RESEARCH ARTICLE

Association of Type II Diabetes Mellitus with Hepatocellular Carcinoma Occurrence - a Case Control Study from Kathmandu Valley

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Abstract

Objective: To assess associations of Type II DM with hepatocellular carcinoma occurrence in Nepal. Materials and Methods: This case control study was carried out using data retrieved from the register maintained in the Department of Biochemistry of Nepalese Army Institute of Health Sciences between 1st January, 2012, and 31st August, 2012. The variables collected were age, gender, HbA1c. All biochemical parameters were analyzed in the Central Laboratory of our hospital by standard validated methods. One way ANOVA was used to examine the statistical significant difference between groups with the LSD post-hoc test for comparison of means of case groups. Odds ratios (OR) were calculated using simple logistic-regression analysis. Results: Etiological factors for HCC were HBV, HCV, alcohol and cryptogenic cirrhosis. The highest age group belonged to the etiological category of HCV with a mean of 71.9±3.6 (CI 69.3, 74.5) years and the lowest age group to the etiological category of HBV with 61.7±5.3(CI 57.9, 65.5) years. The main imperative basis of HCC in present study was HCV (39.5%) and second most significant cause of HCC was alcohol (26%). Glycated hemoglobin was found to be more in males with HCC (7.9%) as compared to females (7.3%). The percentage of Type II diabetes mellitus was greater in HCC patients when compared to controls. This difference was statistically significant with an odd ratio of 4.63 (p<0.001). Conclusion: Type II DM influences incidence, risk of recurrence, overall survival, and treatment-related complications in HCC patients.

Keywords: HCC - type II diabetes - risk factors - Nepal

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Introduction

Hepatocellular carcinoma is the most common major malignant cancer of the liver and its prevalence and mortality rates has increased considerably over the past decades (Dogan et al., 2012). Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer correlated death in the world and more than 80% of HCC cases occur in Asian and African countries. The miserable clinical results of HCC leads to a critical need for in-depth understanding of the pertinent factors affecting HCC occurrence and prognosis (Ye et al., 2012). The well documented risk factors such as hepatitis C virus (HCV), HBV, alcohol certainly plays a role in etiology of hepatocarcinogenesis (Gao et al., 2012). Diabetes has been recommended to be a risk factor for HCC. Diabetes mellitus is mainly of Type I and Type II . Diabetes mellitus (DM) is positively allied with risk of numerous common human malignancies including cancers of the colon, breast, endometrium, pancreas and liver (Mori et al., 2000). Over the last few decades, the prevalence of diabetes mellitus (DM) has augmented considerably in Nepal and is highly suspected to be associated with an increased risk of HCC. Insulin secreted by pancreas absorbs through the portal circulation to the liver and renders the liver to excess of insulin (Xu et al., 2012). Hyperglycemia, hyperinsulinemia, dyslipidemia, obesity , non-alcoholic fatty liver disease, cirrhosis and abnormal fat retention are diabetes-related factors that increase the risk of liver cancer (Kablan et al., 2010). Quite a few other perplexing factors such as diabetes duration, unstable levels of metabolic control, various drugs used for treatment and the likely being there of chronic complications having wide-range or site-specific significance which evaluates cancer risk in diabetic patients (Chiou et al., 2011). The main objective of our present study was to assess the association of Type II DM with hepatocellular carcinoma occurrence.

Materials and Methods

It was a case control study carried out using data retrieved from the register maintained in the Department of Biochemistry of Nepalese Army Institute of Health

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Sciences, Nepal between 1st January, 2012 and 31st August, 2012. The variables collected were age, gender, HbA1c. All these biochemical parameters were analyzed in the Central Laboratory of our hospital by standard and validated methods. The glycated haemoglobin was determined by ion exchange chromatography (Eckerbom et al., 1994). Anti-HBVsurface antigen (anti-HBs), anti-HBV core antigen (anti-HBc), hepatitis B surface antigen (HBsAg), hepatitis Be antigen (HBeAg), (anti-HCV) were determined using commercial assays (Kryger et al., 1981). All these biochemical laboratory parameters were analyzed using Human reagent kits and with the help of semi autoanalyser (Humalyser 3500, Germany) and ELISA. Preceding the study, approval for the study was obtained from the institutional research ethical committee. Analysis was done using descriptive statistics and testing of hypothesis. The data was analyzed using Excel 2003, R 2.8.0, Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version. The One way ANOVA was used to examine the statistical significant difference between groups. Post Hoc test LSD used for the comparison of means of case groups. Odds ratios (OR) were calculated using simple logistic-regression analysis. A p-value of <0.05 (two-tailed) was used to establish statistical significance.

Results

The etiological factor for 200 patients of HCC was HBV, HCV, alcohol and cryptogenic.

Table 1 shows that of the 200 patients of HCC, 170 were males and 30 were females. Glycated hemoglobin was more in males HCC (7.9%) as compared to females (7.3%). The percentage of Type II diabetes mellitus was more in HCC patients when compared to controls. This difference was statistically significant with an odd ratio of 4.63 (p<0.001).

Table 2 illustrates that highest age group belongs to etiological category of HCV with mean of 71.90±3.6 (CI 69.28, 74.52) years and lowest age group belongs to etiological category of HBV with mean of 61.70±5.3 (CI 57.88, 65.52) years. The main imperative basis of HCC in present study was HCV (39.5%) and second most significant cause of HCC was alcohol (26%). HBV infection, HCV infection, alcohol abuse and also DM2 considered to be an independent variables. All associated with an augmented risk of HCC as the maximum frequency of type II diabetes mellitus fall in etiological category of alcohol (32.4), HCV (25%), HBV (16.3%).

Table 1. Type II Diabetes Mellitus Frequency in Cases and Controls

		No. of patients	Dm absent (%)	Dm present (%)	Glycated hemoglobin	Odds Ratio	Relative risk
Total	HCC	200	132 (66)	68 (34)	7.60%	4.63	3.4
	Controls	250	225 (90)	25 (10)	6.80%		
Males	HCC	170	116 (68)	54 (32)	7.90%	3.34	2.6
	Controls	188	165 (88)	23 (12)	7.00%		
Females	HCC	30	23 (75)	7 (25)	7.30%	3.47	3.1
	Controls	62	57 (92)	5 (8)	6.60%		

Table 2. HCC Etiology and Percentage of Type II DM in Various Etiological Factors

Etiology	Age	No. of HCC (%)	% of diabetes mellitus (n=68)
HBV	61.70±5.3 (57.88, 65.52)	11 (5.5)	11 (16.3)
HCV	71.90±3.6 (69.28, 74.52)	79 (39.5)	17 (25.0)
Alcohol	66.20±5.1 (62.49, 69.91)	52 (26.0)	22 (32.4)
HBV+HCV	62.30±5.3 (57.20,65.40)	5 (2.5)	3 (4.4)
HBV+alcohol	62.80±5.9 (58.52, 67.08)	3 (1.5)	2 (2.9)
HCV+alcohol	67.10±5.5 (63.10,71.10)	33 (16.5)	4 (5.8)
HBV+HCV+alcohol	66.10±5.9 (61.82, 70.38)	1 (0.5)	0
Cryptogenetic	67.70±6.6 (62.97, 72.43)	16 (8)	9 (13.2)

Discussion

Alliance between type II DM and cancer has been extensively assumed and explained by various mechanisms. The enhance tumor cell production and metastasis can take place due to the persistent exposure to hyperglycemia and hyperinsulinemia (Richardson et al., 2005). The chances of metastasis was increased as acute exposure to hyperglycemia and IGF increase endothelial cell permeability due to increased generation of reactive oxidative species and structural alteration in the basement membrane (Morss et al., 2007). Our present study had reported the increased occurrence of hepatocellular carcinoma in patients with type II DM. The glycated hemoglobin was more in patients of hepatocellular carcinoma (7.6%) when compared to controls (6.8%). The main causative factor in our current study of HCC was HCV (39.5%), and alcohol (26%). Our results concurred with the findings of Donadon et al (Donadon et al., 2008).

Furthermore, our findings corroborate that patients with DM2 have a significantly increased risk of HCC, independently of cofactors such as HBV and HCV infection and alcohol intake. The patients of HCC with DM had an relative risk of 3.4 of getting the disease when compared to controls with an odd ratio of 4.63. Similarly, in males and females, relative risk was 2.6 and 3.1 with an odd ratio of 3.34 and 3.47 respectively (p<0.001). The increased occurrence of HCC in patients DM Type II can be due to the association of DM with metabolic syndrome. Diabetes augments the oncogenic progression of HCC and transience by accelerating liver fibrosis, enhancing the action of inflammatory markers such as cytokines, genetic and epigenetic changes in malignant cells, (Ma et al., 2012), poor response to treatment, potentiate the incidence of bacterial infections in cirrhotic patients (Yu et al., 2009). In conclusion, Type II DM influences incidence, risk of recurrence, overall survival, and treatment-related complications in HCC patients.

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