

## PANCREATIC CANCER- EPIDEMIOLOGY, FREQUENCY OF ASSOCIATED RISK FACTORS, CLINICAL PROFILE, TREATMENT MODALITY AND SURVIVAL ANALYSIS DONE IN A RESOURCE LIMITED SETTING- A RETROSPECTIVE TERTIARY CARE CENTRE EXPERIENCE

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**Abstract**

**Background:** The objective of the study is to undertake a review on the pancreatic carcinoma regarding its Epidemiology, Clinical profile, Frequency of associated risk factors, treatment modality and survival analysis reported in our institution. **Materials And Methods:** A Single centre, Retrospective study. Analysis of all cases of biopsy proven Pancreatic cancer who presented to the Department of Medical Oncology from January 2019 to December 2023 was done by collection of demographic data, clinical and treatment information. **Results:** A total of 134 cases were studied. Majority of the cases were male (81 patients, 60.4%). The median age group of the study population was 52 years. Habits like smoking and alcohol consumption was confined to the male subset of the patient population. Diabetes and an increased body mass index (BMI) were more prevalent in females in our study population. Family history of cancer was noted in 5 cases (3.73%). There was history of chronic pancreatitis present in 21 patients (15.6%). 66 patients had jaundice on clinical examination (49.2%). Tumour marker CA 19-9 was elevated in 76 patients (57%). Head of the pancreas was the most common site of malignancy observed in our study (126 patients, 94%). Majority of the patient presented in stage III disease (48 patients, 35.8%) and 35 patients had upfront metastasis (26.1%). The most common site of metastasis was found to be the liver (28 patients, 65.1%). Only 31 patients were eligible for upfront surgery (23.1%). 51 patients were treated with neo- adjuvant intent (38.1%). However, at the end of neo-adjuvant treatment, only 14 patients were eligible to be taken up for surgery. 52 patients (38.8%) received palliative chemotherapy. Out of 134 cases 27 cases were lost to follow up. So, survival analysis done for only 107 cases. Median overall survival was 15 months, which was around 28, 14, 13, 4 months for stage 1,2,3, & 4 respectively. In univariate and multivariate analysis showed that Diabetes Mellitus, Jaundice, Smoking and stage grouping were independent prognostic factors for survival in carcinoma pancreas while serum Ca 19.9 level was not. **Conclusion:** Early screening in the population with risk factors like smoking, alcohol consumption, diabetes, raised BMI and history of pancreatitis can help in early diagnosis. Future studies to look for prognostic factors and their impact on survival on pancreatic cancer are the need of the hour.

## INTRODUCTION

Pancreatic cancer is an uncommon cancer. According to the Globocan 2022 world data, pancreatic cancer is 12th in incidence and 6th in mortality.<sup>[1]</sup> In the Indian scenario, pancreatic cancer incidence has seen an increasing trend over the years. The incidence of pancreatic cancer in India is 0.5-2.4/100,000 persons per year in women - 0.2-1.8/100,000 persons per year

in men.<sup>[2]</sup> According to Surveillance, Epidemiology, and End Results (SEER) data, median age for pancreatic cancer is 70 years, only 7% of patients diagnosed with PDAC between 2014 and 2020 were under the age of 50 years. Overall 5 years survival rate for pancreatic cancer is 12.8% for all stages, which is 44%, 16.2% and 3.1% for localized, locoregional and distant metastatic cases respectively.<sup>[3]</sup> The cause for such poor long-term

outcomes is possibly related to the fact that the disease is largely asymptomatic in the early stages and by the time symptoms do develop, the disease is locally advanced or metastatic. Only 10-20% of patients have resectable pancreatic cancer at presentation.<sup>[4]</sup> Despite other gastrointestinal tumors, evidences of risk factors for development of pancreatic cancer are poor and they don't explain the whole pancreatic cancer world. Only in 40% of cases risk factors are identifiable from that 10% have genetics risk factors and rest are environmental (modifiable) factors like smoking, obesity, chronic pancreatitis, diabetes mellitus and other associated factors.<sup>[5]</sup> Although pancreatic carcinoma is one of the leading causes of mortality across the globe and India, very little data are available about its epidemiology. It is hypothesized that due to the changing lifestyle globally and, in India, the rates of pancreatic cancer will increase in the near future. The objective of the study is to undertake a review on the pancreatic carcinoma regarding its Epidemiology, Clinical profile, Frequency of associated risk factors, treatment modality and survival analysis reported in our institution.

## MATERIALS AND METHODS

This study was a Single centre, Retrospective study aimed at analysing the Epidemiology, Frequency of associated Risk factors, Clinical profile, Treatment modality and Survival Analysis of all cases of biopsy proven Pancreatic cancer who presented to the Department of Medical Oncology from January 2019 to December 2023 by collection of demographic data, clinical and treatment information through medical records at a Government Tertiary Hospital in South India.

**Statistical Analysis:** Data collection was done in MS Excel 2016. For patient characteristics, Numerical variables are expressed in Median, and Categorical variables are expressed in percentage. Data analysis was done using SPSS software version 25. The chi-square test was used to identify a statistically significant correlation between variables, with a p-value < 0.05 considered as statistically significant. Survival was plotted using Kaplan Meier curve and Log Rank testing was used for comparison of survival function. The Cox regression model was utilised to determine the correlation between numerous parameters and the mortality risk, as presented.

## RESULTS

A total of 134 cases were studied.

### Patient characteristics

Majority of the cases were male (81 patients, 60.4%). The median age group of the study population was 52 years. Maximum number of cases were seen in the age group of 40-60 years (69 patients, 51.4%) Habits like smoking and alcohol consumption was confined

to the male subset of the patient population. 55 out of 81 males were smokers and 43 out of 81 males were alcohol consumers. Diabetes as a comorbidity was present in 42 patients, 31.3% of the cases. Diabetes and an increased body mass index (BMI) were more prevalent in females in our study population. Family history of cancer was noted in 5 cases (3.73%).

### Presentation

There was history of chronic pancreatitis present in 21 patients (15.6%). 66 patients had jaundice on clinical examination (49.2%). Tumour marker CA 19-9 was elevated in 76 patients (57%). Head of the pancreas was the most common site of malignancy observed in our study (126 patients, 94%). Only 5 patients had uncinate process as the primary site of cancer and only 3 patients had disease originating in the tail of pancreas. Majority of the patient presented in stage III disease (48 patients, 35.8%) and 35 patients had upfront metastasis (26.1%). The most common site of metastasis was found to be the liver (28 patients, 65.1%). Lung, non-regional node and adrenal metastasis were also noted in 9, 4 and 2 patients respectively [Table 1].

### Treatment and Follow-up

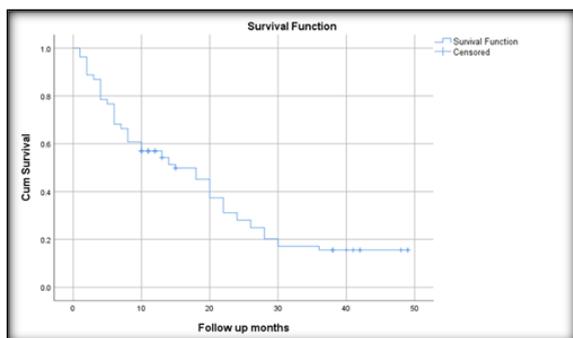
Only 31 patients were eligible for upfront surgery (23.1%). 51 patients were treated with neo-adjuvant intent (38.1%). However, at the end of neo-adjuvant treatment, only 14 patients were eligible to be taken up for surgery. Chemotherapy offered for neoadjuvant treatment was mostly Gemcitabine plus Cisplatin/Carboplatin, only 15% of patients who were young and fit received FOLFIRINIX as neoadjuvant chemo. 52 patients (38.8%) received palliative chemotherapy (gemcitabine plus platinum or single agent gemcitabine according to their performance status). At the end of December 2023, 33 patients (24.6%) remain on treatment or follow up. 74 patients (55.3%) had expired and 27 patients (20.1%) were lost to follow up.

### Survival Analysis

Out of 134 cases 27 cases were lost to follow up. So, survival analysis done for only 107 cases. Median overall survival was 15 months, which was around 28, 14, 13, 4 months for stage 1,2,3, & 4 respectively [Table 2 & Figure 1].

### Univariate and Multivariate Analysis

In univariate analysis Diabetes Mellitus (p=0.013), Jaundice (0.005), Smoking (p=0.04), serum Ca 19.9 levels (<0.01) and Stage grouping (<0.001) showed statistically significant difference in survival. Other factors like Sex (p=0.549), Pancreatitis (p=0.348), alcohol (p=0.201) showed no statistically difference in survival. While in multivariate analysis only Diabetes Mellitus, Jaundice, Smoking and Stage grouping showed statistically significant difference in survival but levels of serum Ca 19.9 did not show any statistically difference in survival. So, ca 19.9 was not an independent prognostic factor but Diabetes Mellitus, Jaundice, Smoking and stage grouping were independent prognostic factors for survival in carcinoma pancreas [Table 3].



**Figure 1: Overall survival**

**Table 1: Patient Characteristics.**

S.no	Patient Characteristics		134 (100%)
1	Sex	Male	81 (60.4%)
		Female	53 (39.6)
2	Age	Median	52 years
3	Diabetes	Yes	42 (31.3%)
		No	92 (68.7%)
4	Smoking	Yes	55 (41%)
		No	79 (49%)
5	Alcohol	Yes	43 (32%)
		No	91 (68%)
6	Pancreatitis	Yes	21 (15.6%)
		No	113 (84.4%)
7	Jaundice	Yes	66 (49.2%)
		No	68 (49.8%)
8	Family History	Yes	5 (3.73%)
		No	129 (96.3%)
9	Site (Pancreas)	Head	126 (94%)
		Uncinate process	5 (3.7%)
		Tail	3 (2.3%)
10	Stage	1	14 (10.4%)
		2	37 (27.6%)
		3	48 (35.8%)
		4	35 (26.2%)

**Table 2: Mean and Median Survival**

Means and Medians for Survival Time						
Meana				Median		
Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval
		Lower Bound	Upper Bound			
18.882	1.691	15.566	22.197	15.000	2.623	9.859

**Table 3: Regression analysis**

Univariate Analysis		Multivariate Analysis	
Parameter	P value	Parameter	P value
DM	0.013	DM	0.020
Sex	0.549	Jaundice	0.004
Pancreatitis	0.348	Smoking	0.045
Jaundice	0.005	Ca 19.9 group 1 (0-35 U/ml)	0.110
Alcohol	0.201	Ca 19.9 group 2 (35-100 U/ml)	0.121
Smoking	0.04	Ca 19.9 group 3 (>100 U/ml)	0.081
Ca 19.9 group 1 (0-35 U/ml)	0.00002	Stage 1	<0.001
Ca 19.9 group 2 (35-100 U/ml)	0.00001	Stage 2	<0.001
Ca 19.9 group 3 (>100 U/ml)	0.013	Stage 3	<0.001
Stage 1	<0.001	Stage 4	<0.001
Stage 2	<0.001		
Stage 3	<0.001		
Stage 4	<0.001		

## DISCUSSION

Although an uncommon cancer, pancreatic cancer in India remains as an area of interest. The majority of patients with newly diagnosed pancreatic cancer present with locoregionally advanced or metastatic

disease, and resection is possible in approximately 10% to 20% of patients at the time of diagnosis.<sup>[6-9]</sup> Most patients who undergo curative intent pancreatectomy will recur between 12 and 22 months postoperatively.<sup>[10,11]</sup> Pancreatic cancer remains an aggressive disease that is potentially curable in

subsets of patients with localized disease who undergo a complete resection. In this study, 67.8% of the patients were in advanced stage (III and IV) at the time of diagnosis. This is a gap that can be filled with increased awareness and screening in people in the population at risk.

Smoking is a modifiable risk factor that is an independent risk factor for acute and chronic pancreatitis. In addition to pancreatitis being a risk factor for pancreatic cancer, Smoking tobacco is also an independent environmental risk factor for pancreatic cancer. A large meta-analysis of 83 studies calculated a relative risk increase at 1.74 for active smokers.<sup>[12]</sup> In our study 41% patients were smokers which was predominant in male sex. Social campaigns and dedicated government programmes in India have made strides in reducing smoking but more needs to be done.

India is the diabetes capital of the world. There have been multiple studies analysing the link between type II diabetes mellitus (DM) and pancreatic cancer, but a causal association has not been clearly established. Two meta-analyses examining more than 30 studies each over four decades have been conducted.<sup>[13,14]</sup> Type II DM was associated with a two-fold risk increase for pancreatic cancer. As with chronic pancreatitis, it appears that the highest risk for pancreatic cancer is in patients with recent onset of DM (<5 years, and particularly within 1 year), as DM is most likely a paraneoplastic manifestation of pancreatic cancer or a result of glandular dysfunction, as opposed to a true risk factor in these patients. In our study Diabetes as a comorbidity was present in 42 patients, 31.3% of the cases. Diabetes and an increased body mass index (BMI) were more prevalent in females in our study population. These numbers suggest that we need to be able to predict and diagnose pancreatic cancer at an early stage by screening of high-risk patients.

In regression analysis done our study both smoking and diabetes came as statistically significant parameters for decreased survival.

Five-year survival of patients with pancreatic cancer has improved marginally over the past two decades, currently estimated to be 10%, 3%, 15%, and 36% for all stages, metastatic, regional, and localized disease, compared to 4%, 2%, 5%, and 12% in 1997.<sup>[15]</sup> As suggested by these data, the largest improvement in survival has been seen in the potential surgical population of patients, likely a multifactorial result of improved patient selection, perioperative care, operative technique, and multi-agent systemic chemotherapy in both the adjuvant and neoadjuvant settings.<sup>[16-18]</sup> In our study median overall survival was 15 months, which was around 28, 14, 13, 4 months for stage 1,2,3, & 4 respectively. So, due to an aggressive nature of the pancreatic cancer diagnosis in early stage is crucial.

## CONCLUSION

Majority of the cases of pancreatic cancer are reported in advanced stage. Early screening in the population with risk factors like smoking, alcohol consumption, diabetes, raised BMI and history of pancreatitis can help in early diagnosis. Future studies to look for prognostic factors and their impact on survival on pancreatic cancer are the need of the hour.

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