International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Research Article

Clinicopathological study of 15 cases of pancreatic tumours including periampullary region tumours

Anu Sumi Issac* and K. Pushpalatha Pai

Department of Pathology, Yenepoya Medical College,Yenepoya University, Nithayananda Nagar, Deralakatte, Mangalore - 575018

***Correspondence Info:**
Dr. Anu Sumi Issac
Final Year Postgraduate,
Department of Pathology,
Yenepoya Medical College, Yenepoya University,
Nithayananda Nagar, Deralakatte, Mangalore - 575018
E-mail: dranuissac@gmail.com

Abstract

Objectives: Most pancreatic tumours are malignant but benign tumours and tumours with variable malignant potential also occur. The objective of this study is to study the morphological variants of exocrine pancreatic tumors and periampullary region tumors with their clinical background.

Methods: This is a retrospective histopathological and clinical evaluation of 15 cases of exocrine pancreatic tumors from 2006-2011. The study was done on haematoxylin and eosin stained sections of paraffin blocks made from the tissue provided (either biopsies or pancreatectomies). WHO Histological Classification of Tumors of Exocrine Pancreas (2000) was followed for categorizing the tumors.

Results: Majority of the tumors were malignant and were adenocarcinomas. The common site of tumour being periampullary region followed by head of the pancreas and was least common in body and tail. Benign and borderline (uncertain malignant potential) tumors were seen only in body and tail of pancreas in this study. Majority of malignant tumors were found in females and all malignant tumors were found in patients above 45 years of age

Conclusion: According to the present study, tumors of the pancreas are more common in females. The benign and borderline tumors are rare and occur in younger age and were seen in body and tail of pancreas, whereas malignant tumors were more common and seen in periampullary region and head of the pancreas. Other tumors which were recorded in the study were pancreatoblastoma, mucinous cystadenoma and solid pseudopapillary tumour.

Key words: exocrine pancreas, tumors, histopathology, clinical correlation

1. Introduction

The pancreas is a glandular organ of dual composition with both exocrine and endocrine components.[1, 2] Tumors of exocrine pancreases are rare with more than 95% being malignant.[3] Several risk factors for pancreatic cancer have been identified, such as smoking [4], age[5], family history [6], and diabetes[7]. The majority of exocrine pancreatic cancers are adenocarcinomas, commonly involving the head and body of the pancreas.[9] Ampullary carcinoma is the term employed for any malignant epithelial tumour centered in the ampulla of vater and it should be distinguished from carcinomas of head of pancreas, terminal third of common bile duct and other portions of the second part of duodenum with secondary involvement of ampulla. Such a distinction may not be possible in advanced cases which is the case in pancreatic tumors most of the time. So the only diagnosis rendered is that of "carcinoma of the pancreato-biliary-ampullary region". [1]In India, the incidence of pancreatic cancer is low (0.5-2.4% per 100,000 men and 0.2-1.8% per 100,000 women), however, recent studies show that this figure is gradually increasing.[9] The purpose of the study is to study exocrine pancreatic tumors clinico-pathologically to know the various types, grades and clinical manifestations.

2. Materials and Methods

This is a retrospective clinico-histopathological study of 15 cases over a period of 5 years. The patients' demographic data and detailed clinical history were recorded. The specimens received in our department included biopsies taken from the suspected tumour site (six cases) and remaining were pancreatectomy specimens. All specimens were received in 10% formalin and fixed for 24-48 hours. The grossing was done according to standard protocol.[10] The biopsies were all embedded. In pancreatectomy specimens, representative sections were taken from every part of the specimen. After routine processing of the sections, paraffin blocks were made, cut and stained with the haematoxylin and eosin stain and Periodic Acid Schiff (PAS) stain and studied with Lynx (Lawrence and Mayo) digital microscope. Gross photographs were taken using a digital camera.

3. Results

Of the total 15 cases of pancreatic tumors received in the study period, 13 cases (86.6%) were malignant with a single benign (6.7%) and a single borderline case (6.7%). The breakup of cases according to demography, site of tumour, type of specimen and diagnosis are summarised in Table 1.

Table 1: Distribution of cases according to demography, site of tumor and diagnosis

S.No	Age (years)	Gender	Site of tumor	Type of specimen	Diagnosis
1	64	F	Periampullary	Biopsy	Periampullary Adenocarcinoma
2	60	F	Periampullary	Whipple	Periampullary Adenocarcinoma
3	88	M	Periampullary	Biopsy	Periampullary Adenocarcinoma
4	45	M	Periampullary	Whipple	Periampullary Adenocarcinoma
5	69	M	Periampullary	Whipple	Periampullary Adenocarcinoma
6	46	M	Periampullary	Whipple	Periampullary Adenocarcinoma
7	48	M	Periampullary	Whipple	Periampullary Adenocarcinoma
8	45	F	Head of pancreas	Biopsy	Ductal Adenocarcinoma
9	67	F	Head of pancreas	Biopsy	Ductal Adenocarcinoma
10	46	F	Head of pancreas	Biopsy	Ductal Adenocarcinoma
11	65	F	Head of pancreas	Whipple	Ductal adenocarcinoma
12	66	F	Tail of pancreas	Distal pancreatectomy + splenectomy	Ductal Adenocarcinoma
13	1	M	Tail of pancreas	Biopsy	Pancreatoblastoma
14	16	F	Body and tail of pancreas	Distal pancreatectomy+splenectomy	Solid pseudopapillary tumor
15	32	F	Body and tail of pancreas	Distal pancreatectomy + splenectomy	Mucinous cystadenoma

Among the malignant cases, periampullary adenocarcinomas including signet ring type constituted the majority accounting for seven cases (53.8%). The youngest patient in this group was a 45 year old male while the oldest was an 88 year old male and the mean age was 60 years. Male predominance was observed in the ratio of 5:2. All of the patients presented with jaundice, abdominal pain, itching and weight loss. Systemic hypertension was found in two male patients. On clinical examination, no mass was palpable per abdomen in any of the cases. Laboratory investigations showed low hemoglobin and deranged liver function test in all patients with elevated serum bilirubin, gamma glutamyltransferase and alkaline phosphatase levels. Ultrasonography and/or computerized tomography findings were suggestive of a growth at the head of pancreas with gross biliary dilatation. On table, surgeons found a mass in the periampullary region with involvement of the duodenum and head of pancreas in all cases. The specimens received for pathological examination consisted of tissue biopsies in two cases and Whipple in five cases. Grossly, all tumors were solid grey white and size less than 2cms. Microscopically, three out of seven cases showed poorly differentiated adenocarcinoma with sheets of pleomorphic, poorly differentiated cells, pleomorphic nuclei with prominent nucleoli and high mitotic rate (Figure 2). Occasional gland formation was seen. Three cases were well to moderately differentiated adenocarcinomas with gland formation and one case was signet ring cell type of adenocarcinoma (Figure 3)

Figure 1: Gross photograph of part of Whipple specimen showing a periampullary tumour around the 2nd part of duodenum with the tumour projecting on the mucosal surface (arrow)

Figure 2: Photomicrograph of periampullary well differentiated adenocarcinoma showing crowded neoplastic glands lined by epithelial cells with vesicular nuclei and prominent nucleoli (arrow) (H&Ex400)

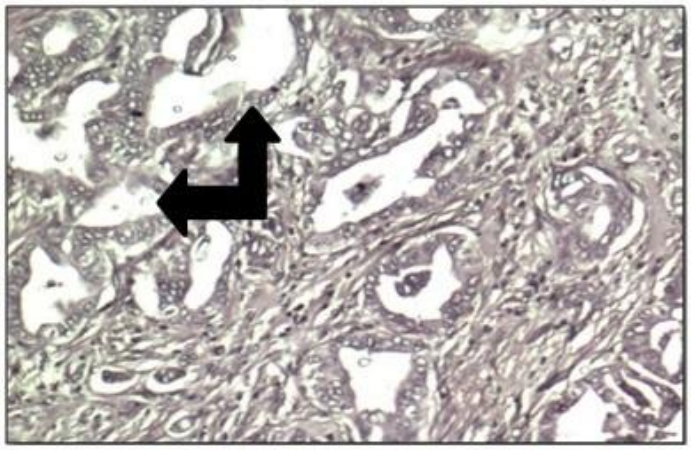
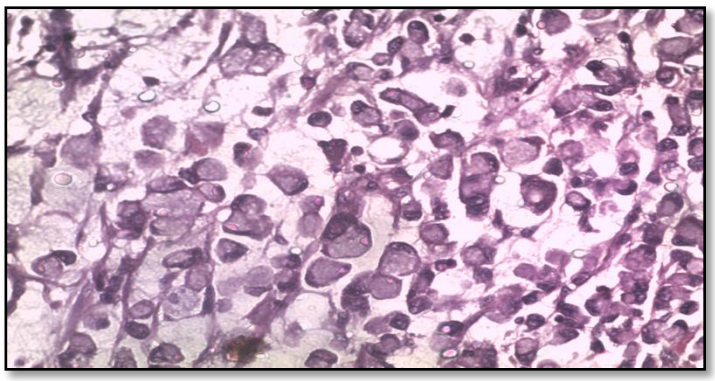


Figure 3: Photomicrograph of periampullary adenocarcinoma with histological features of signet ring cell carcinoma (H&Ex400)



Four cases of adenocarcinoma of head of pancreas (80%) and one case involving the tail of pancreas comprised the next most common set of exocrine pancreatic tumors, all of which were found in females with age ranging from 45 to 67 years with a mean age of 56 years. Four cases of carcinoma head of pancreas patients presented with symptoms of jaundice, vomiting and abdominal pain. One patient was suffering from type 2 diabetes mellitus while two other patients had associated chronic pancreatitis. In all cases, per abdomen examination revealed a palpable mass. In cases of carcinoma head of pancreas, ultrasonographical imaging showed a hypoechoic mass lesion in the head of pancreas with dilatation of pancreatic duct and biliary tree. In case of carcinoma tail of pancreas, no imaging study was done. Out of five cases, the specimens sent for histopathological diagnosis comprised of biopsies from the head of pancreas in three cases, one case of Whipple and one case of distal pancreatectomy. Grossly, Whipple specimen showed tumour less than 5cm and in distal pancreatectomy done for carcinoma tail of pancreas, the tumour was more than 10cm, mainly cystic with necrotic tumour tissue in the cyst (Figure 4).Microscopically, except for one case of carcinoma of head of pancreas which was a moderately differentiated case, the rest were poorly differentiated with occasional glandular pattern with PAS stain showing focal positivity with the tumour mainly showing anaplastic cells arranged in sheets with high mitotic rate (Figure 5).

Figure 4: Gross photograph of distal pancreatectomy with splenectomy for carcinoma tail of pancreas showing a cystic lesion containing necrotic tumour tissue (arrow).

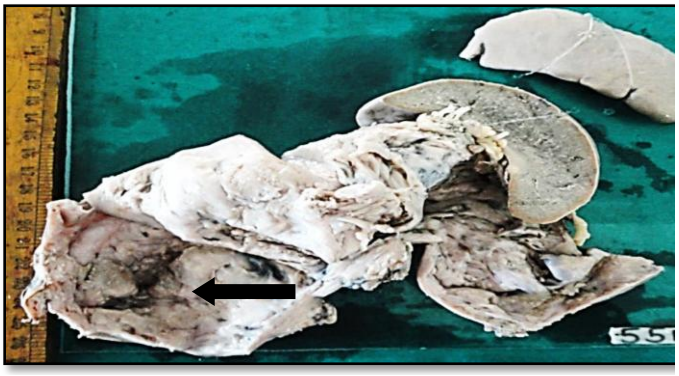
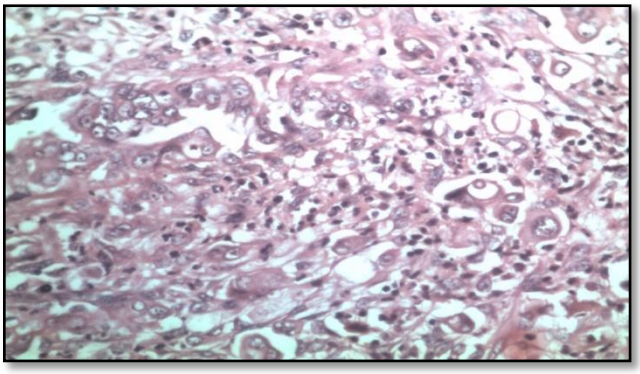
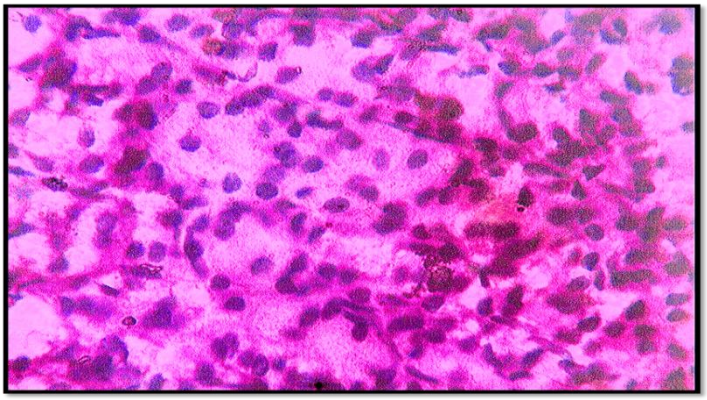


Figure 5: Photomicrograph of carcinoma tail of pancreas showing poorly differentiated tumour cells with pleomorphic nuclei and prominent nucleoli (H&Ex400)



A single case of pancreatoblastoma was diagnosed in a 1 year old boy who presented with vague abdominal pain. On ultrasonography, a growth was detected in the tail of pancreas from where a biopsy was taken and sent for histopathological examination. Microscopically, the tumour was composed of monomorphic, polygonal cells arranged in solid, trabecular and acinar pattern with monotonous round and hyperchromatic nuclei and scanty to moderate cytoplasm. (Figure 6)

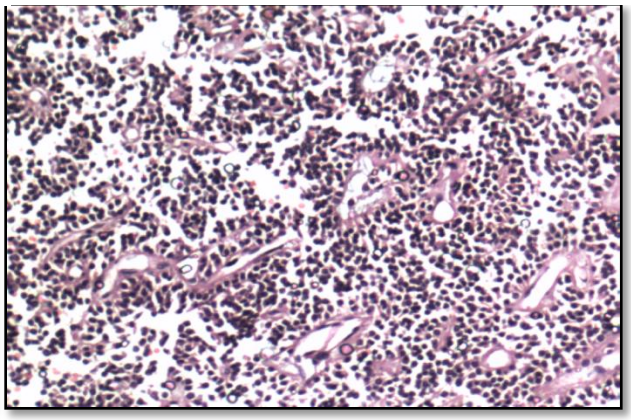
Figure 6: Photomicrograph of pancreatoblastoma showing monomorphic cells arranged in solid, acinar pattern with monotonous round, hyperchromatic nuclei and scanty cytoplasm (H&Ex400)



A solitary case of a borderline tumor - solid pseudopapillary neoplasm of uncertain malignant potential - was found in the body and tail of pancreas of a 16 year old girl who presented with nonspecific symptoms of abdominal pain and dyspepsia. Per abdominal examination revealed a firm mass in the left hypochondrium with extension into the left lumbar region. A well-defined mixed density lesion with enhancing solid components and cystic areas in the tail of pancreas with extension into the body of pancreas was seen on computerized tomography imaging. Specimen of distal pancreatectomy with splenectomy was received which grossly showed a pancreatic mass measuring 11x10x6cms with intact capsule and multiple cystic spaces ranging from 0.2 to 2 cm in diameter with a solid area near the capsule measuring 4x2 cm (Figure 7). Microscopically, the tumor was composed of small to medium sized, monotonous cells with moderate amount of clear to eosinophilic cytoplasm, ovoid nuclei, inconspicuous nucleoli and rare mitotic figures. Tumor cells were seen around blood vessels which gave a pseudo-papillary pattern (Figure8).

Figure 7: Gross photomicrograph of distal pancreatectomy with splenectomy for solid pseudopapillary neoplasm of body and tail of pancreas.

Figure 8: Photomicrograph of solid pseudopapillary neoplasm showing pseudopapillary structures lined by small, monomorphic cells (H&Ex100)



The only benign lesion encountered in this study was a case of mucinous cystadenoma in the body and tail of pancreas diagnosed in a 32 year old lady who presented with right sided abdominal pain radiating to the back. Per abdomen examination detected a palpable mass in the left hypochondrium. Specimen of distal pancreatectomy with splenectomy was received which grossly showed a multilocular cyst measuring 14x9x4cms containing mucoid fluid with the wall showing solid areas (Figure 9). Microscopically, the cyst wall showed a single lining layer of mucin filled columnar cells with basal nuclei and thick fibrocollagenous tissue (Figure 10).

Figure 9: Gross photograph of distal pancreatectomy with splenectomy for mucinous cystadenoma of body and tail of pancreas.

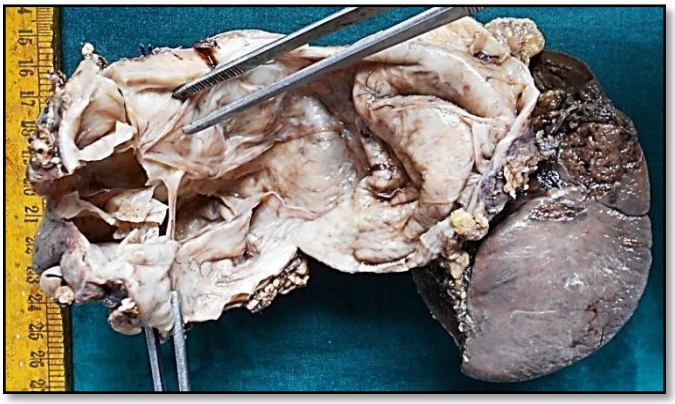
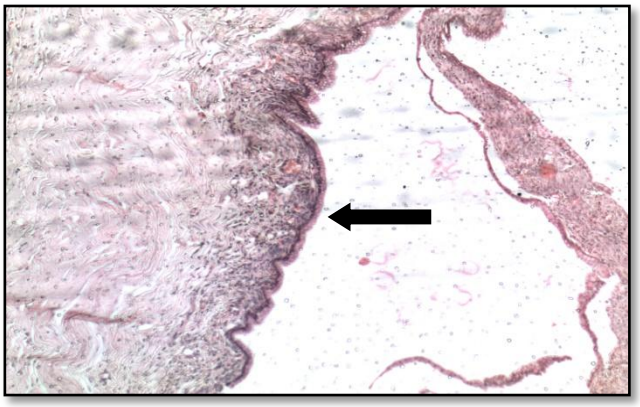


Figure 10: Photomicrograph of mucinous cystadenoma showing mucin filled columnar cells with basal nuclei (arrow) and thick fibrocollagenous tissue (H&Ex100).



4. Discussion

The majority of exocrine pancreatic cancers are adenocarcinomas. These tumours originate in the epithelial cells lining the pancreatic duct, form gland-like structures, and account for 90% of all pancreatic cancers.[1,11,12] Other tumors which rarely occur in pancreas are solid pseudopapillary tumor (borderline malignancy), acinar cell carcinoma and intraductal papillary mucinous neoplasm. In the present study, adenocarcinoma constituted the majority (12/15 cases, 80%) and is comparable to the study by Kumar NV[13] in which 26 (89.7%) out of 29 cases were adenocarcinomas.

Advancing age (60-80 years) and male gender constitute two main demographic risk factors for pancreatic cancer.[14] In the present study, the youngest age at presentation was 45 years for both adenocarcinoma of periampullary region and head of pancreas (Table 1). Majority of cases of adenocarcinomas were found in the fifth and seventh decade (41.7% each). Only one case was found in the ninth decade. None of the cases were found in the eighth decade.

Table 2: Comparison of age incidence of adenocarcinoma in the present study with other author studies

Age in years	Kumar NV [13]	Hassan MM *et al* [15]	Anderson LN *et al* [16]	Present study
< 40	10.3 %	1.9 %	8 %	-
40 – 50	34.5 %	11.9 %	29 %	41.7%
51 – 60	20.7 %	29.2 %	36 %	8.3%
61 – 70	24.1 %	35.7 %	28 %	41.7%
> 71	10.3 %	21.3 %	-	8.3%
Mean age	51.17	61.9	-	59.1

Although male gender has been proved to be of an increased demographic risk, the present study obtained a female preponderance which was higher when compared to other studies (Table 3).

Table 3: Comparison of gender incidence of adenocarcinomas in the present study with other studies

Gender incidence	Total no: of cases	Male	Female
Kumar NV [13]	29	55.2 %	44.8 %
Hassan MM *et al* [15]	808	55.6 %	44.4 %
Anderson LN *et al* [16]	422	55 %	45 %
Dickinson KJ *et al* [17]	31	51.61 %	48.4 %
Present study	12	41.6 %	58.4% %

Clinical presentation depends largely on the location of the tumour. Dickinson *et al* [17]has concluded in their study that there is an increased prevalence of pancreatic body cancer with more advanced disease at presentation. In the present study, out of seven cases of periampullary carcinomas, the tumour was involving lymph nodes in one case (stage III) and remaining tumours were in stage II according to TNM classification. In four cases of carcinoma of head of pancreas, the tumour was found to be confined to the head of pancreas with one case showing lymph node metastasis (stage III). One case of adenocarcinoma from tail of pancreas presented at stage IVB with omental secondaries. These findings in the present study correlate with the statement given by Dickinson KJ *et al*.[17]

Presence of diabetes mellitus and chronic pancreatitis may be possible risk factors for development of carcinoma of exocrine pancreas.[18] In this study there was one case of type 2 diabetes mellitus and two cases of chronic pancreatitis, all of which were seen in female patients who developed pancreatic adenocarcinoma (Table 4).

Table 4: Comparison of clinical presentation and risk factors for adenocarcinoma of pancreas in present study with other studies

Clinical presentation and risk factors	Kumar NV [13]	Hassan MM *et al* [15]	Anderson LN *et al* [16]	Present study
Diabetes Mellitus	31 %	39.2 %	12 %	6.7%
Pancreatitis	24.1 %	4.3 %	5 %	13.4 %
Pain abdomen	75.9 %	90.3 %	-	100 %
Weight loss	82.8 %	90.3 %	-	13.3 %
Jaundice	65.5 %	19.4 %	-	91 %

With the present study it can be concluded that exocrine pancreatic tumours are rare (15 cases in 5 years). Benign tumour of exocrine pancreas (mucinous cystadenoma), pancreatoblastoma (a childhood malignant tumour) and solid pseudopapillary neoplasm (borderline malignancy) were found to be rare in the present study. Female predominance in the present study does not correlate with other studies in the literature. Unlike other studies, this study did not find pancreatic adenocarcinoma below 45 years of age even though one borderline case (solid pseudopapillary neoplasm) was found in a 16 year old female. Since this is a small scale study with limited number of cases, a larger study with more detailed clinical background, risk factors and their interactions is warranted.

References

1. Rosai J. Pancreas and ampullary region. In: Rosai and Ackerman's Surgical Pathology. 10th ed. Missouri: Elsevier Mosby: 2011.
2. Hollingsworth MA. Proteins expressed by pancreatic duct cells and their relatives. *Ann N Y AcadSci* 1999; 880:38-49.
3. Hruban RH, Donahue DL. The Pancreas. In: Kumar, Abbas, Fasuto, Aster, editors. Robbins and Cotran Pathologic Basis of Disease. 8th ed. Philadelphia: Elsevier Saunders; 2010. p. 891-903.
4. Warshaw AL, Castillo CF. Pancreatic carcinoma. *N Engl J Med*1992; 326:455-65.
5. Ghadirian P, Lynch HT, Krewski D. Epidemiology of pancreatic cancer: an overview. *Cancer Detect Prev* 2003; 27: 87-93.
6. Lynch HT, Smyrk T, Kern SE, *et al*. Familial pancreatic cancer: a review. *SeminOncol* 1996; 23:251-75.
7. Everhart J, Wright D. Diabetes mellitus as a risk factor for pancreatic cancer: a meta-analysis. *JAMA* 1995; 273:1605-9.
8. Bastidas JA, Poen JC, Niederhuber JE. Pancreas. In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE, editors. Clinical oncology. 2nd ed. Philadelphia, PA: Churchill-Livingstone; 2000.p. 1749-83.
9. Dhir V, Mohandas K. Epidemiology of digestive tract cancers in India IV. Gall bladder and pancreas. *Indian J Gastroenterol*1999; 18(1): 24-8.
10. Rosai J. Guidelines for handling of most common and important surgical specimens. In: Rosai and Ackerman's Surgical Pathology. 10th ed. Missouri: Elsevier Mosby; 2011. P.2616-7.
11. Cowgill SM, Muscarella P. The genetics of pancreatic cancer. *Am J Surg* 2003; 186: 279-86.
12. Li D, Jiao L. Molecular epidemiology of pancreatic cancer. *Int J Gastrointest Cancer* 2003; 33:3-14.
13. Kumar NV. Clinical study of carcinoma pancreas [dissertation]. Mangalore: Rajiv Gandhi Univ.; 2007.
14. Gold E.B., and Goldin B. Epidemiology of and risk factors for pancreatic cancer. *SurgOncolClin North Am* 1998; 7:67-91.
15. Hassan MM, Bondy ML, Wolff RA, Abbruzese JL, Varuthey JN, Pisters PW, *et al*. Risk factors for pancreatic cancer: Case-control study. *Am J Gastroenterol*2007; 102(12):2696-707.
16. Anderson LN, Cotterchio M, Gallinger S. Lifestyle, dietary and medical history factors associated with pancreatic cancer risk in Ontario, Canada. *Cancer Causes Control* 2009; 20(6):825-34.
17. Dickinson KJ, Gomez D, Lowe A, Gokhale JA, Ausobsky JR, Guillou PH *et al*. Carcinoma of the Body of Pancreas in Evolution: An aggressive disease affecting younger patients?. JOP (Serial Online) 2007 [cited 2007 May 9]; 8(3): 312-9. Available from: http://www.joplink.net/prev/200705/200705_07.pdf.
18. Shi C, Hruban RH, Klein AP. Familial pancreatic cancer. *Arch Pathol Lab Med* 2009; 133: 365–74.