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ORIGINAL ARTICLE

Pancreatic cancer: Incidence, clinical profile, and frequency of associated factors in Kuwait

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Abstract *Background:* Pancreatic cancer is an uncommon tumor, but because the mortality rate approaches 100%, this form of cancer has now become a common cause of cancer mortality. Diabetes has been postulated to be both a risk factor and a consequence of pancreatic cancer, but the degree of risk and associated clinical factors remain unclear.
Objectives: The objectives of this study were to investigate the incidence, clinical profile, and the frequency of associated factors of pancreatic cancer in Kuwait.
Methods: The study design was a retrospective hospital-based record study in which records of 251 pancreatic cancer patients registered, evaluated and treated at Kuwait cancer control center from January 2004 through December 2010 were studied.
Results: The overall pancreatic cancer incidence was 0.9/100000 population. Pancreatic cancer was more frequent in older, obese, smoker, diabetic Kuwaiti males with family history of pancreatic cancer. Metastasis was diagnosed in 67.7% of patients at diagnosis of pancreatic cancer.
Conclusions: Pancreatic cancer in Kuwait is diagnosed in late stages. Screening for this disease was indicated specially in diabetic patients. A comprehensive comparative study is required for determination of risk factors that could be associated with the disease.

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1. Introduction

Worldwide, pancreatic cancer ranks 13th in incidence but 8th as a cause of cancer death.[1] In different areas of the world, pancreatic cancer is quite infrequent; the incidence is highest in North America and Europe (11.8–12.5 cases per 100,000 people) and lowest in southern and eastern Asia and most of Africa (< 3.5 cases per 100,000 people). The incidence in India is less than 2 cases per 100,000 persons per year.[1]

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The relative 1-year survival rate for pancreatic cancer is only 24%, and the overall 5-year survival is 5%.[3] This is due to the fact that pancreatic cancer is hard to catch early. It is notoriously difficult to diagnose in its early stages. At the time of diagnosis, 52% of all patients have distant disease and 26% have regional spread.[4]

Several personal and environmental factors have been associated with pancreatic carcinogenesis. Cigarette smoking is the most well-established environmental risk factor for pancreatic cancer worldwide.[5–8] Estimates indicate that 40% of pancreatic cancer cases are sporadic in nature. Another 30% are related to smoking, and 20% may be associated with dietary factors. Only 5–10% are hereditary in nature.[9] Diabetes mellitus may be associated with a 2-fold increase in the risk of developing pancreatic cancer.[10–12] Less than 5% of all pancreatic cancers are related to underlying chronic pancreatitis.[13,14] Approximately 5–10% of patients with pancreatic cancer have some genetic predisposition to developing the disease.[15–17] In a number of studies, obesity, especially central, has been associated with a higher incidence of pancreatic cancer.[18] It was found that being overweight or obese during early adulthood was associated with a greater risk of pancreatic cancer and a younger age of disease onset, while obesity at an older age was associated with lower overall survival.[19]

In the absence of predisposing conditions, such as familial pancreatic cancer and chronic pancreatitis, pancreatic cancer is unusual in persons younger than 45 years. After an age of 50 years, the frequency of pancreatic cancer increases linearly. The death rate from the disease has risen from 5 per 100,000 population in 1930 to more than 10 per 100,000 in 2003.[3]

To the best of our knowledge, few studies have been done to investigate pancreatic cancer in Kuwait. Therefore, the aim of our study was to assess the incidence, clinical profile, and the frequency of associated factors of pancreatic cancer in Kuwait.

2. Methods

The study design was a hospital-based descriptive one relied upon record study in which cases were retrospectively ascertained. All the necessary approvals for carrying out the research were obtained. The Ethics Committee of the Kuwaiti Ministry of Health approved the research. A total of 276 patients with pancreatic cancer were registered during the study period. Description of 251 patients was available whereas full data for 25 cases were not available.

Cases were recruited from the population of patients diagnosed with pancreatic cancer who were registered, evaluated and treated at Kuwait Cancer Control Center (KCCC) from January 2000 through December 2010. The inclusion criteria were patients with pathologically confirmed diagnosis of pancreatic cancer. The exclusion criteria were presence of other types of pancreatic disease, such as neuroendocrine tumor, adenomas, cysts, or unknown primary tumors; concurrent cancer at another organ site; and past history of cancer.

The necessary data were collected using a structured questionnaire by trained persons who were able to extract the information from the medical record or the data base of KCCC registration center. The collected data included sociodemographic and personal habits (age, gender, residence, nationality, civil status); medical history (family history of cancer or DM, presence of DM and its type and duration). Also it included data related to pancreatic cancer (onset, initial symptoms and signs, diagnosis and treatment).

Data were collected and coded then entered into an IBM compatible computer, using the SPSS version 12 for Windows. Qualitative variables were expressed as number and percentage while quantitative variables were expressed as mean and standard deviation.

3. Results

Kuwait cancer registration center reported 276 new cases from 2000 to 2010, with 0.9/100000 population as an overall incidence of pancreatic cancer. The highest incidence rate reported in 2000 was 1.3/100000 population while, the lowest was reported in the year 2004. No significant trend was detected as shown in Table 1.

Table 2 summarizes the demographic features of the pancreatic cancer patients. The overall ratio of men to women was 1.5:1. The majority of patients were Kuwaiti (52.6%), the Arab patients constituted 38.6% of cases and the non-Arab constituted only 8.8%. Most of patients were from Hawally and Farwaniya (26.3% and 24.7% respectively), and the rest were from other governorates in Kuwait. The mean age of patients was 60.6 ± 7.7 years, the majority of cases were fifty years or older, whereas 31.1% were in the age group between 50 to less than 60 years and 59.4% were 60 years or more.

Table 3 illustrates the frequency of well-known risk factors related to pancreatic cancer. About one fifth of patients 19.9% had positive family history of pancreatic cancer and 44.6% had family history of diabetes mellitus. The mean BMI was 26.8 ± 4.8 and the majority of cases presented with overweight and obesity whereas 36.3% of cases were overweight, 18.7% were obese and 7.2% were very obese.

The proportion of pancreatic cancer patients with a history of cigarette smoking was 38.2%. The majority of smokers gave history of smoking at least one pack per day. Also, 61.4% of smokers had history of smoking for 30 years or more, 25.5% for 20–29 years and only 13.2% for less than 20 years with a mean duration of smoking = 30.3 ± 10.2 years.

Patients with diabetes mellitus constituted 61.4%; and 52.6% of them were type 2. In 62.3% of patients, diabetes mellitus proceeded to pancreatic cancer and the reverse occurred

Table 1 Incidence rate of pancreatic cancer in Kuwait 2000–2010.

Year	No. of new cases	Population	Rate/100,000
2000	29	2189668	1.3
2001	23	2243080	1.0
2002	22	2363325	0.9
2003	24	2484384	1.0
2004	16	2644777	0.6
2005	20	2866888	0.7
2006	33	3051845	1.1
2007	28	3328136	0.8
2008	29	3640427	0.8
2009	25	3442945	0.7
2010	27	3566437	0.8
Average	276	31821912	0.9

Table 2 Socio-demographic characteristics of pancreatic cancer patients.

Variable	No.	%
Age groups		
40-	24	9.6
50-	78	31.1
⩾60	149	59.4
Mean ± SD	60.7 ± 7.7	
Gender		
Male	150	59.8
Female	101	40.2
Nationality		
Kuwaiti	132	52.6
Arab	97	38.6
Non Arab	22	8.8
Place of residence		
Capital	38	15.1
Hawally	66	26.3
Mubarak	37	14.7
Jahra	32	12.7
Farwaniya	62	24.7
Ahmadi	16	6.4
Marital status		
Single	12	4.8
Married	221	88.0
Divorced or widows	18	7.2
Total	251	100.0

Table 3 Frequency of associated factors among pancreatic cancer patients.

Associated factors	No	%
Family history of pancreatic cancer		
Yes	50	19.9
No	201	80.1
Family history of Diabetes mellitus		
Yes	112	44.6
No	139	55.4
BMI		
Normal	95	37.8
Overweight	91	36.3
Obese	47	18.7
Very obese	18	7.2
Mean ± SD	26.8 ± 4.8	
Smoking history		
Yes	96	38.2
No	155	61.8
Amount of smoking[a]		
Non smokers	55	61.8
Half pack	8	3.2
One pack	36	14.3
1.5 pack	12	4.8
2 pack	31	12.4
More than 2 pack	9	3.6
Duration of smoking[a]		
<20	13	13.5
20-	25	26.0
⩾30	58	60.4
Mean ± SD	30.3 ± 10.2	
History of diabetes mellitus		
No	97	38.6
Yes	154	61.4
Type of Diabetes[b]		
Type 2	73	47.4
Type 1	81	52.6
Which is first[b]		
Diabetes mellitus first	96	62.3
Cancer pancreas first	58	37.7
Duration of diabetes[b]		
<2	6	3.9
2-	7	4.5
4-	135	87.7
⩾6	6	3.9
Mean ± SD	5.2 ± 1.3	
Duration of pancreatic cancer		
<2	11	4.4
2-	67	26.7
4-	130	51.8
⩾6	43	17.1
Mean ± SD	4.6 ± 1.4	
Total	251	100.0

[a] Non smokers were excluded.
[b] Non diabetic patients were excluded.

among 37.7% of patients. The mean duration of diabetes mellitus among patients was 5.2 ± 1.3 years with more than 90% having diabetes mellitus for four or more years. The mean duration of pancreatic cancer was 4.6 ± 1.4 with 68.9% having the disease for ⩾4 years.

Table 4 shows the clinical and diagnostic characteristics of pancreatic cancer patients. The majority of patients complained from abdominal pain (91.2%), jaundice (87.6%), anorexia (39.4%) loss of weight (39.4%), and nausea and vomiting (36.3%). Other complaints were less frequently encountered. The same table reveals that 67.7% of patients were complaining from metastasis either in liver (52.6%), lymph node (2.8%) or on other sites (12.4%) at the time of diagnosis of pancreatic cancer.

In slightly more than three quarters of patients (76.1%), cancer was located in the head of the pancreas, 15.1% in the tail and only 8.8% in the body. Only 45.8% of patients were diagnosed clinically and 90% radiologically, where computed tomography (CT) procedure was used in 75.3%. In addition, more than 88.9% were diagnosed through biopsy (33.1%) or tissue pathology (55.8%). The main lines of treatment given to patients were surgery (47.8%), chemotherapy (61.0%) and radiotherapy (18.3%)

4. Discussion

The current work is the first epidemiological study of pancreatic cancer conducted in Kuwait. KCCC reported 276 new cases from 2000 to 2010, with 0.9/1000000 population as an overall incidence of pancreatic cancer. The incidence rates in high-risk countries are about 5–7 times higher than incidence rates in low-risk countries with accurate cancer registration, implying that environmental factors play an important role.[20,21] These wide variations may be due to the study design, setting, population sample and technique used for diagnosis. The low rate reported in Kuwait could be partially attributed to the underestimation as many cases may not be registered as those treated abroad and those who were admitted to the military hospital. However these cases constituted a small proportion to affect the rate significantly.

Table 4 Clinical characteristics of pancreatic cancer patients.

Variables	No.	%
Initial symptoms		
Abdominal pain	229	91.2
Jaundice	220	87.6
Nausea and vomiting	91	36.3
Anorexia	99	39.4
Weakness	32	12.7
Loss of weight	99	39.4
Constipation	27	10.8
Diarrhea	4	1.6
Backache	1	0.1
Fever	8	3.2
Enlarged abdomen	3	1.2
Metastasis	170	67.7
Liver	132	52.6
Lymph nodes	7	2.8
Others	31	12.4
Site of the cancer		
Head	191	76.1
Body	22	8.8
Tail	38	15.1
Clinical diagnosis		
No	136	54.2
Yes	115	45.8
Radiological diagnosis		
No	25	10.0
X ray	8	3.2
Ultrasound	25	10.0
CT	189	75.3
MRI	4	1.6
Pathological diagnosis		
Non	22	8.8
Biopsy	83	33.1
Tissue pathology	140	55.8
Other laboratory methods	6	2.4
Treatment		
Surgery	120	47.8
Chemotherapy	153	61.0
Radiotherapy	46	18.3
Total	251	100.0

In the present study, various factors have been identified and associated with pancreatic cancer as age, gender, family history, duration of diabetes, BMI and smoking history. The study demonstrated an increasing frequency of pancreatic cancer with advanced age. The mean age of patients was 60.6 ± 7.7 years, the majority of them were fifty years or older, where 31.1% were in age group between 50 to less than 60 years and 59.4% were 60 years or more. This was in accordance with the results reported in SEER Cancer Statistics Review that pancreatic cancer is predominately a disease of older individuals and almost all patients are older than 45.[22] In consistent with our results, Albert and Patrick[23] reported that in the absence of predisposing conditions, such as familial pancreatic cancer and chronic pancreatitis, pancreatic cancer is unusual in persons younger than 45 years but the frequency of pancreatic cancer increases linearly after the age of *fifty*.

The results of the present study revealed that males were slightly more likely to develop pancreatic cancer than females. This is due to, at least in part, increased tobacco use in males. The American Cancer Society reported that the incidence of pancreatic cancer in males was 12.1 cases and in females, the rate was 9.1 cases per 100,000 persons per year.[24] In the USA, male rates were 40% higher than female rates while in Japan the corresponding figure was 70%.[22,25] These trends probably represent the effect of changing smoking rates for males than females.

The majority of patients in this study were Kuwaiti (52.6%) and Arab patients (38.6%). The reasons for this are not clear. However, Arnold et al. (26) found that excess pancreatic cancer in certain population group cannot be attributed to currently known risk factors, suggesting the possibility of the underlying frequency of predisposing genetic mutations for pancreatic cancer. Other explanation could be that non-Kuwaiti are mostly healthy individuals in the middle age who came to Kuwait for work and might return to their countries before reaching the age at which usually pancreatic cancer occurs.

A threefold greater risk for pancreatic cancer in subjects with a positive family history of pancreatic cancer was reported.[27] Greer et al.[15] reported that approximately 5–10% of patients with pancreatic carcinoma have some genetic predisposition for developing the disease.[15] The current study showed that about one fifth (19.9%) of patients reported first degree positive family history of pancreatic cancer. This could be due to an inherited syndrome, arranged marriage between the same families, and/or due to a function of a shared environmental exposure such as cigarette smoking.[16,17,26–28]

Studies evaluating the relationship between obesity and pancreatic cancer have been inconsistent.[29–31] In the present study, the mean BMI was 26.8 ± 4.8 and the majority of cases were either overweight and/or obese (36% and 19% respectively). A recent meta-analysis reported that obese people may have a 19 percent higher risk of pancreatic cancer than those with a healthy BMI. The results, however, were not conclusive.[32]

Our results showed that smoking for long duration was encountered among our patients, where 38.2% of patients gave history of smoking from one pack to more than two packs. Moreover, 60.4% of smoking patients used to smoke for 30 years and more. Nearly all published reports showed that smokers had about a 2-fold increased risk, compared to non-smokers.[7,8,10] The findings in these studies, performed in various countries, were highly consistent.[28,33]

Numerous epidemiological studies have reported a positive association between *diabetes mellitus* (*DM*) and the risk of pancreatic cancer.[10,11,34] In the present study, patients with DM constituted 61.4%, 52.6% of them were type 2 (T2DM). Several studies revealed that pancreatic cancer is more common in people with T2DM.[10,11] The estimation of the overall risk of pancreatic cancer among diabetics is consistent with the up to 2-fold increase in risk reported by other investigators.[11,35,36] The present study *showed* that DM proceeded to pancreatic cancer in 62.5% and the reverse occurred among 37.7% of patients. The reason for this link is not known. Most of the risk is found in people with T2DM as in our results. It is often related to being overweight or obese. However, The National Comprehensive Cancer Network (NCCN) guideline also notes an association between sudden onset of T2DM in an adult older than 50 years and a new diagnosis of pancreatic cancer.[13]

Pancreatic cancer is commonly located at the head of pancreas.[35–37] In consistence, our study showed that slightly more than three quarters of patients had cancer in the head

of pancreas, 15.1% in the tail and only 8.8% in the body. Sata et al., reported that pancreatic cancer was located in the head of the pancreas in 71%, in the body in 21% and in the tail in 7%.[38] This could be explained by the possibility of ingested tobacco products that reach the pancreas directly after reflux into the pancreatic ductal system from the duodenum.[38]

In the present study, the majority of patients complained from abdominal pain (91.2%), jaundice (87.6%), anorexia (39.4%) loss of weight (39.4%), and nausea and vomiting (36.3%). This is in agreement with several studies that reported that pancreatic cancer does not manifest as early symptoms and initial symptoms are often nonspecific, such as abdominal discomfort, abdominal pain, weight loss, anorexia, and nausea.[36,37] Pain or jaundice are frequently presenting symptoms with pain usually preceding jaundice.[39,40]

The vast majority of pancreatic cancers extend beyond the pancreas when they are diagnosed.[41,42] Our data showed that liver and lymph nodes were the most common sites of metastases among our patients. Early metastasis to regional and distant lymph nodes is also frequently observed.[2]

Occasionally, a pancreatic cancer is found incidentally during an abdominal ultra sonography (US) examination.[43] In the current study, 45.8% were diagnosed clinically and 90% radiologically; the majority of them by computed tomography (CT) (75.3%), in addition, more than 90% were diagnosed through biopsy (33.1%), tissue pathology (55.8%) and other laboratory methods (2.4%). Researchers reported that US and CT are the imaging modalities that are most frequently used in the diagnosis of pancreatic cancer. Both modalities are useful in detecting the primary tumor as well as extrapancreatic spread and hepatic metastases.[41,44]

The study revealed that the main lines of treatment given to patients were surgery (47.8%), chemotherapy (61.0%) and radiotherapy (18.3%). From all treatment modalities employed in the management of pancreatic cancer, only surgery has curative potential. Unfortunately, only a minority of patients with pancreatic cancer will be suitable candidates for pancreatic resection with curative intent, mostly due to the fact that the disease does not produce distinct symptomatology in its early stages. Subsequently, the vast majority of patients have locally advanced or disseminated disease at the time of diagnosis.[2,45–47]

We acknowledged certain limitations of our study. Firstly, the calculated incidence could be lower than the actual figure due to missing of cases treated in the military hospital and/or private sector. Secondly, as we relied upon record study, the data obtained might be, to certain extent, affected by the quality of recording. Thirdly, as in any descriptive study, conclusion regarding associated variables as risk factors could not be reached. Nevertheless, the results are consistent with those coming from comparative studies.

5. Conclusion

The incidence of pancreatic cancer in Kuwait is relatively low. Pancreatic cancer in Kuwait is diagnosed in late stages. Screening for this disease should be performed specially in patients with T2DM and family history of cancer. Future studies on pancreatic cancer should be done and directed strongly to the assessment of related risk factors hence, concentrating on genetic, environmental and quality of life factors.

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