Elevated Serum Insulin is an Independent Risk Factor for Hepatocellular Carcinoma: A Case Control Study from Nepal

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Abstract

Aim: To investigate associations of fasting insulin and glucose levels in serum with hepatocellular carcinoma risk. Materials and Methods: This hospital based study was carried out using data retrieved from the register maintained in the Department of Biochemistry of the Nepalese Army Institute of Health Sciences, between 1st December, 2011 and 31st June, 2013. The variables collected were age, fasting plasma glucose, fasting plasma insulin and ALT. Quantitative determination of human insulin concentrations was accomplished by chemiluminescence enzyme immunoassay. Results: Of the total 220 subjects enrolled in our present study, 20 cases were of HCC and 200 were healthy controls. The maximum number of cases of hepatocellular carcinoma in category cutpoints of fasting insulin levels fell in the range of >6.10 µU/ml. The highest insulin levels (>6.10 µU/ml) were seen to be associated with an 2.36 fold risk of HCC when compared with fasting insulin levels of (<2.75 µU/ml). Furthermore, the insulin levels (2.75-4.10 µU/ml) of category cutpoints also conferred a 1.57 fold risk for HCC when compared with lowest fasting insulin levels of (<2.75 µU/ml). Conclusions: The effect of an insulin level in increasing HCC risk appeared consistent, influencing incidence, risk of recurrence, overall survival, and treatment-related complications in HCC patients.

Keywords: Insulin - glucose - serum levels - HCC risk - Nepal

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Analysis was done using descriptive statistics and testing of hypothesis. The One way ANOVA was used to examine the statistical significant difference between groups. The Cox proportional hazards model was used to estimate the hazard ratios (HRs) for incident HCC. 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 A p-value of <0.05 (two-tailed) was used to establish statistical significance.

Results

Of the total 220 subjects enrolled in our present study, 20 cases were of HCC and 200 were healthy controls.

Table 1 depicts that the maximum number of cases (11) of hepatocellular carcinoma were above 60 years of age. The fasting plasma glucose ≥126 mg/dL, was observed in 5 cases of hepatocellular carcinoma. Furthermore, the mean value of fasting plasma glucose was 95.5 mg/dL in cases of hepatocellular carcinoma. The mean value of fasting plasma insulin, was 5.78 µU/ml in cases of hepatocellular carcinoma (p value 0.001*).

Table 2 illustrates that fasting insulin levels µU/ml were categorized into category cutpoints and quartile cutpoints. The maximum number of cases of hepatocellular carcinoma in category cutpoints of fasting insulin levels falls in range of >6.10 µU/ml. The highest insulin levels (>6.10 µU/ml) were seen to be associated with an 2.36 fold risk of HCC when compared with fasting insulin levels of (<2.75 µU/ml) of category cutpoints. Furthermore, the insulin levels (2.75–4.10 µU/ml) of category cutpoints also conferred a 1.57 fold risk for HCC when compared with lowest fasting insulin levels of (<2.75 µU/ml) of category cutpoints.

Discussion

Higher trend of numerous malignancies along with individuals with elevated insulin levels, a end result of insulin resistance has been extensively assumed and explained by various mechanisms. The augment tumor cell production and metastasis can take place due to the unrelenting exposure to hyperglycemia and hyperinsulinemia (Richardson et al., 2005). IR, which show the way to the accretion of fat within hepatocytes, is allied to both excess BMI and NAFLD. Hepatic fat accrual generate oxidative stress, ensuing in inflammation and fibrosis. Our present study had reported that the maximum number of cases of hepatocellular carcinoma were above 60 years of age. The mean value of fasting plasma insulin, was 5.78 µU/ml in cases of hepatocellular carcinoma (p Value: 0.001*). The highest insulin levels (>6.10 µU/ml) were seen to be associated with an 2.36 fold risk of HCC when compared with fasting insulin levels of (<2.75 µU/ml) of category cutpoints. Our results concurred with the findings of Chao et al (Chao et al., 2011). Furthermore, the insulin levels (2.75–4.10 µU/ml) of category cutpoints also conferred a 1.57 fold risk for HCC when compared with lowest fasting insulin levels of (<2.75 µU/ml) of category cutpoints. 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 (Mors et al., 2007). IR encourage fibrosis succession, progress of hepatic steatosis, hyperleptinemia, increased TNF production and abridged expression of peroxisome proliferator activated receptors (Hsu et al., 2008). The increased levels of insulin and glucose possibly will endorse fibrogenesis by stimulating the liberation of connective tissue growth factor from hepatic stellate cells (Paradis et al., 2001).

Conclusion: The effect of an insulin level in increasing HCC risk was consistent and influences incidence, risk of recurrence, overall survival, and treatment-related complications in HCC patients.

References


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