapamycin (mTOR) and AMP-activated protein kinase are two more cell growth and metabolic regulators that fat cells may directly and indirectly affect. Obesity may also increase the risk of cancer by reducing tumor immunity and altering the mechanical characteristics of the tissue that surrounds growing tumors (13). Obesity can complicate screening and management in addition to having biological implications. Thus, women who are overweight or obese are more likely to get cervical cancer than women who are of a healthy weight, most likely as a result of less efficient cervical cancer screening in these people (15).

According to a nationwide cross-sectional study using BMI and cancer incidence data from the US Cancer Statistics database, from 2011 to 2015, about 74,690 new cases of cancer in women and 37,670 new cases of cancer in men aged 30 and older, respectively, were attributable to excess body weight (overweight, obesity, or severe obesity). As high as 51% for liver or gallbladder cancer and 49.2% for endometrial cancer in women and 48.8% for liver or gallbladder cancer and 30.6% for esophageal adenocarcinoma in males were among the percentages of cases where increased body weight was blamed (16). According to a recent study by Sung *et al.*, increased body weight contributed to almost 3.9% of all cancer cases globally in 2012 (544,300 cases), with women bearing a greater share of the burden (368,500 cases) than males (175,800 cases). Less than 1% of malignancies related to excess body weight occurred in low-income nations, while 7% to 8% occurred in several high-income Western nations as well as Middle Eastern and Northern African nations (17).

In several studies, it was discovered that obese individuals who reduced weight had lower rates of breast, endometrial, colon, and prostate cancers. For instance, a major prospective study of postmenopausal women found that an intentional weight loss of more than 5% was linked to a decreased risk of malignancies linked to obesity, including endometrial cancer. Unintentional weight reduction, however, was not linked in this study to a higher risk of cancer (18). Teras *et al.*, found that sustained weight loss was linked to a decreased risk of breast cancer among women more than 50 years old (19). Other scientific research has shown that bariatric surgery reduces

the risk of cancer overall, of hormone-related cancers including breast, endometrial, and prostate cancers, and of obesity-related malignancies such as postmenopausal breast cancer, endometrial cancer, and colon cancer in people with obesity, especially in women (20-22).

In conclusion, there is considerable evidence linking cancer, insulin resistance, adipokines, and chronic inflammation brought on by obesity. Determining the ontological function of adipocytokines and their interplay in obesity-related cancer etiology requires additional basic and translational study. It is anticipated that more prospective and long-term research would identify a wide range of obesity-related biomarkers and assess their clinical value in cancer prognosis and monitoring. With regard to public health, lifestyle therapies like weight loss, increased physical activity, dietary changes, and bariatric surgery may be able to reverse the malfunction and inflammation of the adipose tissue that is linked to obesity and may slow the development of cancer.

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