Original Research Paper

VOLUME-6 | ISSUE-4 | APRIL - 2017 • ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

A Study On Risk Factors Of Carcinoma Head of Pancreas

Gastroenterology

KEYWORDS: carcinoma pancreas, alcoholic pancreatitis

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ABSTRACT

Carcinoma head of pancreas is fatal disease and has high mortatality as the disease is being diagnosed at late stages. And even after diagnosis resectability of disease is less and mean survival being 11-20 months after resection. And in unresectable patients mean survival is of 2 to 6 months. Aims of this study were to study alcohol consumption and smoking as risk factors for carcinoma head of pancreas. This was a case control study among patients admitted to surgical wards of Medical College Hospital, Thiruvananthapuram. 68% of cases with carcinoma head of pancreas in our study were smokers and 64% of cases with carcinoma head of pancreas in our study were alcoholics. Age>50, smoking and alcohol consumption were found to be risk factors for carcinoma head of pancreas by univariate analysis.

Introduction

Carcinoma head of Pancreas is a relatively fatal disease with a high mortality and also has poor prognosis, because it is usually diagnosed in the late stage at an unresectable stage. A 10-year study in the USA found that the resectability rate of carcinoma head of pancreas is only 4.8%[1]. A 30-year study in France found that the 5-year survival rate is <5% even after sufficiently early diagnosis[2].In a review by Michaud, over 200 000 people die of carcinoma head of pancreas in the world annually[3]. Only about 10-20% of patients with carcinoma head of pancreas are eligible for resection; after resection, the median survival is 11-20 months and the five year survival is 7-25%. Patients with unresectable locally advanced disease have a median survival of 2-6 months. The cause of carcinoma head of pancreas is not well established, but prior epidemiological studies have shown that cigarette smoking, diabetes mellitus, chronic pancreatitis, obesity, alcohol consumption, hepatitis B virus infection, family history of carcinoma head of pancreas, and genetic disorders are significantly associated with carcinoma head of pancreas. Six genetic syndromes are associated with an increased risk of developing carcinoma head of pancreas[4]. These syndromes include hereditary nonpolyposis colorectal cancer, familial breast cancer associated with the BRCA2 mutation, Peutz-Jeghers syndrome, ataxia-telangiectasia syndrome, familial atypical multiple mole melanoma syndrome, and hereditary pancreatitis.

The association of diabetes to carcinoma head of pancreas has been studied by many investigators. Although the data are somewhat variable, most reports indicate no consistent association of diabetes with cancer of the pancreas, except when cases are included where the diabetes was diagnosed immediately prior to the cancer diagnosis. This relationship suggests that diabetes is more commonly an early symptom of carcinoma head of pancreas rather than a causative influence[5].

Chronic pancreatitis appears to be linked to carcinoma head of pancreas. Patients with chronic pancreatitis followed for several years have up to a 16- fold increased risk of carcinoma head of pancreas. The cumulative 25-year risk of carcinoma head of pancreas in patients with any form of chronic pancreatitis approaches 4 per cent. Other disorders with apparent increased risks of carcinoma head of pancreas include thyroid and other endocrine tumors, cystic fibrosis, elevations of sex hormones, and pernicious anemia. Of all the environmental factors that have been studied, there can be no doubt that cigarette smoking is a risk factor for carcinoma head of pancreas. Case- control studies have found that smoking increases the risk of carcinoma head of pancreas, with an odds ratio between 1.3 and 5.5 for current smokers. There appears to be a dose-response relationship with both the number of cigarettes smoked and the duration of smoking. The relationship between nutrition and diet in carcinoma head of pancreas has been extensively studied. From a number of case-control studies, there appears to be an association between carcinoma head of pancreas and increasing intakes of carbohydrate, cholesterol, meat, salt, dehydrated food, fried food, refined sugar, soybeans, and nitrosamines. The risks are unproven for the excess ingestion of fat, b-carotene, and coffee. A protective influence has been reported for entities such as dietary fiber, vitamin C, fruits, vegetables, no preservatives, raw foods, pressure cooking, and microwave Cooking[6].

Numerous studies have noted an increased risk of carcinoma head of pancreas with certain occupational factors such as exposures to leather tanning, textiles, and various specific chemicals such as ethylene chlorhydrin, halogenated hydrocarbons, chlorinated water and DDT .

Carcinoma head of pancreass are insidious tumors that can be present for long periods and grow extensively before they produce symptoms. The symptoms, once they develop are determined by the location of the tumor in the pancreas. Those in the head or uncinate process of the pancreas make their presence known by causing bile duct, duodenal, or pancreatic duct obstruction. Symptoms include unexplained episodes of pancreatitis, painless jaundice, nausea, vomiting, steatorrhea, and unexplained weight loss. With further spread beyond the pancreas, these patients may note upper abdominal or back pain when peripancreatic nerve plexuses are involved and ascites when peritoneal carcinomatosis or portal vein occlusion develops. Patients with tumors arising in the neck, body, or tail of the pancreas usually do not develop jaundice or gastric outlet obstruction[7]. Their symptoms may be limited to unexplained weight loss and vague upper abdominal pain until the tumor has grown extensively and spread beyond the pancreas. New- onset diabetes mellitus is occasionally the first symptom of an otherwise occult carcinoma head of pancreas. Recent studies have suggested that this form of diabetes may be mediated by a factor released from the tumor that either inhibits insulin release from islets or induces peripheral insulin resistance. Unexplained migratory thrombophlebitis (Trousseau's syndrome) may be associated with pancreatic and other types of malignancy. It is probably a paraneoplastic phenomenon that results from a tumor induced hypercoagulable state.

The physical findings in patients with carcinoma head of pancreas are also dependent on the location, size, and extent of the tumor. Liver nodules indicative of metastases can sometimes be felt. Metastatic subumbilical ("Sister Mary Joseph node")

and pelvic peritoneal ("Blumer's shelf") deposits, as well as left supraclavicular lymphadenopathy ("Virchow's node"), indicate the presence of distant metastases. Malignant ascites, caused by peritoneal carcinomatosis, may also be present. With portal, splenic, or superior mesenteric vein occlusion, mesenteric venous pressures may be increased, and collateral channels, including gastroesophageal varices and caput medusae, may develop. Distal common bile duct obstruction caused by the tumor often leads to bile duct and gallbladder distention. Thus, a palpable gallbladder in a patient with painless jaundice (i.e., Courvoisier's sign) suggests the presence of a periampullary neoplasm.

Patients with pancreatic head lesions frequently have elevated bilirubin and alkaline phosphatase levels suggestive of obstructive jaundice. Other routine laboratory studies are usually normal. The two most widely used carcinoma head of pancreas serum markers are the CEA and the Lewis blood group carbohydrate antigen CA 19-9. Both are frequently elevated in patients with advanced disease, but unfortunately, the circulating levels of these tumor markers are often normal in patients with early, potentially curable, tumors. Thus, using these tumor markers to screen patients with vague symptoms or those in high-risk groups has not been shown to be useful in detecting early disease. With a cutoff value of 37 U/mL, CA 19-9 has been reported to have a sensitivity of 86% and a specificity of 87%. CA 19-9 can also be elevated in patients with cholangitis and jaundice not caused by carcinoma head of pancreas. Extremely high levels of either CA 19-9 or CEA usually indicate unresectable or metastatic disease.

As there is no available screening tool for carcinoma head of pancreas, it seems to be very important to find the risk factors of carcinoma head of pancreas early. Thus, early-targeted intervention can be performed to reduce the risk and suffering of carcinoma head of pancreas. A very few studies were conducted in our country in this regard. Hence this study is an effort to study about risk factors of carcinoma head of pancreas.

Aims of the study

1. To study alcohol consumption as a risk factor for carcinoma head of pancreas
2. To study smoking as a risk factor for carcinoma head of pancreas

Methodology

Study design- Case control study

Study setting- In patients admitted to surgical wards of Medical College, Thiruvananthapuram.

Study subjects- All patients admitted to surgical wards under Medical College Trivandrum with carcinoma head of pancreas.

Study period- One year from 15 December 2014 to 14 December 2015.

Inclusion criteria

Cases- The patients admitted in the surgical wards of Medical College, Trivandrum wards presenting with carcinoma head of pancreas which are clinically, radiologically (CECT Scan abdomen) or histopathologically proved and are willing to participate in the study.

Control- Patients admitted during same period in Medical College Trivandrum wards, those not having carcinoma head of pancreas malignancy.

Exclusion criteria

Those patients not willing to give consent for the study.

Sample size

EPI info for unmatched case control design, assuming 80% power and 5% Alpha error.

Total sample worked as cases 50 and controls 250.

Results

1. Age- 86.0% of the cases were in the age group of ≥50 years where as among the controls 53.2% were in that age group. Age of the cases was significantly higher than that of controls ($p<0.05$).

2. Sex- 84.% of the cases and 81.6% of the controls were male. There was no significant gender difference between the cases and control ($p>0.05$).

3. Alcohol- 64% of cases with carcinoma head of pancreas were alcoholics as compared to 34.8% in control group. The patients who were alcoholics were 4 times(OR=4.39) more at risk of developing carcinoma head of pancreas than others and this was found to be statistically significant($p<0.001$).

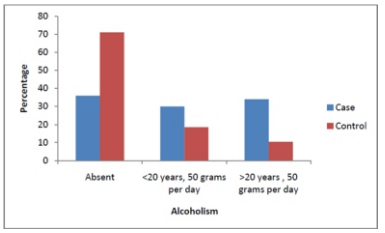

FIGURE 1- Distribution of Alcoholism

4. Smoking- 68% of cases with carcinoma head of pancreas were smokers as compared to 37.85% in control group, with 22% having history of less than 20 pack years and 46% with history of smoking more than 20pack years in cases group. The patients who were smokers were 4.5 times(OR=4.56) more at risk of developing carcinoma head of pancreas than others and this was found to be statistically significant($p<0.001$).

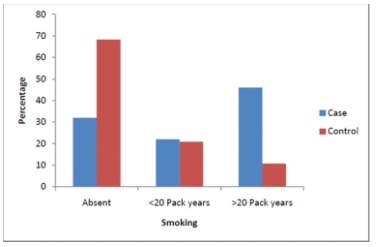

FIGURE 2- Distribution of Smoking

The mean age in cases was 61 years and in control group was 48 years. By univariate analysis age>50 years, smoking and alcohol consumption were found to be the risk factors of carcinoma head of pancreas.

	Category				Total		p	OR	95% CI for OR	
	Case (N=50)		Control (N=250)		(N=300)					
	N	%	N	%	N	%			Lower	Upper
AGE(YRS)≥50	43	86	133	53.2	176	58.7	<0.001	5.404	2.341	12.474
Smoking	34	68	79	31.7	113	37.7	<0.001	4.573	2.384	8.771
Alcohol	32	64	72	28.9	104	34.7	<0.001	4.37	2.306	8.281

TABLE 1- Univariate analysis of risk factors

Discussion

Of the 50 cases studied 42 were males (84%) and 8 were females (16%) and in 250 controls 205 were males and 45 were females. 84.% of the cases and 81.6% of the controls were male. There was no significant gender difference between the cases and control ($p>0.05$). 86.0% of the cases were in the age group of ≥50 years where as among the controls 53.2% were in that age group. Age of the cases was significantly higher than that ofcontrols ($p<0.05$). The mean age was 58.07. In the study conducted by Manal Hassan et al 1.9% were <40yrs, 11.9% between 40-50 years, 29.2% in the age group of 51-60 years 35.7% in the age group 61-70 years and 21.3% above the age of 71 years.

VOLUME-6 | ISSUE-4 | APRIL - 2017 • ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

68% of cases with carcinoma head of pancreas in our study were smokers as compared to 31.1% in control group. In the study conducted by Manal Hassan et al 60% of the cases were smokers and by David et al 38% were smokers.

64% of cases with carcinoma head of pancreas in our study were alcoholics as compared to 28.9% in control group.In the study conducted by Manal Hassan et al only 23.6% of the cases were smokers and that by David et al 24% were alcoholics.

Conclusion

1. Carcinoma head of Pancreas is more common in males as compared to females.
2. Female to male ratio is 1:4.
3. Majority are in the age group >50 years.
4. Average age of incidence is 61years .
5. Age >50years, smoking and alcohol consumption are the risk factors as shown by the univariate analysis.

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