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RESEARCH ARTICLE

CANCER ANTIGEN 15.3 LEVELS IN ALCOHOLIC LIVER CIRRHOSIS

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ABSTRACT

CA 15.3 is a tumour marker useful in monitoring therapy and disease progression in metastatic breast cancer patients. Literature has shown that CA 15.3 levels are affected by liver diseases. This study was a case control study conducted to evaluate CA 15.3 levels in 30 cases of liver cirrhosis in Victoria Hospital attached to Bangalore Medical College and Research institute. There was a statistically significant increase in CA 15.3 levels in cirrhotic patients when compared to age and sex matched healthy controls. Neither cytolysis nor cholestasis, as measured by transaminases and bilirubin respectively, appeared to be related to the increase of the antigen in our patients. A poor metabolism of CA 15.3 due to liver insufficiency can play a role in the increase of this antigen in liver cirrhosis patients. We conclude that liver cirrhosis does not substantially limit the usefulness of this marker in patients with breast cancer as increase in CA 15.3 levels above the reference range was seen in only a small proportion of the patients.

INTRODUCTION

CA 15.3 is a marker for breast carcinoma most useful in monitoring therapy and disease progression in metastatic breast cancer patients (Chan *et al.*, 2006; Ebeling *et al.*, 2002; Molina *et al.*, 2010; Hayes *et al.*, 1992; Porika *et al.*, 2010). Cancer antigen 15-3 is an epitope of a high molecular weight glycoprotein mucin, known as episialin. Elevated CA 15.3 levels are also found in other malignancies, including pancreatic (80%), lung (71%), breast (69%), ovarian (64%), colorectal (63%), and liver (28%) cancer. Elevated CA 15.3 levels are also found in benign liver and breast diseases[1]. This study has been conducted to assess the effect of liver cirrhosis on CA 15.3 levels and also the association between CA 15.3 and clinical and biochemical data in liver cirrhosis.

MATERIALS AND METHODS

Study was done on 30 patients with cirrhosis admitted in the Department of Medicine of Victoria Hospital attached to Bangalore Medical College & Research institute, Bangalore and 30 age and sex matched healthy controls. The diagnosis of liver cirrhosis was based on clinical examinations and laboratory investigations. After obtaining informed consent, 5 ml of venous blood was obtained by venepuncture under aseptic conditions, centrifuged and the separated serum used for estimation of CA 15.3 levels. CA 15.3 was estimated on Beckman Coulter Access 2 fully automated analyser by chemiluminescent immunoassay (Kricka 2006). The upper normal limit for CA 15.3 was taken as 35 U/ml.

Statistical Analysis

The CA 15.3 levels were compared to the liver function tests (Total bilirubin, Serum albumin, liver enzymes AST, ALT, ALP). Cases were also classified into 3 groups based on Child-Pugh classification – Class A (n =0), B (n = 12) and C (n=17) and CA 15.3 levels compared.

Study design: A case control study with 30 cirrhotic patients and 30 age and sex matched healthy controls was undertaken to study the effect of liver dysfunction due to cirrhosis on the levels of breast cancer tumour marker CA 15.3.

Statistical Methods: Results on continuous measurements have been presented as Mean ± SE and results on categorical measurements presented as Number (%). Significance was assessed at 5 % level of significance. Chi-square/ Student 't' test has been used to find the significance of study parameters. Pearson's correlation has been used to compare continuous variables.

Statistical software: Statistical analysis was carried out using Microsoft Excel. Microsoft Word and Microsoft Excel were used to generate graphs, charts, etc.

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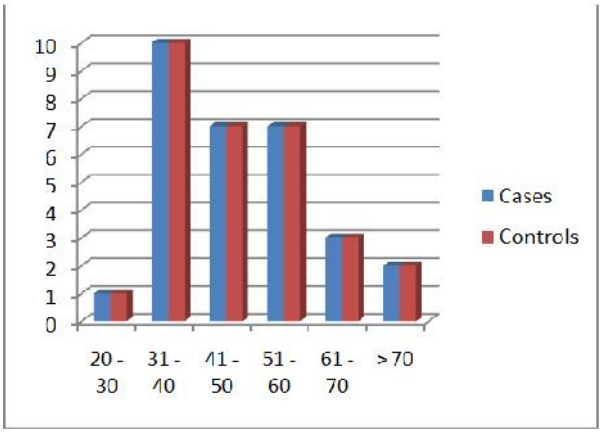
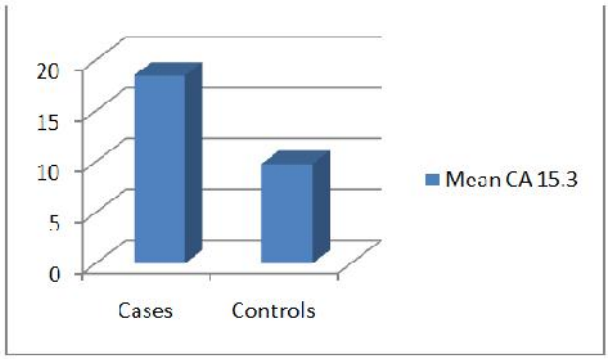
RESULTS

The mean ± SE of CA 15.3 in cases and controls were 18.49 ± 1.74 and 9.75 ± 0.75 U/ml respectively and the difference was statistically highly significant with $p < 0.001$. There was no significant difference in CA 15.3 levels between the different Child-Pugh classes. CA 15.3 levels were increased above the normal limit of 35 U/ml in 3 (10%) of the cases. There was no significant correlation between CA 15.3 levels and liver function parameters such as Total Bilirubin, Direct Bilirubin, Total protein, Albumin, AST, ALT and ALP as assessed by Pearson's correlation.

I. Age distribution of cases and controls



II. Levels of ca 15.3 in cases and controls



III. CA 15.3 Levels in controls and cases classified according to child-pugh scoring

	Number	CA 15.3 Mean ± SE
Controls	30	9.75 ± 0.75
Class B	13	16.0 ± 2.9*
Class C	17	20.4± 2.15*

*- Statistically significant $p < 0.001$ when compared to control group

III. Correlation between ca 15.3 levels and liver function tests

	p value
Total Bilirubin	NS
Direct bilirubin	NS
Total protein	NS
Albumin	NS
AST	NS
ALT	NS
ALP	NS

NS – Not significant

DISCUSSION

CA 15.3 serum levels were slightly increased in a small proportion of our cirrhotic patients without malignancy. Similar results were obtained in studies investigating CA 15.3 levels in benign liver diseases (Collazos *et al.,* 1992; Molina *et al.,* 1986; Ruibal *et al.,* 1986). CA 15.3 is a carbohydrate-related tumour marker. Carbohydrate-related tumour markers are either antigens on the tumour cell surface or secreted by the tumour cells. These markers tend to be more specific than naturally secreted markers, such as enzymes and hormones. Biochemically, they are high molecular weight mucins or blood group antigens. As with other glycoproteins, the metabolism of CA 15.3 can also be impaired by liver dysfunction as liver plays an important role in clearance and excretion of glycoproteins (Thomas and Zamcheck 1983). Also, reduced sialoglycoprotein receptor quantity has been related to the progression of liver disease (Kudo *et al.,* 1989). Therefore a reduced metabolism and clearance of CA 15.3 from the blood due to liver dysfunction could explain the increased levels of this antigen in cirrhotic patients. Neither cytolysis nor cholestasis, as measured by transaminases and bilirubin respectively, appeared to be related to the increase of the antigen in our patients.

Conclusion

This study shows that cirrhotic liver disease is associated with a statistically significant increase in CA 15.3 levels. A poor metabolism of CA 15.3 due to liver insufficiency can play a role in the increase of this antigen in liver cirrhosis patients. But increase above the reference range is seen in only a small proportion of patients (10%). We therefore conclude that liver cirrhosis does not substantially limit the usefulness of this marker in patients with breast cancer.

Limitation

Our study was conducted with a small sample size. Larger studies over longer duration are necessary to study the effect of cirrhosis on CA 15.3 levels.

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