

A STUDY IN THE IMPACT OF DIABETES MELLITUS ON SURVIVAL OF
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ABSTRACT

Background: Pancreatic cancer ranks 11th in women and 12th in men worldwide. Pancreatic cancer patients often have diabetes, which is a risk factor and early symptom. Numerous research have examined the link between diabetes and pancreatic cancer. Diabetes' predictive influence on pancreatic cancer patients' long-term survival is examined. **Patients and method:** A retrospective cohort analysis of pancreatic cancer patient data at Oncology Teaching Hospital. The trial ran from May 1, 2022, until February 1, 2023. It comprised 156 histopathologically confirmed pancreatic cancer patients from January 2018 to September 2022 in two groups. The exposed group included 67 patients who had diagnosed with type 2 diabetes before pancreatic cancer, at same time or after cancer diagnosis; and the non-exposed group with no signs of diabetes. **Results:** This research includes 156 pancreatic cancer patients. The mean age was 56.2 ± 11.2 years. The male percentage was 88 (56.4%) and the female proportion 68 (43.6%). The most prevalent histological picture was 89.1% adenocarcinoma. The average cancer duration was 14.2 ± 9.9 months, while the average diabetes duration was 5.7 ± 3.8 years. This study indicated that the median survival time was 12 months and that diabetes did not affect survival (log-rank test = 0.71). Age (HR = 1.04, P-value <0.001), renal illness (HR=2.6, P-value = 0.01), and palliative care (HR = 7.61, P-value <0.001) increased mortality risk, but not diabetes (HR = 1.11, P-value = 0.6). **Conclusion:** Survival was significantly influenced by age, histopathological picture, cancer stage and treatment modality used but there was no significant effect of the presence of diabetes on the survival.

KEYWORDS: Pancreatic Cancer; Diabetes; Survival; Iraq.

INTRODUCTION

Pancreatic cancer (PanCA) is one of the most aggressive malignancies and remains a major global health challenge due to its poor prognosis and late presentation. It is currently the seventh leading cause of cancer-related mortality worldwide, with a steadily increasing incidence and mortality rate.^[1] PanCA is broadly classified into exocrine and endocrine tumors. Exocrine pancreatic cancers account for the majority of cases, with pancreatic ductal adenocarcinoma (PDAC) representing approximately 85% of all pancreatic malignancies. PDAC is characterized by an extremely poor survival rate, with only about 24% of patients surviving one year after diagnosis and less than 10% surviving beyond five

years.^[2] In contrast, pancreatic neuroendocrine tumors (PanNETs), arising from endocrine tissue, are less common and generally have a better prognosis.^[3] Despite advances in diagnostic and therapeutic strategies, PDAC continues to have dismal outcomes. Most patients present with advanced or metastatic disease at the time of diagnosis, limiting the possibility of curative surgical resection to only 10–20% of cases.^[4] Even among patients undergoing potentially curative surgery, recurrence rates remain high, typically occurring within 12–22 months postoperatively.^[5,6] Although survival rates have modestly improved over the past decades due to better surgical techniques, perioperative care, and systemic therapies, the overall 5-year survival rate

remains approximately 10%.^[6,7] Epidemiologically, pancreatic cancer predominantly affects older individuals, with nearly 74% of cases diagnosed between the ages of 55 and 84 years, while it is rare in individuals under 40 years of age.^[8] Both sexes are equally affected, although certain populations, such as African Americans, exhibit a slightly higher risk.^[8] In Iraq, pancreatic cancer accounted for approximately 530 deaths in 2020, representing 0.36% of total mortality, highlighting its clinical significance within the region.^[9] The etiology of pancreatic cancer is multifactorial, involving genetic, environmental, and medical risk factors. Approximately 10% of cases are familial, with significantly increased risk observed in individuals with affected first-degree relatives.^[10] Several hereditary syndromes, including BRCA2 mutations, Peutz–Jeghers syndrome, and familial atypical multiple mole melanoma, are associated with increased susceptibility.^[11] Environmental risk factors such as cigarette smoking, heavy alcohol consumption, and occupational exposure to carcinogens also play a significant role in disease development.^[12] Medical conditions, particularly chronic pancreatitis, diabetes mellitus, and obesity, have been strongly linked to pancreatic cancer. Chronic inflammation in pancreatitis promotes carcinogenesis through cytokine-mediated pathways.^[13] Diabetes mellitus, especially new-onset diabetes, has been increasingly recognized as both a potential risk factor and an early manifestation of pancreatic cancer.^[14] Long-standing diabetes further increases the risk through mechanisms involving hyperinsulinemia, insulin resistance, and elevated insulin-like growth factor-1 (IGF-1), which promote tumor growth and inhibit apoptosis.^[15] Additionally, obesity contributes to pancreatic carcinogenesis through chronic inflammation and hormonal dysregulation.^[16] The purpose of this study was to analyze the prognostic effect of clinically revealed diabetes on long-term survival in pancreatic cancer patients.

METHOD

This retrospective cohort study was conducted to evaluate the prognostic impact of type 2 diabetes mellitus (T2DM) on survival outcomes among patients with pancreatic cancer. A systematic sampling technique was applied to recruit eligible patients diagnosed between 2018 and 2022. Adult patients with histopathologically confirmed pancreatic cancer were included, while those with incomplete clinical or follow-up records were excluded from the analysis. Data collection was performed using patients' medical records and included demographic characteristics (age and sex), smoking status, and the presence of comorbid conditions such as hypertension, diabetes mellitus, cardiovascular disease, kidney disease, and thyroid disorders. Clinical variables included presenting symptoms, histopathological findings, cancer stage at diagnosis, duration of cancer, duration of diabetes (if present), and treatment modalities received, including surgical intervention, chemotherapy, radiotherapy, or palliative care. Patients were categorized into two main groups

based on diabetes status: an exposed group consisting of patients with T2DM and a non-exposed group comprising patients without a history of T2DM. Additionally, for outcome assessment, patients were divided into two categories according to survival status during the study period: alive and deceased. Statistical analysis was performed using R software (version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria), utilizing packages including *dplyr*, *gtsummary*, and *ggplot2*. Continuous variables were expressed as mean \pm standard deviation for normally distributed data or median (range) for non-normally distributed variables. Categorical variables were summarized as frequencies and percentages. Comparisons between groups were conducted using Welch's t-test for continuous variables and either the chi-square test with Yates' correction or Fisher's exact test for categorical variables, as appropriate. Survival analysis was performed using Kaplan–Meier curves, and differences between groups were assessed using the log-rank test. Hazard ratios were estimated using univariate regression analysis. A p-value of less than 0.05 was considered statistically significant. Ethical approval was obtained from the Scientific Committee of the Department of Medical Oncology, Iraqi Board for Medical Specializations. The study adhered to the principles of the Declaration of Helsinki and its subsequent amendments.

RESULTS

One hundred and fifty-six cases with pancreatic cancer were included in this study. The mean age was 56.2 ± 11.2 years. The proportion of males was 88 (56.4%) and for females was 68 (43.6%). Most of the samples had no history of smoking 55.8% but 28.8% were active smokers. Diabetes was the most prevalent co-morbidity in this study (42.9%) followed by hypertension (27.6%), and heart disease (12.2%). In regard to the presenting symptom weight loss was the most frequent one followed by fatigue, abdominal pain, and polyuria. Adenocarcinoma was the most common image found on histopathological reports with a proportion of 89.1%. The mean duration of the cancer was 14.2 ± 9.9 months; the mean duration of diabetes was 5.7 ± 3.8 years; 10.9% of the cases had diagnosis of diabetes and cancer at the same time. A 76.3% of the cases had undergone chemotherapy treatment and 44.9% had surgical management of the disease while only 35.9% had palliative treatment. An only 30.8% of the cases had survived in this study. As in table 1.

Table 1: Description of study demographics, clinical history and cancer parameters.

Characteristics	Cases (N = 156)
Age (years)	56.2 \pm 11.2
Sex - Male	88 (56.4%)
Sex - Female	68 (43.6%)
Smoking - Non-smoker	87 (55.8%)
Smoking - Active Smoker	45 (28.8%)
Smoking - Ex-smoker	24 (15.4%)
Hypertension	43 (27.6%)

Diabetes	67 (42.9%)
Heart disease	19 (12.2%)
Kidney disease	8 (5.1%)
Thyroid disease	1 (0.6%)
Fatigue	34 (21.8%)
Weight loss	39 (25.0%)
Abdominal pain	28 (17.9%)
Headache	11 (7.1%)
Blurred vision	7 (4.5%)
Polyuria	16 (10.3%)
Polydipsia	4 (2.6%)
Adenocarcinoma	139 (89.1%)
PNET	14 (9.0%)
IPMN	2 (1.3%)
Sarcoma	1 (0.6%)
Stage I	2 (1.3%)
Stage II	31 (19.9%)
Stage III	50 (32.1%)
Stage IV	73 (46.8%)
Surgery	70 (44.9%)
Chemotherapy	119 (76.3%)

Radiotherapy	9 (5.8%)
Palliative	56 (35.9%)
Duration of cancer (months)	14.2 ± 9.9
Duration of diabetes (years)	5.7 ± 3.8
Duration before cancer (years)	4.2 ± 2.3
Duration after cancer (months)	11.2 ± 6.0
Same time diagnosis	17 (10.9%)
Dead	108 (69.2%)
Alive	48 (30.8%)

Patients with and without diabetes were statistically compared and it was revealed that cases with type 2 diabetes were significantly older (mean = 58.9 ± 9.8, P-value = 0.008). No significant association between the presence of diabetes and sex, smoking status, the presence of other co-morbidities, histopathology image of the cancer, and different treatment modalities had been observed (P-value > 0.05). The mean duration of cancer in patients with diabetes was 13.9 ± 9.7 compared to those without diabetes 14.4 ± 10.1 with a P-value of 0.7. Also, survival was not influenced by the presence of diabetes in this study (P-value 0.6). As in table 2.

Table 2: Demographic and clinical profile with or without T2DM.

Characteristics	No T2DM, N = 89 ¹	T2DM, N = 67 ¹	P-value ²
Age, years	54.2 ± 11.9	58.9 ± 9.8	0.008
Sex			
Male	49 (55.1%)	39 (58.2%)	0.7
Female	40 (44.9%)	28 (41.8%)	
Smoking status			
Non-smoker	52 (58.4%)	35 (52.2%)	
Active Smoker	21 (23.6%)	24 (35.8%)	0.2
Ex-smoker	16 (18.0%)	8 (11.9%)	
Co-morbidities			
Hypertension	20 (22.5%)	23 (34.3%)	0.10
Heart disease	7 (7.9%)	12 (17.9%)	0.058
Kidney disease	2 (2.2%)	6 (9.0%)	0.075
Thyroid disease	0 (0.0%)	1 (1.5%)	0.4
Histopathology image			
Adenocarcinoma	79 (88.8%)	60 (89.6%)	
PNET	7 (7.9%)	7 (10.4%)	0.7
IPMN	2 (2.2%)	0 (0.0%)	
Sarcoma	1 (1.1%)	0 (0.0%)	
Cancer stage			
I	0 (0.0%)	2 (3.0%)	
II	19 (21.3%)	12 (17.9%)	0.3
III	31 (34.8%)	19 (28.4%)	
IV	39 (43.8%)	34 (50.7%)	
Treatment			
Surgery	40 (44.9%)	30 (44.8%)	>0.9
Chemotherapy	64 (71.9%)	55 (82.1%)	0.14
Radiotherapy	4 (4.5%)	5 (7.5%)	0.5
Palliative	37 (41.6%)	19 (28.4%)	0.089
Duration of cancer (month)	14.4 ± 10.1	13.9 ± 9.7	0.7
Outcome			
Dead	60 (67.4%)	48 (71.6%)	0.6
Alive	29 (32.6%)	19 (28.4%)	
¹ Mean ± SD; n (%)			

²Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact text

Study parameters was compared according to the survival of the cases and it was observed that age was significantly high in non-survived patients with a mean of 58.9 ± 9.6 years. Regarding histopathological image of the disease, a statistically significant difference was found between alive and dead cohorts (P-value <0.001).

The mortality rate was 66.7% in stage IV disease compared to 4.6% in stage II (P-value <0.001). The duration of cancer was significantly lower in the dead group (mean = 9.7 ± 6.1 months) compared to the alive group (24.3 ± 9.5 months) with a P-value of <0.001. as in table 3.

Table 3: Demographic and clinical profile difference between survived and non-survived patients with pancreatic cancer.

Characteristics	Alive, N = 48 ¹	Dead, N = 108 ¹	P-value ²
Age, years	50.2 ± 12.3	58.9 ± 9.6	<0.001
Sex			>0.9
Male	27 (56.2%)	61 (56.5%)	>0.9
Female	21 (43.8%)	47 (43.5%)	
Smoking status			
Non-smoker	32 (66.7%)	55 (50.9%)	0.070
Active Smoker	13 (27.1%)	32 (29.6%)	
Ex-smoker	3 (6.2%)	21 (19.4%)	
Co-morbidities			
Hypertension	14 (29.2%)	29 (26.9%)	0.8
Diabetes	19 (39.6%)	48 (44.4%)	0.6
Heart disease	4 (8.3%)	15 (13.9%)	0.3
Kidney disease	0 (0.0%)	8 (7.4%)	0.11
Thyroid disease	0 (0.0%)	1 (0.9%)	>0.9
Presenting symptom			
Fatigue	9 (18.8%)	25 (23.1%)	0.5
Weight loss	13 (27.1%)	26 (24.1%)	0.7
Abdominal pain	10 (20.8%)	18 (16.7%)	0.5
Headache	1 (2.1%)	10 (9.3%)	0.2
Blurred vision	1 (2.1%)	6 (5.6%)	0.4
Polyuria	6 (12.5%)	10 (9.3%)	0.6
Polydipsia	2 (4.2%)	2 (1.9%)	0.6
Histopathology image			
Adenocarcinoma	34 (70.8%)	105 (97.2%)	<0.001
PNET	12 (25.0%)	2 (1.9%)	
IPMN	2 (4.2%)	0 (0.0%)	
Sarcoma	0 (0.0%)	1 (0.9%)	
Cancer stage			
I	2 (4.2%)	0 (0.0%)	<0.001
II	26 (54.2%)	5 (4.6%)	
III	19 (39.6%)	31 (28.7%)	
IV	1 (2.1%)	72 (66.7%)	
Treatment			
Surgery	45 (93.8%)	25 (23.1%)	<0.001
Chemotherapy	30 (62.5%)	89 (82.4%)	0.007
Radiotherapy	0 (0.0%)	9 (8.3%)	0.058
Palliative	0 (0.0%)	56 (51.9%)	<0.001
Duration of cancer (month)	24.3 ± 9.5	9.7 ± 6.1	<0.001
Duration of diabetes (year)	6.4 ± 4.3	5.5 ± 3.6	0.4

¹Mean ± SD; n (%)

²Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact text

Kaplan-Meier survival analysis was conducted. It was found that the median survival time in this study was 12 months. No significant difference in survival pattern was observed in those with or without diabetes (log-rank test = 0.71). as in fig 1.

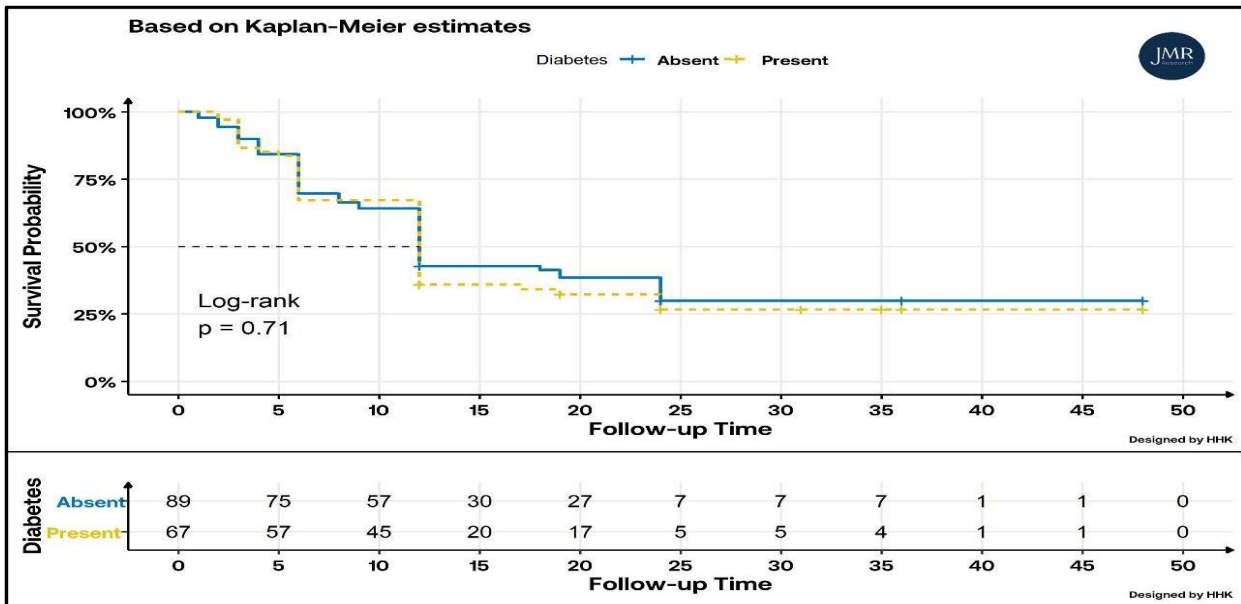


Figure 1: Kaplan-Meier survival curve in patients with or without T2DM. follow-up time is in months.

Regarding the factors that increase the risk of death in pancreatic cancer. It was found that age (HR = 1.04, P-value <0.001), the presence of kidney disease (HR=2.6, P-value = 0.01), patients on palliative care (HR = 7.61,

P-value <0.001) significantly increase the risk of mortality. On the other hand, PNET image of the cancer (HR = 0.08, P-value = 0.014) and surgical management (0.13, P-value <0.001) reduce such risk. As in table 4.

Table 4: Odds for the risk of death in pancreatic cancer patients.

Characteristics	HR1	95% CI1	P-value2
Age, years	1.04	1.02, 1.06	<0.001
Being male	0.98	0.67, 1.43	0.9
Smoking	1.11	0.74, 1.69	0.6
Co-morbidities			
Hypertension	0.89	0.58, 1.36	0.6
Heart disease	1.37	0.79, 2.36	0.3
Kidney disease	2.60	1.26, 5.36	0.010
Diabetes	1.11	0.76, 1.62	0.6
PNET on histopathology	0.11	0.03, 0.45	0.002
Stage	6.70	4.58, 9.80	<0.001
Treatment options			
Surgery	0.13	0.08, 0.21	<0.001
Chemotherapy	1.40	0.85, 2.30	0.2
Radiotherapy	1.65	0.83, 3.26	0.2
Palliative	7.61	5.04, 11.5	<0.001
1HR = Hazard Ratio, CI = Confidence Interval			
2Wald test			
*Unadjusted model			

A logistic model was conducted to investigate the risk factors for death in diabetic patients with pancreatic cancer. Similar to the previous model, the presence of

kidney disease, increasing state, and palliative treatment was associated with higher risk of death in diabetic patients. As in table 5.

Table 5: Odds for the risk of death in diabetic patients.

Characteristics	HR1	95% CI1	P-value2
Age, years	1.03	1.00, 1.06	0.090
Being male	0.76	0.43, 1.34	0.3
Smoking	1.11	0.74, 1.69	0.6
Total duration of diabetes	0.99	0.92, 1.06	0.7
Duration of DM after diagnosis of cancer	0.88	0.71, 1.09	0.3

Duration of DM before diagnosis of cancer	1.02	0.91, 1.13	0.8
Co-morbidities			
Hypertension	0.59	0.32, 1.11	0.10
Heart disease	1.05	0.51, 2.16	>0.9
Kidney disease	2.63	1.11, 6.22	0.028
PNET on histopathology	0.10	0.01, 0.73	0.023
Stage	5.51	3.09, 9.83	<0.001
Treatment options			
Surgery	0.13	0.08, 0.21	<0.001
Chemotherapy	1.40	0.85, 2.30	0.2
Radiotherapy	1.65	0.83, 3.26	0.2
Palliative	7.61	5.04, 11.5	<0.001
1HR = Hazard Ratio, CI = Confidence Interval			
2Wald test			
*Unadjusted model			

DISCUSSION

Pancreatic cancer remains one of the most lethal malignancies worldwide, with high mortality and poor survival outcomes largely due to late-stage presentation and limited therapeutic options.^[17] In the present study, we evaluated the association between type 2 diabetes mellitus (T2DM) and survival outcomes in patients with pancreatic cancer, alongside other clinicopathological factors. The demographic characteristics of our cohort showed a relatively younger mean age (56 years) compared to other studies reporting ranges between 64 and 71 years.^[18] Male predominance (56.4%) was observed, consistent with previous reports.^[19,20] Interestingly, more than half of our patients were non-smokers, aligning with findings by Hsieh *et al.*^[21], although other studies reported higher smoking prevalence.^[18,19] Diabetes mellitus was the most common comorbidity in our cohort (42.9%), which is comparable to findings by Nakai *et al.*^[20] and higher than some international and local reports.^[18,21] Advanced disease at diagnosis was evident, with stage IV being the most frequent (46.8%), consistent with other studies.^[18] This reflects the aggressive nature of pancreatic cancer and the lack of effective early detection strategies. Most patients received chemotherapy, which remains the cornerstone of treatment in advanced disease, while fewer patients underwent surgical intervention, similar to previous findings.^[18] Regarding the association between diabetes and clinical variables, diabetic patients in our study were significantly older, consistent with Hwang *et al.*^[22] However, no significant association was observed between diabetes and sex or smoking status, which aligns with some studies^[20] but contrasts with others reporting higher prevalence among males and smokers.^[22] Importantly, our primary analysis did not demonstrate a significant association between diabetes and overall survival. This finding is consistent with studies by Nakai *et al.*^[20] However, other researchers have reported a modest negative impact of diabetes on survival.^[22,23] Differences in findings may be attributed to variations in sample size, study design, and particularly the duration of diabetes, which has been suggested as an important determinant of prognosis.^[23] Several factors were significantly associated with survival outcomes in our

cohort. Increasing age and advanced cancer stage were strong predictors of poor survival, consistent with previous literature.^[24] Surgical treatment and chemotherapy were associated with improved survival, highlighting the importance of active treatment strategies even in advanced disease.^[20] Conversely, smoking status was not significantly associated with survival, although conflicting evidence exists.^[18] In terms of mortality risk, older age, advanced disease stage, and the presence of kidney disease significantly increased the risk of death. These findings are supported by previous studies demonstrating the adverse impact of comorbidities and disease burden on outcomes.^[24,25] However, diabetes itself was not significantly associated with increased mortality risk in our cohort, which may be influenced by the relatively small sample size and unmeasured confounding factors. This study has several limitations, including the relatively small sample size, lack of detailed assessment of diabetes duration, and potential confounding by other comorbidities. Further large-scale, prospective studies are needed to better clarify the complex relationship between diabetes and pancreatic cancer outcomes.

CONCLUSION

Pancreatic cancer was more common in males, with diabetes as the most frequent comorbidity. Adenocarcinoma predominated, and mortality was high. Diabetes correlated with older age but not survival. Survival depended on age, stage, histology, and treatment. Mortality risk increased with age, kidney disease, advanced stage, and palliative care, while surgery improved outcomes.

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