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CHOLANGIOCARCINOMA -RETROSPECTIVE ANALYSIS FROM A TERTIARY CARE CENTRE

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ABSTRACT Fifty patients with Cholangiocarcinoma(CCA) was retrospectively analyzed. Incidence was equal in both sexes. Median age was 53 years. Most common presentation was jaundice and abdominal pain. Fourteen patients (28%) had Perihilar CCA and 36(72%) had distal CCA. Seventeen patients (34 %) were smokers and 15(30%) were alcoholics. Thirty four patients (68%) were farmers and 16(32%) were painters, weavers and carpenters. Thirty five (70%) patients had stage III and IV disease. Whipples surgery was done for 26(52%) patients, palliative triple bypass procedure was done for 15(30%) patients. ERCP was the main procedure for relieving biliary obstruction. Chemotherapy was given to 27 patients (54%) and the remaining 23 (46%) received best supportive care.

KEYWORDS : Cholangiocarcinoma, pCCA, dCCA, Farmer, Jaundice.

Introduction:

Cancers of biliary tract are called as Cholangiocarcinoma(CCA) that are associated with intrahepatic or extrahepatic bile ducts(1). Cancers of the biliary tract are rare. CCA often diagnosed at an advanced stage and is associated with dismal prognosis. This cancer requires multidisciplinary approach by team with experience in their management.

CCA incidence rates vary among different areas of world and related to variation in distribution of risk factors and interplay between genetic differences and geographical risk factors(2).

High incidence rates of over 6.0 per 100,000 are reported in Thailand, Korea, and China. In Thailand, the incidence rate varies by region, ranging from 5.4 to 85.0 per 100,000(16).

In India incidence rate is 1.6/1,00,000. The age-adjusted Incidence rate at Chennai is 0.8/1,00,000 (3,4)

Environmental toxins, chemical carcinogens ,chronic biliary tract inflammation and congenital causes have been suggested to play a role in the pathogenesis of CCA(4-7).Viral infection like hepatitis C has also been implicated Cholangiocarcinoma (iCCA)(8-10). Primary sclerosing cholangitis is an inflammatory disorder of the biliary tree that leads to fibrosis and stricture of the intrahepatic and extrahepatic biliary tree(11,12), is another cause for iCCA.

CCA of biliary tract is usually adenocarcinoma and further divided into sclerosing, nodular,and papillary type and less commonly squamous cell carcinoma, sarcoma,small cell carcinoma and lymphoma (13-15). CCA is one of the main cause for malignant obstruction of biliary tract apart from pancreatic adenocarcinoma, gall bladder adenocarcinoma, lymphoma and compressive metastatic proximal lymph nodes(25,26).

Surgical resection is complex and associated with morbidity and mortality in perihilar Cholangiocarcinoma(pCCA). Surgical resection can be considered for locally confined distal Cholangiocarcinoma(dCCA) without major vascular and distant metastases.

Whipples procedure has a reasonable chance of providing a negative resection margin for dCCA.For unresectable dCCA, palliation by stenting for biliary decompression, or combination with chemotherapy can be considered. Palliative bypass procedure for biliary decompression may be performed.

Chemotherapy with gemcitabine and Cisplatin should be considered in CCA after resection with or without radiation,In advanced stages palliative chemotherapy with gemcitabine based or fluoropyrimidine can be given.

Objective:

To identify the epidemiological, clinicopathological features and outcome of CCA.

Materials and methods:

Retrospective analysis of 50 patients with CCA treated from January 2014 to December 2015 was done. Detailed history, occupation, history of use of pesticides and modes of exposure, clinical exam findings, biochemistry, imaging, pathology report and treatment details i.e. surgery, chemotherapy, palliative procedure were taken from case records. Staging was made according to AJCC cancer staging system (seventh edition). Chemotherapy regimens used in this study were Cisplatin and Gemcitabine or Cisplatin and 5FU or single agent 5FU.patients characteristics are given in table .1.

RESULTS:

Table -1. Patient characteristics are given below

NO	PARAMETERS	PERIHILAR Number (percentage)	DISTAL Number (percentage)	Total
1.	Number of patients	14(28%)	36(72%)	50(100%)
2.	Age (median)	52(27-58)	53(40-70)	
3.	Sex Male Female	 6(12%) 8(16%)	 19(38%) 17(34%)	 25(50%) 25(50%)
4.	Occupations Farmers Others (painters, weavers, carpenters)	10(20%) 4(8%)	24(48%) 12(24%)	34 16
	Modes of pesticides exposure Spraying Dispose container,mixing, Loading,	Total (both sex) 21(60%) 13(40%)		
5.	Jaundice Yes No	 14(28%) 0(0%)	 35(70%) 1(2%)	 49 1
6.	Abdominal pain Yes No	 10(20%) 4(8%)	 19(38%) 17(34%)	 29 21

7.	Stage I/II Stage III/IV	4(8%) 10(20%)	11(22%) 25(50%)	19 31
8.	ERCP stent Yes No	 3(6%) 11(22%)	 18(36%) 7(14%)	 31 19
9.	Whipples procedure	0(0%)	26(75%)	26
10.	Bypass procedure	11(22%)	4(8%)	15
11.	No surgery	3(6%)	6(12%)	9
12.	Chemotherapy Cisplatin + gemcitabine Cisplatin +5Fu 5FU(palliative)	7(14%) 2(4%) 3(6%) 2(4%)	20(40%) 8(16%) 5(10%) 7(10%)	27 17 10
13.	Best supportive care	7(14%)	16(32%)	23

Results :

A total of 50 patients were analysed. Out of 50 patients, 25(50%) were males and 25(50%) were females. Among the 50 patients, 36(72%) had dCCA,, 14(28%) had pCCA and no one had(iCCA).Thirty four (68%) were farmers and 16(32%) had other occupation (painters,weavers and carpenters) or unemployed. Among the farmers 10(20%) and 24(48%) had pCCA and dCCA respectively. Twenty one(60%) farmers had history of spraying pesticide in the field. Skin is the most exposed organ while spraying the fields. Thirteen(40%) farmers handled pesticides directly.

Fourty nine (98%) patients presented with jaundice [perihilar: 14(28%) & distal: 35(70%)] and 29(58%) patients had abdominal pain[perihilar: 10(20%) & distal: 19(38%)] According to TNM stage,15(30%)patients had stage I/II and 35(70%) had stage III/IV. In this study, 21(42%) patients underwent ERCP stenting[perihilar: 3(6%) & distal : 18(36%)] ,26(52%) underwent whipples surgery and all of them were dCCA patients. 15(30%) underwent palliative triple bypass surgery[perihilar: 11(78.5%) & distal: 4(11.2%)] Twenty seven (54%) patients received chemotherapy [perihilar: 7(14%) & distal: 20(40%)] and 23(46%)patients had best supportive care [perihilar: 7(14%) & distal: 16(32%)].The chemotherapy regimen includes Cisplatin and gemcitabine in 10 (20%), Cisplatin and 5FU in 8 (16%) and single agent 5FU in 9 (14%).

Discussion:

The median age of the patients was 53 years with range of 27 to 70 years .The age at presentation is much younger than what is reported in the literature i.e. 65 years. (18,19)

CCA is classified into three types like iCCA, pCCA and dCCA site. CCA incidence is low but it is on the rise globally (20). In India the incidence is rate is 1.6/1,00,000. The age-adjusted Incidence rate at Chennai is 0.8/1,00,000 (Globocan 2012, ICMR 2014). This study shows dCCA is the most common site than pCCA region but it differs from other studies (21). Incidence is equal in male and female. Present study shows 68% of patients were farmers and 32% were painter, weaver and carpenter. Sixty percentage of farmers had history of spraying pesticide in the field. Skin is the most exposed organ while spraying the fields. Thirty percentage of farmers handled pesticides directly.Case control study by Kornthip Jeephet et al , found no association between pesticides exposure and CCA(24). Most common symptoms were jaundice and abdominal pain. In this study, 21 (42%) patients underwent ERCP stenting for palliative biliary drainage and for relieving obstruction. Distal CCA is best palliated with biliary stenting compared to pCCA(25).Twenty six (75%) dCCA patients underwent Whipples surgery. Fifteen(30%) patients underwent palliative triple bypass surgery.

Twenty seven (54%) patients received chemotherapy and 23(46%) had best supportive care. In adjuvant setting, Eight (16%) patients received chemotherapy(Cisplatin and gemcitabine or Cisplatin and 5FU).Adjuvant chemotherapy in CCA has been associated with survival benefit especially in lymph node positive patients(26). Ten (20%) advanced stage patients received Cisplatin and Gemcitabine regimen and 4(8%) Cisplatin and 5FU . In palliative setting , single agent 5FU used in 9(14%) .

Two year median survival for stage I/II was 16 months (range 12-18 months) and in stage III/IV it was 11 months (range 8 -15months). Two year median survival for stage III/IV was 5 months (range 3-8 months) in best supportive care.

In UK ABC-02 trial, advanced /metastatic disease patients had received either Cisplatin and gemcitabine or gemcitabine alone. Median overall survival was 11.7months in cisplatin/gemcitabine compared to 8.1 months in gemcitabine alone (22,23).

Conclusion:

This study results showed more younger patients were affected (median age 53 years) and distal bile duct was the most common site which is in-contrast to other studies. Farmers by occupation were commonly affected. Seventy percent presented in advanced stage. Seventy five percent of dCCA could undergo Whipples surgery. Gemcitabine and 5- FU based regimens were commonly used. Two year median survival was 16 months in the adjuvant setting and 11 months in metastatic disease and 5 months with best supportive care.

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