RESEARCH ARTICLE

Clinical, Laboratory Biomarkers and Imaging Findings of Pancreatic Adenocarcinoma in Iran

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Abstract

Background: Pancreatic cancer has a high mortality rate because it is usually diagnosed late. Since little is known about this cancer in Iran, with the aim of improving this knowledge deficiency, we evaluated clinical, laboratory biomarkers, imaging findings and treatment modalities in Iranian patients with pancreatic adenocarcinoma. Materials and Methods: 131 cases of pancreatic adenocarcinoma in 2010-2013 were obtained from the Taleghani Hospital Record Department. Cases confirmed by histopathology from CT-guided biopsy, EUS-FNA and surgery examination were included. We excluded those with incomplete medical records. Results: The study included 131 subjects between 24 and 97 years of age and a mean age of 63±13.4 years. Eighty (61.1%) were male and 51 (38.9%) female. Previous history included diabetes mellitus in 36 (27.5%), alcohol drinking in 5 (3.9%), smoker in 28 (21.4%) and opium addiction in 13 (10%) . The common presenting history included weight loss in 79 (60.3%), abdominal pain in 77 (58.8%), fever in 11 (8.4%), nausea in 30 (22.9%), jaundice in 72 (55%), pruritus in 52 (39.7) and anemia in 33 (25.2%) . CA19-9 levels with cut offs of 50, 100 and 200 U/ml were increased in 81%, 72% and 66% of patients, respectively. Tumor staging was: stage I, 3 (2.3%); stage II, 10 (7.6%); stage III, 58 (44.3%); and stage IV, 60 (45.8%). From 45 patients, 17 received ERCP inserted metallic stents and 22 plastic stents, the remaining 6 failed that PTC was done. Whipple surgery and chemotherapy were conducted for 10 and 29 patients, respectively. Conclusions: This disease affected older people and there was a male preponderance. The commonest risk factors were diabetes mellitus, smoking and cholelithiasis. The majority of patients presented with loss of appetite, loss of weight, jaundice, abdominal pain and discomfort. Almost all presented at late stages of the disease so that curative surgery was impossible. Also chemotherapy was only performed in a few patients as a neoadjuant treatment.

Keywords: Pancreatic adenocarcinoma - diabetes mellitus - EUS-tumor staging - Iran

Introduction

In Worldwide, Pancreatic carcinoma causes more than 220000 deaths annually and is the sixth major cause of cancer-related mortality in 2005 (Taghavi et al., 2011). It is the fourth leading cause of cancer-related death in the United States (Atlanta: American Cancer Society, 2007), and 6th in Europe (Bray et al., 2002). Based on the GLOBOCAN 2012 estimates, about 330372 persons pancreatic cancer cases deaths are estimated to have occurred in 2012; and is the12th leading cause of cancer deaths in men (173812 deaths annually) and women (156560 deaths annually). This increase is because of the aging and growth of the world population alongside an increasing adoption of cancer-causing behaviors, particularly smoking.

In Asia, incidence and mortality rate of pancreatic carcinoma was 143363 and 137251 respectively.

China, Japan, India, Indonesia and Korea are the first to fifth, That Iran among Asian countries in terms of mortality and incidence of pancreatic cancer is ranked eleventh (incidence 1138 and Mortality rate 1096). Pancreatic cancer is cancer of the twelfth leading to death in Iran (Globocan, 2012).Table 1 shows a comparison between incidence and mortality of pancreatic cancer patients in worldwide, Asia and Iran.

In 2003, pancreatic cancer incidence rate per 100,000 population was 0.40% in females and 0.46% in males, in 2004; 0.42% in females and 0.46% in males and in 2005

Table 1. Estimated Pancreatic Cancer-Related Incidence, Mortality and 5-Year Prevalence(GLOBOCAN 2012)

	Incidence	Total %	ASR (w)	Mortality	Total %	ASR (w)	5-y prevalence	Total
World	337872	2.4	4.2	330372	4	4.1	211544	0.7
Asia	143363	2.1	3.2	137251	3.1	3	97541	0.7
Iran	1138	1.3	1.8	1096	2.1	1.8	775	0.5

*ASR: Age -standardised rate(w) per 100000

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the pancreatic cancer incidence rate was 0.39% in females and 0.56% in males (Parkin et al., 2005; Jamali et al., 2009).

Most pancreatic cancers occur in older people, The investigations show that age is a risk factor for this cancer (Vincent et al., 2011). Another factor, cigarette smoking has proven epidemiological correlation with development of pancreatic cancer (Momi et al., 2012). Other factors include positive family history (Schenk et al., 2001) and type 2 diabetes mellitus (Huxley et al., 2005). Pancreatic cancer symptoms are vague and unknown, this is a reason for that diagnosed in the final stages. The high mortality rate of pancreas cancer is nearly the same as the incidence rate (Lowenfels et al., 2002).

In recent years, few studies have been conducted in relation to pancreatic cancer in Iran. This study is a review of all cases of pancreatic adenocarcinoma admitted in Taleghani hospital to describe the epidemiological. We can hopefully develop targeted strategies and activities for the early management of pancreas cancer in Iran.

Materials and Methods

This study was conducted at Taleghani Hospital, which is located in Tehran, Iran. It is a tertiary referral centre and the main provider of cancer care services in the area. A list of pancreatic cancer patients admitted to Taleghani Hospital in 2010-2013 was obtained from the Department of Records. We included only confirmed cases of pancreas adenocarcinoma by histopathology examination. We excluded those with incomplete medical record. A standardized check list was used to collect data from the records. The data that extracted were sociodemographic factors such as age, sex, marital status; smoking status, alcohol intake, other risk factors, clinical characteristics such as family history of pancreatic cancer, presenting symptoms, method of diagnosis and the treatment received. Data entry and analysis was conducted using the Statistical Package for the Social Science (SPSS) version 17.0. Data distributions and frequencies (%) were examined. All continuous variables were expressed as mean and standard deviation (SD) or as median while categorical variables as frequency and percentage.

Results

The study included 131 subjects between 24 and 97 years of age and a mean age of 63±13.4 years with Range 73 years. 80 (61.1%) were male and 51 (38.9%) female. The majority of pancreas cancer patients 96.4% married. Regarding the risk factors; 28 (21.4%) had smoked, 5 (3.9%) had been taking alcohol, opium addiction in 13 (10%) patients, 36 (27.5%) had diabetes, 24 (18.3%) had cholelithiasis, 23 (17.5%) had cholesyctectomy and only 5 (3.8) % had family history of pancreas cancer. The majority of patients 88 (67.1%) presented with complain of loss of appetite, 79 (60.3%) had loss of weight, nausea in 30 (22.9%), fever in 11 (8.4%), 72 (55%) presented with jaundice, 52(39.7) with pruritus, 77 (58.8%) presented with abdominal pain and 33(25.2%) had anemia.

CA19-9 level with cut off 50, 100, and 200 U/ml were increased in 81%, 72% and 66% of patients respectively. Table 3 shows important laboratory test in this review. Most tumors 94 (71.8%) located at head, 14 (10.7%), 10 (7.6%), 13 (9.9%), located at body, tail and unicate of pancreas respectively. Pancreatic duct dilation was

Table 2. Risk Factors and Symptoms of Pancreatic Adenocarcinoma Cases

Risk factors	No.	%	Presenting symptoms	No.	%
Diabetes mellitus	36	27.5	Loss of appetite	88	67.1
smoker	28	21.4	Loss of weight	79	60.3
Cholelithiasis	24	18.3	Abdominal pain	77	58.8
cholesyctectomy	23	17.5	Jaundice	72	55
opium addiction	13	10	Anemia	33	25.2
Alcohol drinker	5	3.9	Nausea	30	22.9
Family history	5	3.9	Fever	11	8.4

Table 3. Laboratory Finding

	Mean±SD
ESR	41.3±25
AST	102±11
ALT	133±18
ALP	886±87
Bil T	9.3±9.6
LDH	389±40
CA19-9	442±53

Table 4. Clinical Characteristics

		Frequency	(%)
Location of tumor:	Head	94	(71.8)
	Unicate	13	(9.9)
	Body	14	(10.7)
	Tail	10	(7.6)
Staging:	I	3	(2.3)
	II	10	(7.6)
	III	58	(44.3)
	IV	60	(45.8)
Treatment:	Stenting		
	Plastic	22	(16.7)
	Metallic	17	(12.9)
	Failed	6	(4.5)
	Whipple	10	(7.6)
	Chemotherapy	29	(22.1)

Table 5. Estimated Pancreatic Cancer-Related Incidence, Mortality and 5-Year Prevalence (GLOBOCAN 2012)

	Incidence PC	ASR	Mortality	ASR	Mean age of PC patients	Median age in Population(yr)
China	65727	3.6	63662	3.5	72	36.3
Japan	32899	8.5	31046	8.2	60.5	45.8
India	11936	1.2	10828	1.1		26.7
Indonesia	5829	2.7	5642	2.6		28.9
Korea	5379	6.7	5086	6.2	62.3	33.2
Turkey	3174	4.5	3064	4.3	56- 59.6	29.2
Iran	1138	1.8	1096	2.1	60.7- 63	27.8

Table 6. Estimated Pancreatic Cancer-Related Incidence, Mortality on Based Sex

		Incidence	%Total	ASR(w)	Mortality	%Total	ASR(w)
World	Men	178161	2.4	4.9	173812	3.7	4.8
	women	159711	2.4	3.6	156560	4.4	3.4
Asia	Men	80704	2.2	3.8	76698	2.9	3.6
	women	62659	2	2.6	60553	3.3	2.5
Iran	Men	635	1.4	2.1	608	2	2
	women	503	1.3	1.6	488	2.1	1.6

seen in 116(88%) patients. The majority of cancers 60 (45.8%) and 58 (44.3%) were in stage IV and stage III and only 10(7.6%) and 3(2.3%) were stage II and stage I respectively, From 45 patients underwent ERCP, metallic stent inserted in 17 patients and plastic stent in 22 patients and 6 patients failed that PTC was done. Whipple surgery and chemotherapy was done for 10 and 29 patients respectively.

Discussion

The incidence of pancreatic cancer is on the rise (Helmstaedter et al., 2008). On the other hand, five-year survival rate has not changed in 30 years ago (14). In recent years, much research has not been in Iran and the countries of the region. In this study, we are providing a review on risk factors, clinical, Laboratory Biomarkers and Imaging finding of pancreatic adenocarcinoma in Iran.

The incidence of pancreatic cancer increases steadily with age; approximately 80% of cases are diagnosed between 60-80 years of age. In our study, mean age of patients was 63 years. This result is almost identical to another researches in Iran (Jamali et al., 2009; Ahmadloo et al., 2011; Taghipour et al., 2013) and in Asia (Inoue et al., 2003; Engin et al., 2012; Emine et al., 2013; Woo et al., 2013). China ranked first the incidence of pancreatic cancer with a mean age of 72 years is different from other countries in the region and had highest fatality rate (9.6%) (Jianfeng et al., 2013; Wang et al., 2013) pancreatic cancer is still the disease of elderly people in Iran and Asia but patients are comparatively younger at the time of diagnosis than in western countries. This may suggest that Some genetic and environmental factors could contribute to the development of pancreatic cancer (Jamali et al., 2009).

Our present study showed that there were more males having pancreas adenocarcinoma compared to females with a male-to-female ratio of between 1.56. Throughout the world, pancreas cancer is more common among males, with a male-to-female ratio of between 1.3 and 2 (Barkin et al., 1999).

Therefore, similar to western countries, pancreatic cancer in Iran occurs slightly more commonly in men than in women. This male preponderance is probably related to the fact that there is a higher prevalence of smoking and some other risk factors among males (Lowenfels et al., 2002).

The important risk factors in worldwide studies are smoking, diabetes mellitus, pancreatitis, pernicious anemia, cholecystectomy, alcohol, family history of pancreas cancer, and previous laparatomy (Lin et al., 2001; Lowenfels et al., 2002; Ghadirian et al., 2003).

Cigarette smoking is widely known as a risk factor of pancreatic cancer in Japanese studies (p<0.001) (Lin et al., 2002; Matsuo et al., 2011; Nakao et al., 2013). Another study in Turkey confirmed this related between smoking and pancreatic cancer (p<0.0001)(Engin et al., 2012) and according to a study in Iran, too. (Jamali et al., 2009). Smoking is less common in the Iranian population. This may contribute to lower incidence of pancreatic cancer in Iran compared to western countries (Fotouhi et al., 2009).

Another important risk factor of pancreatic cancer is diabetes mellitus. A study conducted in Taiwan reported that pancreatic cancer was significantly associated with diabetes mellitus with more than three times of risk compared to the non diabetics (Chiou et al., 2011). The increased risk of pancreatic cancer seems related to the duration of diabetes mellitus (Lin et al., 2001). Among region countries, Korean (Woo et al., 2013) and Japanese (Matsuo et al., 2011) studies reported a meaningful relation between diabetes and pancreatic cancer (p<0.01 and p<0.001 respectively), but in a study of Turkey (Engin et al., 2012) do not confirmed result (p<0.9).

Other risk factors that have been mentioned sporadically in worldwide literature, Included: Drinking alcohol, family history, blood group (p<0.01), HCV (p<0.01), HBV infection can cause about 40.7% increase in the risk of pancreatic cancer (Matsuo et al., 2011; Engin et al., 2012; Lei et al., 2013; Woo et al., 2013). Trace elements significant increase (p<0.0001) in blood Cd in PC patients compared with controls (Farzin et al., 2013). Also the protective effects of physical activity on pancreatic cancer risk are hypothesized in some articles (Inoue et al., 2008; Jiao et al., 2009; Stevens et al., 2009; Kruk et al., 2013). In our study, many of the patients were discovered having Diabetes mellitus (27.5%) at presentation of pancreas cancer. The prevalence of smoking was (21.4%) in the present study which was the second highest risk factor after Diabetes mellitus. Unfortunately, the risk factors of the disease are not extensively studied in Iran.

The clinical presentation of pancreatic adenocarcinoma patients in our study was almost similar to other studies (Jamali et al., 2009; Taghipour et al., 2013). The majority of our patients presented to the hospital with complaints of loss of appetite and loss of weight. In addition, patients also presented with abdominal pain, abdominal discomfort and fever. On examination, half of the pancreas cancer patients presented with jaundice. Currently, there is no screening program for the early detection of pancreatic cancer in Iran.

The diagnosis of pancreas cancer is challenging as the pancreas is located in a relatively inaccessible site within the abdominal cavity, thus this cancer is usually diagnosed in the advanced stage. In the early stage of disease, most patients have very few symptoms, which are usually non specific. The non-specific symptoms include generalized dyspepsia, early satiety and nausea which are unlikely to be acted on seriously by the patient or general practitioner. Most of our patients were diagnosed pancreas cancer by histopatology. The majority of our patients were in stage III and IV. Most of them had liver metastases. This is probably related to the delay of presentation of symptoms and the difficulty of diagnosing pancreas cancer. Surgical resection is the best choice of treatment for pancreas cancer. However, many patients were not candidates for surgery because of local spread and disease metastases. Only 10 patients had the Whipple procedure because of advanced disease and other complications. In addition, 29 patients had some palliative treatments such as chemotherapy. Survival of pancreatic cancer is poor especially in untreated patients.

There were some limitations in this study. This was a review of medical records and has some inherent

weaknesses such as missing variables, in particular, socio-economic details and blood investigations. We could not also examine the effects of diet and obesity on the occurrence of pancreatic cancer.

We are advocating early detection of pancreatic cancer by using an imaging modality or molecular markers especially in a high risk population. Our institution also needs to improve surgical intervention for pancreatic cancer.

The awareness about pancreas cancer should be raised among the Iranian population especially with regards common presenting symptoms and risk factors. Pancreas cancer represents a considerable challenge to the clinician. Surgical advancement is needed that can be performed safely in patients who are fit for surgery in a specialist centre. In view of the poor survival rate of this disease, special attention must also be given to the advancement of palliative care and the training of specialized hospice care personnel. Advances in symptom palliation and novel treatments may improve the survival and quality of life for those patients who cannot undergo surgery.

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