Review Article

A Confront on Cancer allied Diabetic Patients

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Abstract

Insulin resistance, hyperinsulinemia and changes in signaling of different hormones associated with diabetes may affect the risk of breast cancer. We reviewed epidemiologic studies of the association between and risk of different types of cancers and the available evidence on the role of certain mediators of an association between diabetes and cancer. Many evidences supports the modest association between type 2 diabetes and the risk of cancer, the mechanisms underlying an association between diabetes and cancer risk remain unclear, particularly because the 2 diseases share several risk factors, including obesity, a sedentary lifestyle. Although the metabolic syndrome is closely related to diabetes and embraces additional components that might influence cancer risk.

Keywords: Diabetes; Insulin; Liver; Pancreatic cancer; Carcinoma; Endometrial cancer; Tumor; Hormone; Obesity; Radiation therapy

Abbreviations: NASH: Nonalcoholic Steatohepatitis; HCC: Hepatocellular carcinoma; BMI: Body Mass Index; TURBT: Trans Urethral Resection of Bladder Tumor.

Introduction

People with Diabetes tend to have high levels of the blood-sugar-regulating hormone insulin [1, 2] as well as related hormones called insulin-like growth factors. Those hormones cause cells to grow and spread, and that may include cancer cells. About 80% of cancer patients have glucose intolerance or frank diabetes [3]. People with diabetes [4] have high blood sugar because their body cannot move sugar into fat, liver and muscle cells to be stored for energy. This is because either:

- Their pancreas does not make enough insulin

- Their cells do not respond to insulin normally [5]

There are three major types of diabetes. The causes and risk factors are different for each type

Type 1 diabetes can occur at any age, but it is most often diagnosed in children, teens, or young adults. In this disease, the body makes little or no insulin. Daily injections of insulin are needed. The exact cause is unknown [6].

Type 2 diabetes is the commonest form of diabetes. It most often occurs in adulthood, but teens and young adults are now being diagnosed with it because of high obesity rates. Many people with type 2 diabetes do not know they have it [7].

Gestational diabetes is high blood sugar that develops at any time during pregnancy in a woman who does not have diabetes.

People are now aware that the lack of physical activity that plagues the globe is directly related to the increase in obesity. Obesity has been linked to health problems such as heart disease and type 2 diabetes. People with lower muscle mass on their bodies have increased risk of developing insulin resistance, which put them at risk of developing diabetes. So, building muscles specifically could help keep diabetes away the fact that the muscle plays an important role in glucose breakdown, thus affecting the body's ability to manage blood glucose level [8].

People with diabetes [9] have twice the risk of cancers of liver [10], pancreas and the uterine lining and are at a greater risk for colorectal, breast and bladder cancers than the normal population. A link to other cancers is inconclusive at present. High insulin levels, high glucose levels and chronic inflammation often seen in diabetes may influence cancer development [11].

Present review converses on cancers in diabetic patients, mainly focusing on liver cancer, pancreatic cancer, endometrial cancer, colorectal cancer and bladder cancer.

Liver Cancer

Liver cancer (Hepatocellular carcinoma) is a cancer [12,13] arising from the liver. It is also known as primary liver cancer or hepatoma. The liver is made up of different cell types such as bile ducts, blood vessels, and fat-storing cells. Liver cells (hepatocytes) make up 80% of the liver tissue. Thus, the majority of primary liver cancers over 90%-95%arises from liver cells and is called hepatocellular cancer or carcinoma [14]. Chronic infection with hepatitis B and C virus [15,16], alcohol consumption [17,18] and cirrhosis of the liver are recognized risk factors for primary liver cancer. Patients with diabetes are at increased risk of developing primary liver cancer and perhaps cancers of the biliary tract. Patients with insulin-dependent diabetes mellitus and those with non-insulin-dependent diabetes mellitus differ in their risk for primary liver cancer and the risk is also affected by the type of diabetes treatment [19]. Diabetes can be the result of metabolic syndrome, and this increases the risk of nonalcoholic steatohepatitis (NASH) [20]. NASH can lead to various forms of liver cancer such as Acute Liver Failure, Abnormal Liver enzymes, and Hepatocellar Carcinoma. i.e., acute liver failure can be associated with diabetes [21]. This is the quick deterioration of the liver that is followed by or linked

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to liver cancer [22-24]. Abnormal liver enzymes can be found in the blood as a direct result of cholesterol-reducing medicine. This medicine is used to control symptoms of diabetes. Hepatocellar Carcinoma (HCC) is a type of liver cancer greatly associated with diabetes. A study done by The American Association for the Study of Liver Diseases found that hyperinsulinemia is a possible reason for the increase of HCC in diabetic patient [25]. Particularly type 2 diabetes and cancer [26-28] share many risk factors. Some medications or drugs [29-31] used to treat hyperglycemia are associated with either an increased or reduced risk of cancer. Cancer and diabetes are diagnosed within the same individual more frequently than would be expected by chance, even after adjusting for age [32,33]. Both diseases are complex, with multiple subtypes. Diabetes is typically divided into 2 major subtypes, type 1 and type 2, along with less common types, whereas cancer is typically classified by its anatomic origin such as lymphoma, leukemia, lung, breast and liver cancer [34-37] within which there may be multiple subtypes. This is because insulin is produced by pancreatic β cells and then transported via the portal vein to the liver. Both the liver and the pancreas are exposed to high concentrations of endogenously produced insulin. Diabetes-related factors including steatosis, nonalcoholic fatty liver disease, and cirrhosis may also enhance susceptibility to liver cancer [38-41]. Various symptoms of liver cancer [42-45] are Ascites ,Jaundice, Fever, Fatigue, Nausea ,Abdominal pain ,Loss of appetite ,Weight loss ,Pain in the back or abdomen or around the right shoulder blade, A hard lump just below the rib cage, Dark-coloured urine ,Internal bleeding . The **treatments for liver cancer** are Surgery, Radiation therapy, Chemotherapy and Percutaneous ethanol injection [**46-48**]. The new types for liver cancer treatment still in clinical trials are Hyperthermia therapy and Biologic therapy. So, the Patients with diabetes are at increased risk of developing primary liver cancer [49-52].

Pancreatic Cancer

Diabetes is a disease in which the body does not make or properly use a pancreatic hormone called insulin. Insulin helps the body utilize glucose efficiently. Normally, insulin allows glucose to enter cells to be used for energy. In people with diabetes, either the body does not produce enough insulin or the amount that is produced is not fully effective. Instead of entering cells, the glucose remains in the blood resulting in high blood glucose levels. High blood glucose can lead to cell damage and long-term complications. In general pancreatic cancer is two times more likely to occur in people who have diabetes than in people who do not have diabetes. Type 2 diabetes is associated with being overweight and is caused when the body becomes less responsive to the action of insulin, leading to high blood sugar levels. Type 1 diabetes arises, often in childhood, when the insulin-producing cells in the pancreas are damaged, usually by an aberrant immune reaction [53]. In pancreatic cancer the cancer [54-56] patients who have diabetes for less than five years, it is unclear if the diabetes contributed to the cancer or if the precancerous cells caused the diabetes. Cutting all forms of sugar out of the diet will not result in the death of cancer cells because cancer cells cannot be starved [57,58]. Glucose is the basic food source for all cells, including cancer cells and is provided by eating foods containing carbohydrates. It may be necessary to avoid foods high in simple sugars. If the patient is experiencing weight loss unrelated to blood sugar control, it may be caused by cancer induced weight loss, called cancer cachexia [59,60]. Chemical changes in the

body cause the breakdown of body fat and lean body mass to make energy for cancer and healthy cells [61]. Different types of treatment are available for patients with pancreatic cancer [62]. Some treatments are standard. Three types of standard treatment are used: Surgery are as total pancreatectomy, distal pancreatectomy. Whipple procedure Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy. They are Chemotherapy is a cancer treatment that uses drugs [63,64] to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing [65].

Endometrial Cancer

Endometrial cancer is the most common type of uterine cancer. Increased levels of estrogen appear to play a key role in endometrial cancer [66]. Estrogen helps stimulate the buildup of the lining of the uterus. High level of estrogen results in excessive endometrial growth and cancer [67-69]. Obesity also has an adverse effect on both the diabetes and endometrial cancer. Diabetes was independently associated with endometrial cancer. Elevated levels of circulating insulin were a mechanism. Through which diabetes imparted an excess risk of various kinds of cancers [70-72]. Diabetes in particular was associated to endometrial cancer to some extent. With an elevation in risk of endometrial cancer among both users and nonusers of unopposed estrogens and elevations in risk among diabetics in all bmi Strata would be expected, since the diagnosis of type 2 diabetes is preceded by a period of hyperinsulinemia regardless of a person's Body Mass Index (BMI). The general symptoms of endometrial cancer are Abnormal uterine bleeding, abnormal menstrual periods, Bleeding between normal periods before menopause, Vaginal bleeding or spotting after menopause, Extremely long heavy, or frequent episodes of vaginal bleeding after age 40,Lower abdominal pain or pelvic cramping, Thin white or clear vaginal discharge after menopause. Treatment options involve surgery, radiation therapy, and chemotherapy [73,74].

Colorectal Cancer

Colorectal cancer is a disease in which cells in the colon or rectum become abnormal and divide without control, forming a mass called a tumor [75,76]. Colorectal cancer cells may also invade and destroy the tissue around them. In addition, they may break away from the tumor and spread to form new tumors in other parts of the body.

Colorectal cancer is more likely to occur as people get older; Polyps are abnormal growths that protrude from the inner wall of the colon or rectum [77]. They are relatively common in people over age 50, a person who has already had colorectal cancer is at an increased risk of developing colorectal cancer a second time, and Ulcerative colitis is a condition that causes inflammation and sores (ulcers) in the lining of the colon. Increasing evidence from epidemiologic studies suggests that cigarette smoking; particularly long-term smoking increases the risk of colorectal cancer. People with diabetes have a greater chance of developing colon cancer. They also tend to have lower survival rates and higher recurrence rates. Better blood sugar control would mean lower insulin levels, which might affect colon cancer risk. Obesity is also a risk factor for both diabetes and colon cancer. Association of type 2 diabetes with colon and rectal cancer [78] incidence among men suggests that insulin use is associated with a slight, but not a substantially increased, risk of colorectal cancer among men with type 2 diabetes. Sometimes surgery is an option for a person whose colorectal cancer has spread

in a limited way outside of the intestine. Chemotherapy may be recommended before surgery in some cases [79-81].

Bladder Cancer

Diabetes mellitus may alter the risk of developing a variety of cancers, and their associations are biologically plausible [82]. Bladder cancer is a major health concern for older males in Western populations [83,84]. Bladder cancer is a cancer [85-87] that starts in the bladder wherein body part holds and releases urine. It is in the center of the lower belly area. It is a disease in which abnormal cells multiply without control in the bladder. Based on types of fluids consumed many observed development of bladder cancer. It is hypothesized that the dietary components of beverages may lead to the development of bladder cancer [88]. Standard diagnosis for bladder cancer is biopsy which is obtained during cystoscopy [89]. In some cancer cases patients are generally treated by removing only part of the bladder, and that procedure is followed by radiation, chemotherapy and immunological therapy [90-92]. Surgical therapy includes Trans Urethral Resection of Bladder Tumor (TURBT), partial or complete Cystectomy.

Conclusion

There is a significant association between diabetes, diabetes therapies and cancer. In general diabetes seems to be linked to a variety of cancers including liver, pancreatic, colorectal, endometrial and bladder cancer. The proposed mechanism of action includes hyperinsulinemia and the effects that insulin has on the IGF axis to promote survival and progression of early malignant cells by increasing tumor growth and decreasing cellular apoptosis. Several studies are available to elucidate a correlation with cancer and insulin, it is important to continue treating diabetes with insulin analogs in order to avert the long-term complications of the disease. Possible mechanisms for a direct link between diabetes and cancer include hyperinsulinemia, hyperglycemia, and inflammation. Healthy diet, physical activity, and weight management reduce the risk and improve outcomes of type 2 diabetes and some forms of cancer and should be promoted for all.

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