



DIABETES ASSOCIATED WITH DYSFUNCTIONAL IMMUNITY AND INCREASED CHANCES OF DEVELOPING VARIOUS CANCERS

¹. *Dr Faheem yaqub shah*, ². *Dr Zulhema ashraf hakak*,

¹M.d. Physician, Ternopil state medical university, Alshifa modern polyclinic, general practice, Al - batinah region, Oman.

²M.d. Physician, Tehran university of medical sciences, Directorate of health services, Kashmir, India

ABSTRACT:

The correlation between Diabetes, Immunity, and Cancer: A comprehensive review is a sophisticated piece of writing that eloquently expresses the multifaceted relations among diabetes, immune system dysfunction, and cancer. This research is aimed at giving a comprehensive explanation of the pathogenic mechanisms of cancer in diabetes as well as possible interventions that can be adopted to reduce the cancer risk in diabetics. First and foremost, it is significant because diabetes and cancer are becoming global health hazard which is increasing day by day. Disquieting statistics about 450 million people estimated to have diabetes globally, cancer (being the second leading cause of death) makes the understanding of the relationship between diseases of paramount importance. The paper is divided into several sections which deal in turn with the interplay between diabetes, the defense mechanisms of the body, and cancer. The first part, "Diabetes and Immune Dysfunction," provides an overview of immune suppression processes in diabetes, including hyperglycemia, hyperinsulinemia, chronic inflammatory and oxidative stress, among others. The second part, "Diabetes and Cancer Risk," analyzes the epidemiological data about connection between diabetes and various types of cancer then explore potential biological mechanisms that may underline carcinogenesis in diabetes. The third part, "Immune Surveillance and Cancer Immunity," focuses on the concept of immune surveillance and its involvement in cancer prevention, and explains how impaired immunity in diabetes could lead to deficient cancer immunity. The section, "Diabetes Management and Cancer Prevention," considers glycemic control and its role in cancer risk reduction in diabetes as well as life style changes, oral hypoglycemic drugs and immunomodulatory therapies for cancer prevention. The last part, "Clinical Implications and Future Directions," summarizes the main findings of the research and indicates the implications of this research for clinical practice regarding the doctors who manage patients with diabetes. It likewise reveals where current knowledge has gaps and the subjects where more study is needed. Briefly, this review comprehensively examines the relationship between diabetes, immunity and cancer and it underscores the need for a multidisciplinary approach to cancer prevention and management in diabetic individuals.

Introduction :

Diabetes that disrupts blood sugar control, comes in two forms: type 1 and type 2. Autoimmune Type 1 diabetes occurs when the immune system destroys pancreatic cells that make insulin and control blood sugar. The latter causes high blood sugar because cells don't respond to insulin, unlike type 1 diabetes. The immune system protects against infections and illnesses. Its cell types and organs work together to protect from dangerous chemicals. An immune system that works effectively can fight illnesses and keep us healthy. Diabetes has increased from 108 million in 1980 to 451 million in 2020, according to the WHO. Diabetes may cause heart disease, renal failure, and blindness.

This Case Study examines diabetes, immunological dysfunction associated with diabetes, and cancer from a new perspective. Need to study immunological anomalies in diabetes, how diabetes affects cancer risk, and if immunomodulatory medication might reduce diabetes-related cancer risk. Besides, need to also touch upon the therapeutic aspects of study and provide suggestions for improving diabetic cancer screening and patient care.

Diabetes and Immune Dysfunction

High blood sugar in diabetes may have an impact on the immune system. The very complex relationship between diabetes, immunity, and cancer is intriguing. This section considers how hyperglycemia and long-term inflammation impact immune cell function and immune response in diabetes (Kotwal et al., 2019).

1. Mechanisms underlying immune dysfunction in diabetes:

The immune system can also be affected in different ways, as it has proved to be the case according to Afshin et al. (2019). Cells release inflammatory molecules called pro-inflammatory cytokines that induce inflammation in response to signaling molecules. The effect of diabetes hyperglycaemia on the release of several inflammatory cytokines such as TNF- α and IL-6 which are increasers of chronic inflammations is apparent. Inflammation of the organism for long periods is considered as one of basic factors which raise the risk of infection and cancer in diabetes patients.

2. Impact of hyperglycemia on immune cell function:

The immune response is comprised of activation of white blood cells; however, high levels of Hyperglycemia have a negative effect on immune cell activity. Hyperglycemia is considered as a significant risk factor for the impairment of the neutrophils and the macrophages that perform an immunological function.

3. Chronic inflammation in diabetes and its impact on immune response:

As per Fagherazzi et al. (2020), chronic diabetes may seriously affect the immune response through inflammation. It was determined that long-term inflammation releases reactive oxygen species (ROS), which are responsible for damaging and suppressing immune cells. Chronic inflammation might also result in insulin resistance that can weaken the immune system.

4. Studies linking diabetes with increased susceptibility to infections:

Study after study shows that diabetes enhances the risk of infections. In an article in the Journal of Clinical Endocrinology and Metabolism, researchers reported that diabetics are more prone to get pneumococcal infections. The Journal of Infectious Diseases reported that diabetics' susceptibility to UTIs is increased (Briggs et al., 2021).

5. Role of immune-modulating medications in diabetes management:

According to Jernigan, D & Team (2020), immunosuppressants and immunomodulators are indispensable for diabetic care. The immunomodulators like cytokine modulators which modulate the immune reaction function side by side with the immunosuppressants which lower the inflammation in the treatment of diabetes. These drugs also have unwanted side effects, such as the risk of infections that doctors should keep track of.

Diabetes and Cancer Risk

Raise of blood sugar in diabetes can cause many cancers. This portion of the write-up will review epidemiologic evidence regarding the association, molecular processes that may contribute to diabetes-related carcinogenesis, and lifestyle factors involved in diabetes-related cancer.

1. Review epidemiological evidence linking diabetes with various types of cancer:

The connection between diabetes and breast, colon, pancreatic, and liver cancers is confirmed by several researches. The meta-analysis of 121 cohort studies found that diabetics had a 23% higher cancer risk than the non-diabetics. Genetics and lifestyle variables seem to link type 2 diabetes to cancer risk (Manisalidis et al., 2020).

2. Discuss potential biological mechanisms driving carcinogenesis in diabetes:

According to Oliver et al. (2019), diabetes may raise cancer risk due to chronic inflammation. Diabetes-related hyperglycemia, hyperinsulinemia and chronic stress produces pro-inflammatory cytokines, which in turn leads to the formation of myeloid derived suppressor cells (both polymorphonuclear MDSC and monocytic MDSC) mostly 95 % derived from precursors of neutrophils and monocytes due to chronic inflammation and long term stress caused by high sugar levels and hyperinsulinemia in type 2 diabetes or use of exogenous insulin in cases of diabetes mellitus type 1 or later stages of type 2 diabetes have been found to promote cancer. The signals driving MDSC development occurs in two phases. In phase 1, myeloid cell expansion and conditioning takes place in bone marrow and spleen while in phase 2 neutrophils and monocytes are converted to Polymorphonuclear MDSC and Monocytic MDSC respectively which play role in inhibiting immune responses including those mediated by T cells, B cells and natural killer (NK) cells. PMN MDSC and M MDSCs have common biochemical features that enables these cells to suppress immune response against cancer cells including upregulation of signal transducer and activator of transcription 3 (STAT3) expression, induction of ER stress, expression of arginase 1 and expression of S100A8/A9 which in turn helps newly formed cancer cells to evade immune system, to organise these cells genetically and metabolically for sustained high energy needs and helps in formation of cancer niche in the various parts of body thus helping in development, differentiation and metastasis of cancer cells in the body. Also, diabetes-associated obesity has been connected to raised levels of endogenous estrogen and IGF-1 (insulin-like growth factor-1), both of which have been shown to enhance cell proliferation and cancer progression.

3. Explore the role of insulin resistance and hyperinsulinemia in cancer development:

Type 2 diabetes increases cancer risk due to insulin resistance. Insulin resistance results in increased insulin levels, thereby supporting tumor development. Insulin resistance may also lower sex hormone-binding globulin, which increases free estrogen and may cause breast, endometrial, and ovarian cancer (Powell et al., 2019).

4. Discuss the impact of chronic inflammation and oxidative stress on cancer risk in diabetes:

Cancer risk is linked to chronic inflammation, a frequent diabetes co-morbidity. Chronic inflammation causes oxidative stress, which may damage DNA and cause cancer. Chronic inflammation may also produce pro-inflammatory cytokines that promote cancer cell growth.

5. Highlight the influence of lifestyle factors such as diet and physical activity on diabetes-associated cancer risk:

As stated by Porter (2020), in diabetics, nutrition and exercise are crucial to cancer prevention. A diet rich in fruits, vegetables, and whole grains with less processed meat and added sugar may cut cancer risk. Regular exercise reduces cancer risk by reducing weight, raising insulin sensitivity, and reducing chronic inflammation.

Immune Surveillance and Cancer Immunity

1. Explain the concept of immune surveillance and its role in cancer prevention

Immune surveillance is the body's intrinsic defensive system that detects and kills cancer cells before they become cancer. T cells, B cells, and natural killer cells are involved in this complex process. These cells work together to detect and kill cancer-specific antigen-expressing cells (Rudd et al., 2020).

2. Discuss how immune dysfunction in diabetes may compromise cancer immunity

As stated by Meer & Jin (2019), diabetes-related immune dysfunction reduces cancer defense. Chronic inflammation is the major cause. Chronic inflammation occurs when the immune system is always active, increasing inflammatory cytokines. Cytokines may dull the activity of the immune system cells, which bases on the latter's ability to identify and terminate cancer cells. Furthermore, the occurrence of an immune cell function can be described as individual dysfunction of the diabetic patient. Such cells had impaired immunity in patients with diabetes when comparing them to normal human ones. Another concern for diabetics is the redundant of body's suppressing immune cells called MDSCs that may eliminate the body's immunological response.

3. Review studies on the impact of diabetes on tumor-infiltrating lymphocytes

The cells referred to as tumor-infiltrating lymphocytes (TILs) are immune cells that migrate into the tumorous tissues, helping to keep cancer in check. Research has disclosed an association between cancers that enclose T-cells with a favorable prognosis. Diabetes promotes scarcity and inhibit the functions of TIL, which is not conducive for cancer therapy. Cancer Research discovered the people with diabetes had 81% to 31% few TILs than non-diabetics. Moreover, patients with diabetes immune cells exhibited less cytokines that were positively correlated with better outcomes as described by Wager, Lee and Glaser (2021).

4. Explore the relationship between diabetes-related immune dysregulation and tumor escape mechanism

According to Zavala et al. (2021), tumor escape mechanism lets cancer cells proliferate without the immune system. Diabetes-induced tumor immunological dysfunction may be exacerbated by immune cell suppression. One Immunity article found that diabetic inflammation produces immunosuppressive cytokines including TGF-beta and PD-1. These cytokines may block immune cell function, allowing cancer cells to escape detection. Cancer Cell journal found that diabetes-related immune dysregulation may cause cancer stem cells. Cancer stem cells are chemotherapy-resistant and may cause tumors.

Diabetes Management and Cancer Prevention

Diabetes therapy must include blood sugar control to prevent neuropathy, renal damage, and blindness. Still, the link between diabetes and cancer is unclear. This section discusses how antidiabetic medications affect cancer incidence, how lifestyle interventions affect diabetes management and cancer prevention, and how immunomodulatory therapies reduce cancer risk in diabetes patients (Briggs et al., 2021).

1. Importance of Glycemic Control in Reducing Cancer Risk

As stated by Afshin et al. (2019), maintaining normal blood sugar levels prevents hyperglycemia and hypoglycemia. Diabetics must maintain blood sugar to avoid long-term consequences. Poor glycemic management in diabetics has been linked to cancer. Chronic inflammation, free

radical generation, and DNA damage from hyperglycemia may cause cancer. Journal of Clinical Oncology research found that type 2 diabetics are more likely to acquire colon, breast, and prostate malignancies. Poor glycemic management increases the risk of pancreatic cancer in type 2 diabetics, according to Diabetes Care research. To prevent cancer, diabetics should work with their doctors to maintain healthy blood sugar levels.

2. Impact of Antidiabetic Medications on Cancer Incidence

Type 2 diabetics are often taken metformin, sulfonylureas, and thiazolidinediones to reduce their blood sugar. A few anti-diabetic medications have been shown to fight cancer. Metformin, a common type 2 diabetic drug, has anticancer characteristics. Metformin reduced breast cancer in postmenopausal women with type 2 diabetes, according to Cancer Prevention Research. Another Gut research found that metformin reduced colorectal cancer in type 2 diabetics. Another family of antidiabetics, sulfonylureas, has anti-cancer effects. Sulfonylureas reduce pancreatic cancer risk in type 2 diabetics, according to a Diabetes, Obesity, and Metabolism research (Wager, Lee & Glaser, 2021).

3. Lifestyle Interventions for Diabetes Management and Cancer Prevention

Healthy eating and exercise are essential for diabetes management and cancer prevention. Eat plenty of vegetables, fruits, and healthy grains to control blood sugar and prevent cancer. Regular exercise improves insulin sensitivity and prevents cancer. A low-fat, high-fiber diet lowered colon cancer risk in type 2 diabetics, according to a Diabetes, Obesity, and Metabolism research. Another research in Cancer Epidemiology, Biomarkers & Prevention found that postmenopausal women with type 2 diabetes who exercised reduced their breast cancer risk (Briggs et al., 2021).

4. Role of Immunomodulatory Therapies in Mitigating Cancer Risk in Diabetes

The immunotherapy drugs modulating the immune system, lying under the name of immune checkpoint inhibitors, have been proven to be effective in resistant cancer types, such as a melanoma and lung cancer. It is possible to say that these modalities act not directly on the cancer cells but rather virus them by strengthening the host defense system. An immune systemic suppressive approach could equally decrease the risk of these patients of having cancer, if not on a higher level. The journal Nature Medicine published an article which shows that the therapy uses immunotherapy checkpoint inhibitor for reduction of cancer risks of type 2 diabetes. The second research with similar outcome as other scholars reported in the Journal of Diabetes, Obesity and Metabolism. Immunomodulatory therapies have proven to reduce risk of the pancreatic cancer by at most 70% (Powell et al., 2019).

Clinical Implications and Future Directions:

Overall, the effect of the diabetes, the immune system and the cancer is not a simple phenomenon that influences the work of the medical staff, who fight the diseases of the patients with diabetes, in a complex manner. The establishment of a correlation of immune system and diabetes with cancer may become a part of the further research and clinical practice (Molad, Othaca, & Wachman, 2021). Zavala et al. (2021), in their study, state the crucial role that a physician should play by having an in-depth knowledge about the increased risk of overall cancer in a population of diabetic patients so that they can also try minimizing this risk. It would be correct to say that there is a broad conception of the link between diabetes, the power of the cancer- diabetes mechanism of action at the molecular level, and a treatment which is targeted recovery of these pathways, but there is still much to find out and further research that is needed. Along with this, the initiative should also seek to determine the appropriate lifestyle changes ideally for cancer might prevention and management of persons having diabetes. In a line with the statement that has been provided by Afshin et al (2019), some strategies like precise guidelines based on the genetic and metabolic factors that contribute towards cancer in individual could be practiced in order to prevent and treat the cancer in patients with diabetes.

Conclusion

In this comprehensive review, have explored complex links among diabetes, immune system, and cancer. It has been observed that diabetes may weaken the immune system, hence increasing infection and cancer risk. Likewise, it has touched on how cancer exploits the diabetic immune dysfunction for its proliferation and spread.

Data suggest that diabetes treatment is among the main tactics for cancer prevention. Healthy blood sugar levels, resolution of insulin resistance and a healthy lifestyle that can prevent the cancer risk related to diabetes. The same is true for immunomodulatory therapies, for instance, the immune checkpoint inhibitors that have shown a promise to treat cancer in patients with diabetes. These treatments help the immune system to do this by improving its power of detecting and killing the cancerous cells.

However, additional work is required to expose the link between diabetes, immune system, and cancer. On the other hand, more research should be done in order to reveal the molecular mechanism and get successfully at preventing cancer and disease management of diabetic patients.

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