

Diabetes as a Risk Factor of Pancreatic Cancer

MUHAMMAD ASIF¹, SYED WHAJ AHMAD², SYED FARAZ AHMAD³, AHMED NAWAZ BANU⁴, MAHEEN JAMIL⁵, NAHAL ARSHAD⁶

¹Medical Officer, Tehsil Headquarter Hospital Minchinabad

²Medical Officer, Institute: Surgicare hospital, Dgkhan

³Medical Officer, Rural health center, Basira, Muzaffargarh

⁴Medical Officer (MO), Bahawal Victoria Hospital, Bahawalpur

⁵Woman Medical Officer, Fatima Memorial Hospital Lahore

⁶Woman Medical officer, Jinnah Hospital Gujranwala

Corresponding author: Muhammad Asif, Email: drasifnaich@gmail.com, Cell: 03025584845

ABSTRACT

Objective: The aim of this study is to determine the relation between diabetes and pancreatic cancer.

Study Design: Retrospective study

Place and Duration: Tehsil Headquarter Hospital Minchinabad. May 2021-Dec 2021

Methods: There were two hundred and fifty patients of pancreatic cancer were included in this study. Age of the patients was between 20-90 years. Informed written consent was taken from all the patients for detailed demographics age, sex, body, mass index. Patients were underwent for CT scan and ultrasonography. Outcomes were association of diabetes among enrolled cases was measured. Age duration of diabetes among all the cases were measured. Prevalence of cancer among different regions of pancreas was studied. SPSS 24.0 version was used to analyze complete data.

Results: There were 160 (64%) males and 90 (36%) cases were females. Mean age of the patients was 65.4±6.45 years with mean BMI 27.3±4.67 kg/m². Tobacco smoking was found in 151 (60.4%) among. Frequency of diabetes was found among 80 (28%) cases. Among 80 cases of diabetes, 72 (90%) patients had recent onset diabetes. Mean age of diabetes diagnose was 56.34±5.34 years and mean age of pancreatic cancer diagnosed was 58.9±6.77 years. Head in pancreas was the most common affected side of tumor among 58 (72.5%), followed by body 12 (15%) and tail in 10 (12.5%) cases.

Conclusion: In this study we concluded that frequency of diabetes among pancreatic cancer patients was 28% and majority of the cases had new-onset diabetes. Except this tobacco smoking was significant causing factor for pancreatic cancer. It may be possible to screen for pancreatic cancer in new-onset diabetes by identifying a particular biomarker for pancreatic cancer.

Keywords: Diabetes Mellitus, Pancreatic cancer, Causes

INTRODUCTION

As a result of the obesity pandemic, the number of persons with diabetes worldwide has risen to 285 million, or 6.6 percent of the population aged 20 to 79, according to the World Health Organization. More than 95% of diabetes cases are caused by type 2 diabetes mellitus. Several malignancies, including liver, pancreatic, endometrial, colorectal and breast, are related with type 2 diabetes mellitus. Type 2 diabetes mellitus may be the third modifiable risk factor for pancreatic cancer, behind smoking and obesity. Diabetic pancreatitis is closely linked to pancreatic cancer, yet the two diseases are not mutually exclusive. On the one hand, diabetes may be a sign of pancreatic cancer before it has even developed. Diabetics have been linked to an increased risk of pancreatic cancer [1–3].

In both epidemiological and biological terms, diabetes and cancer have been connected. Diabetes (primarily type 2) has been linked to an increased risk of several cancers (colorectal, breast, endometrium, liver, pancreas, and bladder) [4], and diabetes can advance cancer stages and increase mortality [5,6]. There is also convincing evidence that diabetes (primarily type 2) can increase cancer mortality [5,6]. Individuals with glucose intolerance, such as obesity, diabetes mellitus (DM), and high blood glucose levels, have a higher chance of developing pancreatic cancer (PC). Hyperglycemia's tumorigenic impact, obesity's mitogenic effect, and persistent, subclinical inflammation induced by pancreatic fat infiltration are some of the mechanisms behind these connections.. In spite of this lack of proof, various processes have been proposed.

Despite the fact that PC is one of the most common causes of cancer deaths globally, it has a 5-year overall survival rate of less than 1% [7]. The best treatment option for PC is surgical resection, which has shown significant progress in lowering the disease's death rate. Even though surgical resection has a modest effect on overall survival, it may nevertheless have a 50% to 80% failure probability, resulting in a poor quality of life for patients who successfully undergo the procedure [8].

Obesity has been shown to raise the risk of type 2 diabetes (T2D). Reduced insulin sensitivity causes an increased demand on pancreatic islets to release more insulin, resulting in

hyperinsulinemia, which is generally the first event in the pathogenesis of T2D, which is caused by genetic and environmental variables. [9]

Glucose and lipid metabolism, as well as cell proliferation and angiogenesis, can be regulated by insulin, which is also a potential growth factor. Although diabetes and obesity have been linked to a variety of diseases, pancreatic cancer is regarded to be the most dangerous. [10] When insulin from the endocrine pancreas' islets causes malignant transformation of the exocrine pancreas' ductal epithelial cells, it grows fast, and this relationship is likely the source of pancreatic cancer's fatal prognosis. [11] It's unclear how T2D and pancreatic cancer are linked, since some research suggests it shortens survival time, while others say it doesn't. [12] A higher incidence of pancreatic cancer in diabetics and a higher incidence of pancreatic cancer in those with diabetes have been found in epidemiological research, therefore it's unclear if diabetes is a cause or effect of pancreatic cancer. [13]

Recent research has focused on the prevalence and mortality of PC related with diabetes, however few studies have conclusively proven a link between diabetes duration and PC. PC and diabetes have been linked in three meta-analyses [14]. To begin, Batabyal et al. looked at illness duration in terms of specific ranges, such as 1, 1–4, 5–9, and 10 years. Although the individual relative risk (RR) ranged from 6.69 at 1 year to 1.36 at 10 years [15], this group observed that there was a significant risk of PC early following the diagnosis of DM. They did not look at the relationship between PC and diabetes duration in the other two meta-analyses.

We conducted this study to determine prevalence of diabetes associated among patients with pancreatic cancer.

MATERIAL AND METHODS

This Retrospective study was conducted at Tehsil Headquarter Hospital Minchinabad and comprised of 160 patients. Informed written consent was taken from all the patients for detailed demographics age, sex, body mass index. Patients had other severe medical illness and <20 years of age were not included in this study.

Age of the patients was between 20-90 years. All the study subjects were questioned individually about their medical history; specific attention was paid to the existence of diabetes, the patient's age at the time of diagnosis, the type of diabetes, and the therapy received for it. Members of the close family were also questioned in most cases. When feasible, the findings of earlier blood tests, particularly the glucose levels, were documented. An unambiguous rise in plasma glucose concentration (200 mg per deciliter [11.1 mmol per litre]) was used to diagnose diabetes, along with the classic signs and symptoms of the disease, such as polydipsia, polyuria, polyphagia, and weight loss. A fasting plasma glucose concentration greater than or equal to 140 mg per deciliter (7.3 mmol per litre) was also considered, as was a history of polydipsia. Prevalence of cancer among different regions of pancreas was studied. SPSS 24.0 version was used to analyze complete data.

RESULTS

There were 160 (64%) males and 90 (36%) cases were females. Mean age of the patients was 65.4±6.45 years with mean BMI 27.3±4.67 kg/m². Tobacco smoking was found in 151 (60.4%) among.(table 1)

Table 1: Characteristics details of enrolled cases

Variables	Frequency	Percentage
Mean age (years)	65.4±6.45	
Mean BMI (kg/m ²)	27.3±4.67	
Sex		
Male	160	64
Female	90	36
Tobacco Smoking		
Yes	151	60.4
No	99	39.6

Frequency of diabetes was found among 80 (28%) cases with pancreatic cancer and the remaining cases did not show any symptoms of diabetes.(fig 1)

Figure 1: Association of diabetes with cases of pancreatic cancer

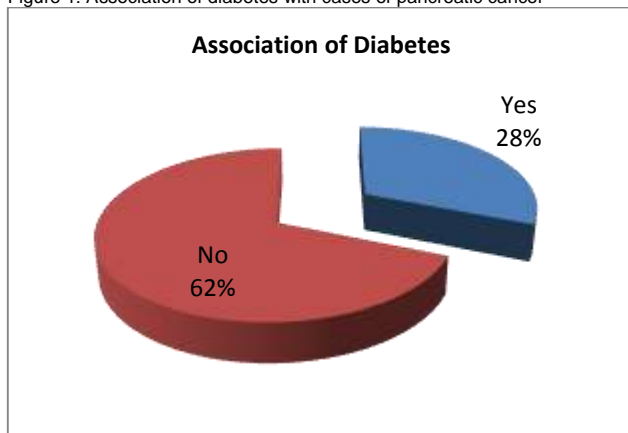


Table 2: Age and frequency of diabetes among the cases

Variables	Frequency	Percentage
Mean age of pancreatic cancer (years)	58.9±6.77	
Mean age of diabetes diagnose (years)	56.34±5.34	
Type of Diabetes		
Recent onset diabetes	72	90
Long term diabetes	8	10
Family History of diabetes		
Yes	51	63.8
No	29	36.2

Among 80 cases of diabetes, 72 (90%) patients had recent onset diabetes. Mean age of diabetes diagnose was 56.34±5.34 years and mean age of pancreatic cancer diagnosed was 58.9±6.77 years. Family history of diabetes found among 51(63.8%) cases.(table 2)

We found that head in pancreas was the most common affected side of tumor among 58 (72.5%), followed by body 12 (15%) and tail in 10 (12.5%) cases.(table 3)

Table 3: Prevalence of pancreatic cancer among diabetic cases

Variables	Frequency	Percentage
Affected Side of Pancreas		
Head	58	72.5
Body	12	15
Tail	10	12.5

DISCUSSION

Diabetic patients were shown to have an increased risk of developing pancreatic cancer. There was, however, no correlation between diabetes and pancreatic cancer in persons with long-term diabetes. Patients with pancreatic cancer are more likely to have diabetes of recent start, which may have been triggered by the tumour, according to recent studies. Pancreatic cancer is thought to be more likely in those with diabetes than in those who don't. It was not determined how long a patient had diabetes prior to being diagnosed with pancreatic cancer in these studies. Methodological differences between our study and prior research include the limited number of patients, the use of postal questionnaires and death certificates, and perhaps unrepresentative control groups in previous studies. [16,17]

In this retrospective study 250 patients of both genders had pancreatic cancer were presented. There were 160 (64%) males and 90 (36%) cases were females. Mean age of the patients was 65.4±6.45 years with mean BMI 27.3±4.67 kg/m². Tobacco smoking was found in 151 (60.4%) among. Results of current research showed resemblance to the previous studies.[18,19] Frequency of diabetes was found among 80 (28%) cases with pancreatic cancer and the remaining cases did not show any symptoms of diabetes. Diabetic individuals who were diagnosed at the same time as or shortly before their tumours are more likely to have diabetes as a result of their disease. When pancreatic cancer attacks the islet cells in the pancreas, it may result in the development of diabetes. When the illness progresses, insulin resistance is common, which may explain why diabetes might develop before the pancreatic tumour symptoms.[20,21]Mean age of diabetes diagnose was 56.34±5.34 years and mean age of pancreatic cancer diagnosed was 58.9±6.77 years.

The findings of this study support the idea that newly diagnosed diabetes (before to a pancreatic cancer diagnosis) is related with a higher risk of pancreatic cancer than diabetes that has been present for two years or more previous to a cancer diagnosis. Diabetic symptoms are more often a sign of pancreatic cancer, rather than the cause or risk factor for cancer, according to this study The incidence of pancreatic cancer was higher in long-term T2D patients than in short-term T2D patients (2–5 years), which supports the idea that the diabetic condition that encompasses insulin resistance and hyperglycemia are likely risk factors for the development of pancreatic cancer, as previously indicated. Family history of diabetes found among 51(63.8%) cases.[19,22]

We found that head in pancreas was the most common affected side of tumor among 58 (72.5%), followed by body 12 (15%) and tail in 10 (12.5%) cases. Patients with early-stage pancreatic cancer who had carcinoma of the head of the pancreas were more likely to acquire diabetes than those who had carcinoma of the body and/or tail of the organ, according to earlier research.[23]

Diabetes and PC have been linked in epidemiological research. Previously published systematic reviews [24,25]

aggregated research with populations with new-onset or long-term diabetes. Those findings showed a 1.5-fold greater incidence of PC in diabetic individuals, indicating a stronger link between diabetes and PC than our study found. This data suggests that the link between long-term diabetes and PC development is as strong as the link between new-onset diabetes and PC development.

CONCLUSION

In this study we concluded that frequency of diabetes among pancreatic cancer patients was 28% and majority of the cases had new-onset diabetes. Except this tobacco smoking was significant causing factor for pancreatic cancer. It may be possible to screen for pancreatic cancer in new-onset diabetes by identifying a particular biomarker for pancreatic cancer.

REFERENCES

- 1 Noy A, Bilezikian JP. Clinical review 63: Diabetes and pancreatic cancer: clues to the early diagnosis of pancreatic malignancy. *J Clin Endocrinol Metab.* 1994;79:1223–31. [PubMed] [Google Scholar]
- 2 Gullo L, Pezzilli R. Diabetes and pancreatic cancer. *Pancreas.* 2004;28:451. author reply 451-2. [PubMed] [Google Scholar]
- 3 Fisher WE. Diabetes: risk factor for the development of pancreatic cancer or manifestation of the disease? *World J Surg.* 2001;25:503–8.
- 4 Giovannucci E, Harlan DM, Archer MC, Bergenstal RM, Gapstur SM, Habel LA, et al (2010) Diabetes and cancer: a consensus report. *Diabetes Care* 33:1674–1685 pmid:20587728
- 5 Griffiths RI, Danese MD, Gleeson ML, Valderas JM (2012) Epidemiology and outcomes of previously undiagnosed diabetes in older women with breast cancer: an observational cohort study based on SEER-Medicare. *Biomedcentral Cancer* 12:613–626
- 6 Toriola AT, Stolzenberg-Solomon R, Dalidowitz L, Linehan D, Colditz G (2014) Diabetes and pancreatic cancer survival: a prospective cohort-based study. *Br J Cancer* 111:181–185
- 7 Gudjonsson B (2009) Pancreatic cancer: survival, errors and evidence. *Eur J Gastroenterol Hepatol* 21:1379–1382
- 8 Asiyabola B, Gleisner A, Herman JM, Choti MA, Wolfgang CL, Swartz M, et al (2009) Determining pattern of recurrence following pancreaticoduodenectomy and adjuvant 5-fluorouracil-based chemoradiation therapy: effect of number of metastatic lymph nodes and lymph node ratio. *J Gastrointest Surg* 13:752–759
- 9 Stumvoll M, Goldstein BJ, van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. *Lancet.* 2005;365:1333–1346
- 10 Burney S, Irfan K, Saif MW, Masud F. Diabetes and pancreatic cancer. *JOP.* 2014;15:319–321
- 11 Walter U, Kohlert T, Rahbari NN, Weitz J, Welsch T. Impact of preoperative diabetes on long-term survival after curative resection of pancreatic adenocarcinoma: a systematic review and meta-analysis. *Ann Surg Oncol.* 2014;21:1082–1089.
- 12 Nakai Y, Isayama H, Sasaki T, Mizuno S, Sasahira N, Kogure H, Kawakubo K, Yamamoto N, Hirano K, Ijichi H, et al. Clinical outcomes of chemotherapy for diabetic and nondiabetic patients with pancreatic cancer: better prognosis with statin use in diabetic patients. *Pancreas.* 2013;42:202–208.
- 13 Chari ST, Leibson CL, Rabe KG, Timmons LJ, Ransom J, de Andrade M, Petersen GM. Pancreatic cancer-associated diabetes mellitus: prevalence and temporal association with diagnosis of cancer. *Gastroenterology.* 2008;134:95–101.
- 14 Ben Q, Xu M, Ning X, Liu J, Hong S, Huang W, et al (2011) Diabetes mellitus and risk of pancreatic cancer: A meta-analysis of cohort studies. *Eur J Cancer* 47:1928–1937
- 15 Fokas E, O'Neill E, Gordon-Weeks A, Mukherjee S, McKenna WG, Muschel RJ. Pancreatic ductal adenocarcinoma: from genetics to biology to radiobiology to oncoimmunology and all the way back to the clinic. *Biochim Biophys Acta.* 2015;1855:61–82.
- 16 Huxley R., Ansary-Moghaddam, A., Berrington de González, A. et al. Type-II diabetes and pancreatic cancer: a meta-analysis of 36 studies. *Br J Cancer* 92, 2076–2083 (2005).
- 17 Salvatore T, Marfella R, Rizzo MR, Sasso FC. Pancreatic cancer and diabetes: A two-way relationship in the perspective of diabetologist. *Int J Surg.* 2015 Sep;21 Suppl 1:S72-7.
- 18 Tan J, You Y, Guo F, Xu J, Dai H, Bie P. Association of elevated risk of pancreatic cancer in diabetic patients: A systematic review and meta-analysis. *Oncol Lett.* 2017;13(3):1247-1255. doi:10.3892/ol.2017.5586
- 19 Li D, Mao Y, Chang P, Liu C, Hassan MM, Yeung SJ, Abbruzzese JL. Impacts of new-onset and long-term diabetes on clinical outcome of pancreatic cancer. *Am J Cancer Res.* 2015;5:3260–3269.
- 20 Lu Y, García Rodríguez LA, Malgerud L, González-Pérez A, Martín-Pérez M, Lagergren J, Bexelius TS. New-onset type 2 diabetes, elevated HbA1c, anti-diabetic medications, and risk of pancreatic cancer. *Br J Cancer.* 2015;113:1607–1614.
- 21 Choi Y, Kim TY, Oh DY, Lee KH, Han SW, Im SA, Kim TY, Bang YJ. The impact of diabetes mellitus and metformin treatment on survival of patients with advanced pancreatic cancer undergoing chemotherapy. *Cancer Res Treat.* 2016;48:171–179.
- 22 Sadr-Azodi O, Gudbjörnsdóttir S, Ljung R. Pattern of increasing HbA1c levels in patients with diabetes mellitus before clinical detection of pancreatic cancer - a population-based nationwide case-control study. *Acta Oncol.* 2015;54:986–992.
- 23 Wakasugi H, Funakoshi A, Iguchi H. Clinical observations of pancreatic diabetes caused by pancreatic carcinoma, and survival period. *Int J Clin Oncol.* 2001;6:50–4.
- 24 Huxley R, Ansary-Moghaddam A, Berrington de Gonzalez A, Barzi F, Woodward M (2005) Type-II diabetes and pancreatic cancer: a meta-analysis of 36 studies. *Br J Cancer* 92:2076–2083
- 25 Batabyal P, Vander Hoorn S, Christophi C, Nikfarjam M (2014) Association of diabetes mellitus and pancreatic adenocarcinoma: a meta-analysis of 88 studies. *Ann Surg Oncol* 21:2453–2462