In the name of GOD

Cholangiocarcinoma predictive factors in primary sclerosing cholangitis patients who underwent liver transplantation in Abu Ali Sina Hospital of shiraz between 2016-2021

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Introduction

Primary sclerosing cholangitis (PSC) is an idiopathic chronic cholestatic liver disease characterized by diffuse inflammation and fibrosis of hepatobiliary system which leads to biliary cirrhosis. PSC is associated with many malignancies such as: cholangiocarcinoma (CCA), colorectal cancer, hepatocellular carcinoma, gall bladder cancer and pancreatic cancer. Among these CCA is the lethal one and has known as the main mortality factor in PSC patients.

Introduction

Approximately half of PSC patients are diagnosed to have CCA only 2 years after their own underlying disease ,these patients often have categorizes as poor prognosis ones since the tumors are frequently diagnose at an advance stage. Unfortunately the only treatment for the patients is surgical resection which due to early disease progression it cannot be used. Cholangiocarcinoma (CCA) is a malignancy of biliary system which occurs due to hyperplasia of bile ducts epithelial cells.

Methods

This current retrospective cross sectional study has been conducted on 450 PSC patients of ABU-ALI SINA specialized and sub-specialized organ transplant hospital (a medical therapeutic branch of Shiraz university of medical science) between years of 2016-2021. The information include age, gender, PSC period, medications, CA 19-9 level, Alkaline phosphates level, Total bilirubin level , MRCP report, CT Scan report, explanted liver pathology.

Methods

After collecting correlated data, we gather all the information in SPSS statistical software so unused data has adjusted automatically and then after making sure of putting all the information correct data analyzing starts. Hypothesis test with P lower than 0/05 as a meaningful level , for describing data we use descriptive statistical methods (frequency , central indicators and dispersion) and if data weren't normal we use average and quarterly range for reporting. For analyzing the connection between variables we use X2 methods and to investigating the terms between variables we use logistic regression model.

Results

In this study we gather the information of 450 PSC patient who underwent liver transplant surgery in ABU-ALI SINA specialized and sub-specialized organ transplant hospital including 268 (59.6%) male and 182 (40.4%) female who fulfill the study protocol.

In this study 82 of PSC patients who underwent liver transplant surgery develop with CCA, so the prevalence of CCA in these patients was equal to 18.2% (14.76, 22.10%). Among these 82 patient 52 (63.4%) was male and 30 (36.6%) female.

Results

Significant risk factors in univariate analysis included Carbohydrate antigen 19-9 (CA 19.9), Hilar lymph node in CT Scan & MRCP, Stricture in CT scan & MRCP, mass in CT scan & MRCP, and age of PSC diagnosis, taking medication (azaram, sulfasalazine, mesalazine, ursoflor). In our study azaram medicine proved to have a remarkable protective effect among PSC patients against cholangiocarcinoma. Multiple logistic regression analysis showed that factors of CA 19-9(OR: 4.888 ; 95% CI:1.816-13.157), Hilar lymph node in CT Scan & MRCP (OR: 2.652 ; 95% CI:1.406-5.004),Stricture in CT scan (OR: 5.153 ; 95% CI:1.634-16.244) and Mass in CT scan & MRCP (OR: 2.565 ; 95% CI:1.328-4.953) are important predictors of cholangiocarcinoma.

Results

Table 1: comparison of mean age in PSC patients with liver transplant

Variable	All PSC patients (N=450)	Patients without CCA (N=368)	Patients with CCA (N=82)	P-value
Age (average± standard deviation)	35±11.4	34.5±11.1	41.3±10.8	0.034

- Independent Sample t test

Results

Table 2: Frequency distribution of prescribed drugs

Prescribed drugs	Whole patients (N=450)	Patients without CCA (N=368)	Patients with CCA (N= 82)	P-value
Ursoflor	294	244	50	0.371
mezalasine	266	368	82	0.214
azaram	76	69	7	0.023
sulfasalazine	18	15	3	0.999
2 drug	366	307	59	0.019

- Fisher's exact test

Results

Table 4: MRCP and CT Scan reports frequency distribution

MRCP and CT report simultaneously (%)	All PSC patients (N=450)	Patients without CCA (N=368)	Patients with CCA (N=82)	P- value
Thickening of bile duct	222	176	46	0.536
Mass	84	54	30	<0.001
Hilar lymph node	109	74	35	<0.001

- Fisher's exact test

Results

Table 3 : CA19-9 frequency distribution

CA19-9 (%)	All PSC patients (N=450)	Patients without CCA (N=368)	Patients with CCA (N=82)	P-value
Positive (>200)	24	13	11	0.001
Negative(<200)	370	309	61	

- Fisher's exact test

Table 5: Multivariate table

variable	Crude OR (95% CI)	P value	Adjust OR (95% CI)	P value
T-bill	1.005(0.984-1.026)	0.641		
ALK.PH	1.00(1.00-1.00)	0.697		
biliarydx	1.737(0.953-3.169)	0.072		
liverdx	1.034(0.480-2.228)	0.933		
inflammation	1.130(0.642-1.986)	0.672		
DM	0.657(0.191-2.265)	0.506		
IBD	0.652(0.397-1.072)	0.092		
Hep C	1.117(0.123-10.129)	0.921		
Hep B	0.807(0.175-3.711)	0.783		
GALL STONE	1.533(0.629-3.738)	0.347		
BMI	0.989(0.921-1.063)	0.769		
PSC DURATION	0.995(0.989-1.00)	0.063		
Age diagnosis of psc	1.024(1.002-1.045)	0.028		
sex	1.220(0.744-2.001)	0.432		
thickening of bile duct wall in MRCP&CT	1.187(0.728-1.936)	0.491		
bile duct dilatation in MRCP	1.626(0.823-3.213)	0.162		
filling defect in MRCP	0.566(0.214-1.499)	0.252		
stricture in MRCP	0.710(0.428-1.179)	0.186		

Table 5: Multivariate table

variable	Crude OR (95% CI)	P value	Adjust OR (95% CI)	P value
Stricture in CT scan	3.715(1.297-10.638)	0.014	5.153(1.634-16.244)	0.005
ursoflur	0.794(0.485-1.301)	0.360		
mezalazin	0.717(0.443-1.160)	0.175		
sulfasalazine	0.894(0.253-3.161)	0.862		
Ca19-9	4.286(1.835-10.011)	0.001	4.888(1.816-13.157)	0.002
Azaram	0.404(0.179-0.916)	0.030		
Hilar lymph node in CT Scan and MRCP	2.684(1.612-4.464)	<0.000	2.652(1.406-5.004)	0.003
Mass in CT scan and MRCP	3.050(1.783-5.218)	<0.000	2.565(1.328-4.953)	0.005
Age of diagnosis PSC	1.024(1.002-1.045)	0.028		
Drug(4Drug)	0.510(0.293-0.888)	0.017		

Discussion

Since that only 4 of our variants become meaningful statistically, it conveys the meaning that high level of CA19-9 and important details of MRCP and CT Scan also patients age meanwhile diagnosis of PSC play an important role in indicating patients prognosis and possibility of CCA occur.

Diagnosis of CCA in patients with PSC is a major challenge and base on other researches using MRCP and CT Scan is very helpful and based on our survey having mass and hilar lymph node in MRCP/CT Scan report will play a predictive role in CCA occurrence in PSC patients.

In the other hand also high level of CA 19-9 (>200) in PSC patients before transplantation can predict CCA occurrence too.

Among all the drugs we significantly find a protective effect against CCA in patient who has azaram as their prescription.

Discussion

PSC is more common in men as our survey shows 58.7% of all the PSC patients were men and among these CCA has occur in 63% of these population.

Also we found out that the average age of patients when PSC diagnoses as well as other surveys is about 35±11/4 in all patients and CCA reveals at about 41/3±10/8 in these population, which is considerably younger than the age of CCA diagnosis in the general population (70-80) so it conforms that we should have expect CCA in PSC patients much more sooner than the patients with out PSC.

Conclusion

Several risk factors for CCA have been identified. Due to the late diagnosis of cholangiocarcinoma by regular examining of PSC patients and considering clinical trials and combining CT scan and MRCP reports, people at higher risk of this cancer can be identified.

Azaram shows to have a protective effect in PSC patients against CCA.

For further researches we recommend that it will be better not to research as a limited time line on this subject because the effect of time line on statistical calculations is inevitable.

Thanks for your attention