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RISK FACTOR ASSOCIATED WITH AMPULLA OF VATER CARCINOMA

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ABSTRACT

BACKGROUND:

Biliary tract cancers, which include tumors of the gallbladder, extra hepatic bile duct, and ampulla of Vater, are uncommon but deadly diseases. Tobacco and alcohol are well-known risk factors for a variety of cancers, and the International Agency for Research on Cancer has classified them as group 1 carcinogens. Tobacco use is the leading cause of cancer in the world. Despite a large body of research on tobacco and alcohol, the link between these exposures and biliary tract cancers remains unknown.

METHODOLOGY:

Respondents were interviewed in-person by trained interviewers using a structured questionnaire to obtain information on demographic characteristics, lifestyle behaviors, and medical histories. Based on the responses of the respondents the sample size was 66 from Coimbatore city. SPSS version 17 was used to carry on the statistical analysis for the study.

RESULT:

In the current study it was identified that among the selected respondents majority were from age group of above 56 years, 60.61 percent were female respondents and were married 43.94 percent were from middle income family and have attained middle education and 65.15 percent were from rural area. 56.06 percent did not have any comorbidities and they were not alcohol consumers and were not smokers and the majority of them were non vegetarians. There was relationship between general characteristics and Co morbidity and there was an association between comorbidity, consanguinity, stage of tumor and size of tumor.

Keywords: AMPULLA, VATER CARCINOMA, TUMOR, SMOKER AND ALCOHOLIC

Introduction

Biliary tract cancers, which include tumors of the gallbladder, extrahepatic bile duct, and ampulla of Vater, are uncommon but deadly diseases (Hsinge et.al 2006, Castro et.al. 2013 and Valle et.al. 2017). Several lines of evidence point to inflammation playing a role in the aetiology of biliary tract cancers. Although the global incidence of biliary tract cancer is low, it is significantly higher in certain geographic regions and among certain ethnic and racial subgroups (Njei 2014). Cancers of the biliary tract (BTC) include gallbladder (GBC), intrahepatic bile duct (IHBDC), extrahepatic bile duct (EHBDC), and ampulla of Vater

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(AVC). BTCs account for 3% of all adult cancers worldwide, with incidence varying greatly by geography and ethnicity (Patel 2001 and Ferlay et.al. 2015).

Tobacco and alcohol are well-known risk factors for a variety of cancers, and the International Agency for Research on Cancer has classified them as group 1 carcinogens. Tobacco use is the leading cause of cancer in the world (Secretan 2009, IARC et.al. 2012, Castro et.al. 2013 and Praud et.al.2016). Although alcohol consumption accounts for a smaller proportion of new cancer cases, the global prevalence of alcohol use is high, with approximately 38% of the world's population aged 15 and older regularly consuming alcohol (McGee et.al. 2019).

Infectious agents such as Helicobacter pylori (H. pylori), Salmonella typhi, hepatitis B and C, and liver flukes are thought to cause inflammatory responses in the gastrointestinal and biliary tracts that can lead to cancer (Grimble 2002, Portincasa 1997). Furthermore, inflammatory biliary and gastrointestinal conditions such as cholecystitis, primary sclerosing cholangitis, and ulcerative colitis have been linked to the development of biliary tract malignancies, with the latter two conditions being more closely linked to bile duct cancer (Fox 1998, Hising et.al. 2006 and Burak et.al. 2004)

Despite a large body of research on tobacco and alcohol, the link between these exposures and biliary tract cancers remains unknown. Previous research into the links between tobacco smoking and alcohol consumption and the risk of biliary tract cancer has produced inconsistent or inconclusive results (Chow et.al.2004, Shaib et.al. 2007 andIARC 2012). The majority of previous studies were small, retrospective case-control studies, limiting their ability to detect minor associations and perform analyses individually by anatomic site. Prior meta-analyses relied almost entirely on case-control data and compared ever vs never smoking and alcohol consumption (Li et.al. 2011, Palmer et.al. 2012, Ye et.al. 2013 and Wenbin et.al. 2013)

Understanding the socio demographic characteristics of people will provide a platform for more research focusing on the risk associated with smoking and alcohol consumption in accordance with ampulla of vater carcinoma.

REVIEW OF LITERATURE

Ye et.al. (2013) studied on association between smoking and alcohol consumption and extrahepatic cholangiocarcinoma (ECC) through a meta-analysis of clinical observational studies. A total of 12 eligible articles (11 case-control studies and one cohort study) were included in this meta-analysis. Eleven studies reported the association between smoking and ECC. Pooled analysis indicated that smokers had an increased risk of ECC development as compared with non-smokers (summary RR = 1.23; 95%CI: 1.01-1.50). This correlation was present in population-based studies (n = 5; summary RR = 1.47;

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95%CI: 1.06-2.05) but not in hospital-based studies (n = 6; summary RR = 1.10; 95%CI: 0.88-1.37) and in non-Asian regions (n = 7; summary RR = 1.39; 95%CI: 1.03-1.87) but not in Asia (n = 4; summary RR = 1.08; 95%CI: 0.85-1.38). Seven studies reported an association between consuming alcohol and ECC. Pooled analysis indicated that alcohol drinkers had a similar risk of ECC development as did individuals who did not drink alcohol (summary RR = 1.09; 95%CI: 0.87-1.37). There was moderate heterogeneity among the studies and no evidence of publication bias. Smoking is associated with an increased risk of ECC, but alcohol consumption is not. Further population-based studies, particularly cohort studies, are warranted to enable definitive conclusions.

A family history of gallstones was associated with increased risks of biliary stones (odds ratio (OR) =2.8, 95% confidence interval (CI) =2.1-3.8), gallbladder cancer (OR=2.1, 95% CI=1.4-3.3), and bile duct cancer (OR=1.5, 95% CI=0.9-2.5), after adjusting for age, gender, marital status, education, smoking, alcohol drinking, and body mass index. For gallbladder cancer, subjects with gallstones but without a family history of gallstones had a 21-fold risk (95% CI 14.8-30.1), while those with both gallstones and a positive family history had a 57-fold risk (95% CI 32.0-110.5). Significant risks for gallbladder cancer persisted after additional adjustment for gallstones, and when the analysis was restricted to subjects with first-degree relatives whose gallstones were treated with cholecystectomy. The significant associations with a family history of gallstones were seen for all first-degree relatives, including parents, siblings, and offspring, but not spouses (Heing et.al. 2007).

Adiposity was measured using baseline body mass index, waist circumference, hip circumference, and waist-to-hip and waist-to-height ratios. Hazard ratios (HR) and 95% confidence intervals (95%CI) were estimated using Cox proportional hazards models adjusted for sex, education, race, smoking, and alcohol consumption with age as the time metric and the baseline hazard stratified by study. During 37,883,648 person-years of follow-up, 1,343 GBC cases, 1,194 EHBDC cases, 784 IHBDC cases, and 623 AVC cases occurred. For each 5 kg/m2 increase in body mass index there were risk increases for GBC (HR: 1.27 [95% CI: 1.19, 1.36]), IHBDC (HR: 1.32 [95% CI: 1.21, 1.45]), and EHBDC (HR: 1.13 [95% CI: 1.03, 1.23]), but not AVC (HR: 0.99 [95% CI: 0.88, 1.11]). Increasing waist circumference, hip circumference, waist-to-hip ratio, and waist-to-height ratio were associated with GBC and IHBDC but not EHBDC or AVC. These results indicate that adult adiposity is associated with an increased risk of biliary tract cancer, particularly GBC and IHBDC. Moreover, they provide evidence for recommending weight maintenance programs to reduce the risk of developing these cancers.

METHODOLOGY

Respondents were interviewed in-person by trained interviewers using a structured questionnaire to obtain information on demographic characteristics, lifestyle behaviors, and medical histories. Based on the responses of the respondents the sample size was

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66 from Coimbatore city. SPSS version 17 was used to carry on the statistical analysis for the study.

RESULTS

The social and demographic characteristics of the selected respondents can be identified as follows,

Table – 1Social and Demographic characteristics

S. no	Social and Demographic characteristics	Frequency	Percentage
1	Age		
	Below 35 yrs	12	18.18
	36 yrs to 55 yrs	23	34.85
	Above 56 yrs	31	46.97
2	Gender		
	Male	26	39.39
	Female	40	60.61
3	Marital status		
	Married	54	81.82
	Single	1	1.52
	Others	11	16.67
4	SES		
	Lower	14	21.21
	Middle	29	43.94
	Upper	23	34.85
5	Education		
	Lower	14	21.21
	Middle	28	42.43
	High	24	36.36
6	Locality		
	Rural	43	65.15
	Urban	23	34.85

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Source: Primary Data 2021

One of the important aspects in understanding the Ampulla of vater carcinoma patient's age is one of the concerns. The age wise distribution showed that among the selected target group 46.97 percent were above 56 years of age followed by 34.85 percent respondents between the age of 36yrs to 55yrs and 18.18 percent of the respondents were below the age of 35years. The gender wise distribution of the respondents showed that 60.61 percent were female respondents and 39.39 percent were male respondents. Marital status of the respondents indicated that 81.82 percent were married, 16.67 percent were divorced or separated and 1.52 percent was single. Socio Economic Status of the respondents stated that 43.94 percent were from middle income family followed by 34.85 percent were belonging to upper class and 21.21 percent were lower income group. Education of the respondents showed that 42.43 percent have attained middle education followed 36.36 percent have attained high education and 21.21 percent have attained lower education. The locality of respondent's details showed that 65.15 percent were from rural area and 34.85 percent are from urban area.

Thus from the study it was identified that among the selected respondents majority were from age group of above 56 years, 60.61 percent were female respondents and were married 43.94 percent were from middle income family and have attained middle education and 65.15 percent were from rural area.

After examining the social demographic characteristics of the respondents the investigator has identified the general characteristics of the selected group. Result of the general characteristics can be identified in table (2).

Table – 2General Characteristics

S. no	General characteristics	Frequency	Percentage

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1	Comorbidity Yes No	 29 37	 43.94 56.06
2	Alcohol Current Never Former	 8 43 15	 12.12 65.15 22.73
3	Smoking Current Never Former	 4 52 10	 6.06 78.79 15.15
4	Diet Vegetarian Non-vegetarian	 17 49	 25.76 74.24
5	Consanguinity Yes No	 22 44	 33.33 66.67

Source: Primary Data 2021

Figure 1

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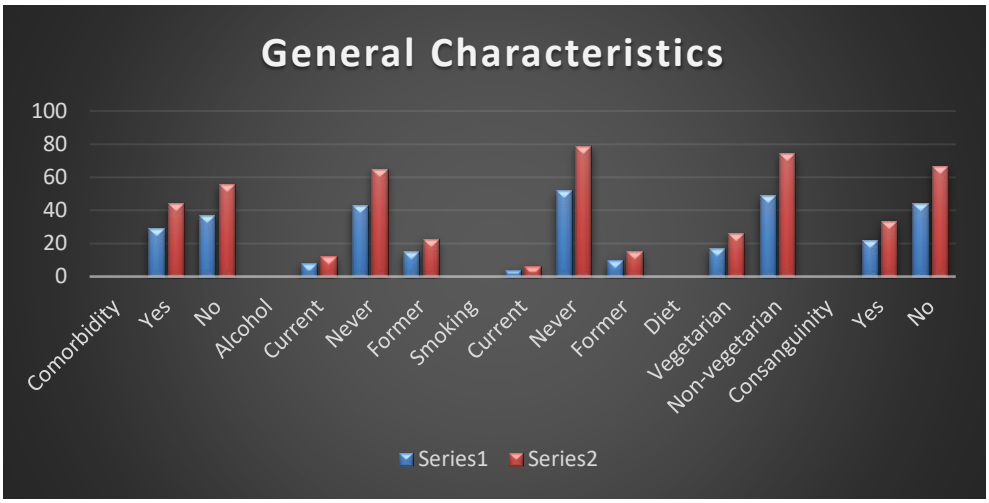

Detail on co morbidity among the selected respondents showed that 56.06 percent were not co morbidity and 43.94 percent were from co morbidity. Information on alcohol consumption among the selected respondents showed that 65.15 percent had never consumed alcohol whereas 22.73 percent were former alcohol addicted person and 12.12 percent were consuming alcohol currently during the investigation. Detail on smoking showed that 78.79 never smoked whereas 15.15 percent were former smokers and 6.06 percent are currently into smoking habit during the investigation. Diet habit of the respondents showed that 74.24 percent were non-vegetarian and 25.76 percent were vegetarian. Detail on consanguinity showed that 66.67 were not from consanguinity and 33.33 percent were from consanguinity.

2. DETAIL OF HEALTH CONDITION

Health condition of the respondents identified during the investigation has been shown in the following table (3).

Table – 3 Health condition

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S. no	Health condition	Frequency	Percentage
1	Stage of Tumor		
	Stage I	32	48.48
	Stage II	19	28.79
	Stage III	15	22.73
2	Size of tumor		
	Less than 2	42	63.64
	More than 2	24	36.36
3	Comorbidity		
	Never	37	56.06
	DM, HTN	13	19.70
	DM, Asthma	3	4.55
	BPPV, DM	2	3.03
	HTN	4	6.06
	DM	7	10.67

Source: Primary Data 2021

Information on stages of tumor showed that among the selected respondents 48.48 percent were in Stage I of tumor followed by 28.79 percent were from Stage II and 22.73 percent were from stage III of tumor. Detail on the size of tumor showed that 63.64tumor was less than 2cm whereas 36.36 percent tumor was more than 2cm. detail on co morbidity showed that 56.06 percent were from never from comorbidity whereas 19.70 percent had DM and HTN followed by 10.67 percent having DM, whereas 6.06 percent had HTN, 4.55 percent had DM, Asthma and 3.03 percent had BPPV, DM.

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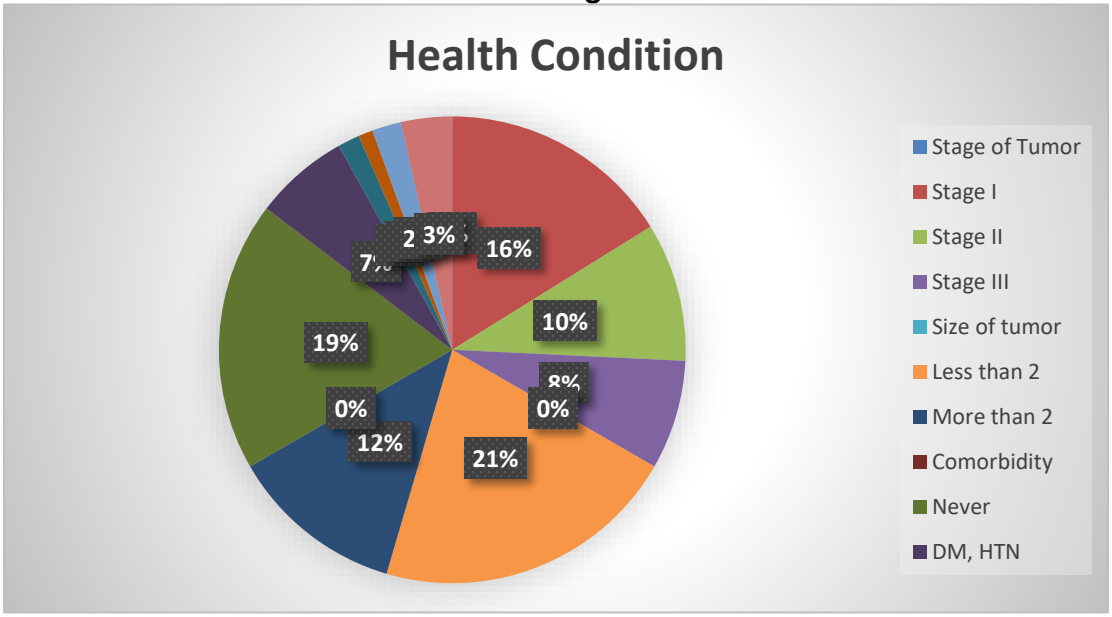
Figure



Relationship between general characteristics and Co morbidity

In order to examine the relationship between the general characteristics and Co morbidity the investigator has implied multiple regression models. Result of the model can be identified in the following table.

Null hypothesis Ho: There is no significant relationship between independent variables (alcohol, smoking, diet pattern and Consanguinity) and dependent variable of Co morbidity of the selected respondents

Regression

Table No: Model Summary

R	R Square	Adjusted R Square	Std. Error of the Estimate
.756	.648	.379	11.256

Table shows, R is the correlation, its value is 0.756 and R square is degree of determination, its value is 0.648. The degree of determination shows the extent to which alcohol, smoking, diet pattern and Consanguinity influences the Co morbidity among the selected respondents

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Table No: 2 ANOVA

Model	Sum of Squares	Df	Mean Square	F	Sig.
Regression	5.342	2	1.065	13.411	.000
Residual	48.125	63	.074		
Total	53.345	65			

ANOVA table shows that the significant value is less than 0.05, which means dependent variable that is participation in decision making is significantly predicted by independent variables which alcohol, smoking, diet pattern and Consanguinity at 95 % of confidence level. This indicates that the regression model for participation in decision making is significant.

Table No: 3 Coefficients

Variables	Unstandardized Coefficients	Standardized Coefficients	T	Sig.
Alcohol	.383	.429	4.903	.000*
Smoking	-.136	-.241	-2.729	.008**
Diet	.200	.310	5.413	.000*
Consanguinity	.213	.542	4.963	.003*

* Dependent Variable: Co morbidity

*=Significant at 1% level, **=Significant at 5% level, ^{NS}=Not Significant

It can be identified from the table that variables such as alcohol (P=0.000), diet (P=0.000) and consanguinity (P=0.003) are statistically significant at 1 percent level of significance and variable Smoking (P=0.008) is statistically significant at 5 percent level of significance. Through the multiple regression analysis it can be identified that the selected independent variable influences the dependent variable. There is positive relationship between general characteristics and Co morbidity. The `R` squared value gives the

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goodness of fit of the model and the value being 0.648 which indicated that 64 percent of the variation was influenced by the combined effect of all the independent variables.

Relationship between the comorbidity, consanguinity, stage of tumor and size of tumor

In order to examine the relationship between the comorbidity, consanguinity, stage of tumor and size of tumor of the targeted group the investigator has used correlations. Result of the correlation can be seen in table.

Correlations

		Comorbidity	Consanguinity	Stage of Tumor	Size of Tumor
Comorbidity	Pearson Correlation	1	.107**	.123*	.116**
	Sig. (2-tailed)		.005	.002	.000
Consanguinity	Pearson Correlation	.107**	1	-.145*	.066
	Sig. (2-tailed)	.005		.000	.087
Stage of Tumor	Pearson Correlation	.123*	-.145*	1	.333*
	Sig. (2-tailed)	.002	.000		.000
Size of Tumor	Pearson Correlation	.116**	.066	.333*	1
	Sig. (2-tailed)	.000	.087	.000	

The correlation between the education and variables co morbidity, consanguinity, stage of tumor and size of tumor was examined. Co morbidity is correlated with consanguinity, stage of tumor and size of tumor at 1 percent and 5 percent level of significance. Consanguinity is correlated with comorbidity, stage of tumor at 1 percent and 5 percent

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level of significance. Stage of tumor is correlated with co morbidity, consanguinity and size of tumor at 1 percent and 5 percent level of significance. The size of tumor is correlated with commodity and stage of tumor at 1 percent and 5 percent level of significance.

CONCLUSION

Biliary tract cancers, which include tumors of the gallbladder, extra hepatic bile duct, and ampulla of Vater, are uncommon but deadly diseases. Tobacco and alcohol are well-known risk factors for a variety of cancers, and the International Agency for Research on Cancer has classified them as group 1 carcinogens. Tobacco use is the leading cause of cancer in the world. Despite a large body of research on tobacco and alcohol, the link between these exposures and biliary tract cancers remains unknown. In the current study it was identified that among the selected respondents majority were from age group of above 56 years, 60.61 percent were female respondents and were married 43.94 percent were from middle income family and have attained middle education and 65.15 percent were from rural area. 56.06 percent did not have any comorbidities and they were not alcohol consumers and were not smokers and the majority of them were non vegetarians. There was relationship between general characteristics and Co morbidity and there was an association between comorbidity, consanguinity, stage of tumor and size of tumor.

REFERENCES

1) Burak K, Angulo P, Pasha TM, Egan K, Petz J, Lindor KD Am J Gastroenterol. 2004 Mar; 99(3):523-6.
2) Castro FA, Koshiol J, Hsing AW, Devesa SS Int J Cancer. 2013 Oct 1; 133(7):1664-71.
3) Chow WH, McLaughlin JK, Menck HR, et al. Risk factors for extrahepatic bile duct cancers: Los Angeles County, California (USA). Cancer Causes Control. 1994;5(3):267–272. [PubMed] [Google Scholar]
4) Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F Int J Cancer. 2015 Mar 1; 136(5):E359-86.
5) Fox JG Aliment PharmacolTher. 1998 Feb; 12 Suppl 1():37-60.
6) Grainge MJ, West J, Solaymani-Dodaran M, et al. The antecedents of biliary cancer: a primary care case–control study in the United Kingdom. Br J Cancer. 2009; 100(1):178–180. [PMC free article] [PubMed] [Google Scholar]
7) Grimble RF CurrOpinClinNutrMetab Care. 2002 Sep; 5(5):551-9.
8) Hsing AW, Rashid A, Devesa SS, Fraumeni JF Jr (2006) Biliary tract cancer In: Schottenfeld D, Fraumeni JF Jr (eds) Cancer epidemiology and prevention, 3rd edn Oxford University Press, Oxford, pp 787–800 [Google Scholar] [Ref list]
9) IARC Working Group on the Evaluation of Carcinogenic Risks to Humans.IARCMonogrEvalCarcinog Risks Hum. 2012; 100(Pt E):1-538.

ISSN:1673-064X
E-Publication: Online Open Access
DOI/10.5281/zenodo.5746768

10) Li Y, Yang H, Cao J.. Association between alcohol consumption and cancers in the Chinese population–a systematic review and meta-analysis. PLoS One. 2011;6(4):e18776.. [PMC free article] [PubMed] [Google Scholar]
11) McGee EE, Jackson SS, Petrick JL, et al. Smoking, Alcohol, and Biliary Tract Cancer Risk: A Pooling Project of 26 Prospective Studies. J Natl Cancer Inst. 2019;111(12):1263-1278. doi:10.1093/jnci/djz103
12) Njei B. Changing pattern of epidemiology in intrahepatic cholangiocarcinoma. Hepatology. 2014;60(3):1107–1108. [PubMed] [Google Scholar]
13) Palmer WC, Patel T. Are common factors involved in the pathogenesis of primary liver cancers? A meta-analysis of risk factors for intrahepatic cholangiocarcinoma. J Hepatol. 2012; 57(1):69–76. [PMC free article] [PubMed] [Google Scholar]
14) Patel T. Increasing incidence and mortality of primary intrahepatic cholangiocarcinoma in the United States. Hepatology. 2001;33(6):1353–1357. [PubMed] [Google Scholar]
15) Portincasa P, van de Meeberg P, van Erpecum KJ, Palasciano G, VanBerge-Henegouwen GP Scand J Gastroenterol Suppl. 1997; 223():60-9.
16) Praud D, Rota M, Rehm J, Shield K, Zatoński W, Hashibe M, La Vecchia C, Boffetta P Int J Cancer. 2016 Mar 15; 138(6):1380-7.
17) Secretan B, Straif K, Baan R, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V, WHO International Agency for Research on Cancer Monograph Working Group. Lancet Oncol. 2009 Nov; 10(11):1033-4.
18) Shaib YH, El-Serag HB, Nooka AK, et al. Risk factors for intrahepatic and extrahepatic cholangiocarcinoma: a hospital-based case-control study. Am J Gastroenterol. 2007; 102(5):1016–1021.
19) Valle JW, Lamarca A, Goyal L, Barriuso J, Zhu AX Cancer Discov. 2017 Sep; 7(9):943-962.
20) Wenbin D, Zhuo C, Zhibing M, et al. The effect of smoking on the risk of gallbladder cancer: a meta-analysis of observational studies. Eur J GastroenterolHepatol. 2013; 25(3):373–379.
21) Ye XH, Huai JP, Ding J, Chen YP, Sun XC. Smoking, alcohol consumption, and the risk of extrahepatic cholangiocarcinoma: a meta-analysis. World J Gastroenterol. 2013 Dec 14; 19(46):8780-8. doi: 10.3748/wjg.v19.i46.8780. PMID: 24379600; PMCID: PMC3870528
22) Ye XH, Huai JP, Ding J, et al. Smoking, alcohol consumption, and the risk of extrahepatic cholangiocarcinoma: a meta-analysis. World J Gastroenterol. 2013; 19(46):8780. [PMC free article] [PubMed] [Google Scholar]