DOI: https://doi.org/10.53350/pjmhs2023174474

ORIGINAL ARTICLE

Diagnostic Implications of Enhanced CD34 Expression in Hepatocellular Carcinoma: A Cross-Sectional Study

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ABSTRACT

Background: Hepatocellular carcinoma is the most prevalent primary cancer of the liver globally and is responsible for the majority of cancer-related fatalities. The purpose of the research was to establish the frequency of enhanced cd34 expression in sinusoid-like vascular endothelial cells in Hepatocellular carcinoma.

Methods: CMH Multan's Department of Histopathology carried out a cross-sectional study. Histochemical staining was performed. Before beginning the staining technique, sections were washed in phosphate buffer saline for 5 minutes. The usual immunohistochemistry staining method - Avidin Biotin Complex Method - was employed following hospital protocols.

Results: 85 (67.5%) male and 41 (32.5%) female patients were among the 126 studied cases. 54 (42.9%) were from rural areas, while 72 (57.1%) were from urban areas. Diabetes was prevalent in 43 (34.1%), and smoking was found in 10 (7.9%). Obesity was found in 18 (14.3%), and hypertension was identified in 74 (58.7%). Only 5 (4.0%) of our research's cases had a family history of HCC. Enhanced cd34 expression was noted in 106 (84.1%).

Conclusion: There found a very high frequency of enhanced cd34 expression of sinusoid-like vascular endothelial cells in HCC. The enhanced cd34 presentation can aid in the early recognition of HCC and the proper care of these patients to improve their quality of life.

Keywords: Enhanced Expression, Hepatocellular carcinoma, cd34, Risk factors.

INTRODUCTION

In Western countries, hepatocellular carcinoma (HCC) is the most widespread primary liver cancer and the third-highest reason for mortality associated with malignancy.(1) Chronic hepatic infections, for instance, hepatitis-b (Hep-B) infection or hepatitis-c (Hep-C) infection, non-alcoholic fatty liver disease (NAFLD), aflatoxins consumption, and cigarette smoking, are all well-known causes of HCC.(2) The clinical presentation varies significantly; individuals may be symptom-free or show symptoms ranging from upper-right quadrant abdomen pain and loss of weight to jaundice with obstruction and fatigue. The use of tomography is the foremost and essential step in all HCC diagnosing, treatment, and later follow-up visits.(3) "The Barcelona Clinic Liver Cancer Staging System" is still the most widely used grading approach for HCC therapy recommendations.(4) HCC has been challenging to detect and treat efficiently in the past; current treatment focuses on hepatectomy, hepatic transplantation, ablation therapies, embolisation therapy, and systemic treatment using cytotoxic medicines and targeted agents.(5) CD34 is a type I transmembrane sialomucin produced by hematopoietic stem-cells, microvascular and lymphoid endothelial cells. CD34 is missing from typical sinusoidal endothelial cells in healthy livers. Still, expression rises during capillarisation in chronic inflammatory illness and sinusoidal-type vasculature in HCC. CD34 expression has also risen in various cases following chronic inflammation, including the rheumatoid joint and areas of neo-lymphoid formation.(6) CD34 expression has previously been linked to vasculogenic and angiogenic processes, with mesenchymal CD34+ stem cells mainly linked to vascularisation recently; vasculogenic and angiogenic mechanisms are required for cancer development. Multiple studies have also described CD34 expression in cancer cells, even though the loss of this molecule has been associated with an invasive malignant character. In this perspective, the CD34 molecule can be considered a dedifferentiation marker in neoplastic cells. Endothelial cells and endothelial progenitors may also express CD34 as a possible cancer vascularisation marker. Because HCC is a hyper vascular malignancy, staining for vascular endothelium with CD34 is often positive or significantly positive, as unpaired arteries are more easily identifiable—however, the sinusoidal epithelium stains weakly with CD34 antibodies in benign tissue.(7) Due to a lack of local data on this topic and the simple fact that extensive internet studies found that elevated CD 34 expression has not been completely clarified, data on its function in HCC in Pakistan are rare. The findings of this study will create a helpful baseline database of our local community, which will aid clinicians in the early detection of HCC.

MATERIAL AND METHODS

Following ethics committee permission, a cross-sectional study was carried out at the Combine Military Hospital (CMH), Multan's Department of Histopathology during the period of January 2021 to March 2022. The sample was selected from individuals with HCC who presented to CMH Multan's outpatient department (OPD) or the indoor general medicine department. Informed consent was obtained, and they were instructed on the study's aims and the patient's confidentiality. On a standardised proforma, all information such as gender, age groups, residence status, family history, diabetes, smoking, hypertension, and obesity was entered. Immunohistochemistry was carried out on formalin-fixed and paraffin-embedded 3 – 4 µ m sections cut, dewaxed, and hydrated. Before starting the staining, sections were washed in phosphate buffer saline for 5 min. The standard Immunohistochemistry staining method – Avidin Biotin Complex Method- was used per hospital protocols. The data was entered and analysed using the latest version of the SPSS. The mean with standard deviation for patient age was calculated using descriptive statistics for categorical variables like gender, age groups, residential status, cigarette smoking, family history, hypertension, diabetes, obesity, and enhanced cd34 expression percentages and frequencies were determined. Stratification was used to control effect modifiers such as gender, age groups, residence status, family history, diabetes, hypertension, obesity, and smoking. Chi-square tests were used after stratification to evaluate how they affected enhanced expression.

RESULTS

There were 126 patients included in the study, of which 85 (67.5%) were male while 41 (32.5%) were females. The mean age was 54.18 ± 9.13. The minimum age was 39, while the maximum age was 70 years, as shown in Table 1.

The male patient's mean age was 53.88 ± 9.54 years, whereas the female patient's mean age was 54.80 ± 8.28 years. Most of the cases, 79 (62.7%), were over the age of 50 years. Of the 126 study cases, 54 (42.9%) were from rural, while 72 (57.1%) were from urban areas. Smoking was observed in 10 (7.9%) of our research cases. Diabetes was found in 43 (34.1%) of the patients. In our research, hypertension was present in 74 (58.7%) cases. The patients' mean Body Mass Index (BMI) was 25.43 ± 2.13 kg/m^2, and obesity was observed in 18 (14.3%) participants. Only 5 (4%) people had a family history of HCC, as shown in Table 2. Enhanced cd34 expression of sinusoid-like vascular endothelial cells in HCC was stratified by age, gender, residential status, diabetes, hypertension, obesity, smoking, and family history, as shown in Table 3.

Table 1: Age and Gender Distribution of Participants

Risk Factors		Frequency	Percentage
Age	Up to 50 years	18	37.3
	More than 50 years	108	62.7
Gender	Male	85	67.5
	Female	41	32.5

Table 2: Distribution of factors associated with Hepatocellular Carcinoma

Risk Factors		Frequency	Percentage
Hypertension	Yes	74	58.7
	No	52	41.3
Smoking	Yes	10	7.9
	No	116	92.1
Diabetes	Yes	43	34.1
	No	83	65.9
Obesity	Yes	18	14.3
	No	108	85.7
Residential Status	Urban	72	57.1
	Rural	54	42.9
Family History	Yes	5	4.0
	No	121	96.0
Enhanced cd34 expression	Yes	106	84.1
	No	20	15.9

Table 3: Stratification of Enhanced expression with regards to Risk factors

Risk Factors	Enhanced cd34 Expression		P – value
Gender	Yes	No	
Male	70	15	0.604
Female	36	5	
Age			
Up to 50 years	27	20	0.001
More than 50 years	79	00	
Residential Status			
Rural	44	10	0.623
Urban	62	10	
Diabetes			
Yes	43	00	0.001
No	63	20	
Hypertension			
Yes	74	00	0.001
No	32	20	
Obesity			
Yes	15	03	
No	91	17	
Smoking			
Yes	10	00	0.362
No	96	20	
Family History			
Yes	02	03	0.028
No	104	17	

DISCUSSION

HCC is the ninth most common reason for cancer-related mortality in the United States.[8] It was projected that 30,640 new hepatic and biliary malignancies were diagnosed in 2013, with 21,670 fatalities.[9] Females were less likely than males to develop HCC (1:2.4), with greater rates in East and South Asia, Central and West Africa, Melanesia, and Micronesia/Polynesia.[10] The age-adjusted incidence of hepatic malignancies has increased from 1.6 per 100,000 people to 4.6 per 100,000 people among American Indians and Alaska Natives, followed by blacks, Whites, and Hispanics.[11]

HCC screening methods include both radiological tests and serological indicators. Ultrasound (US), computerised tomography (CT), and magnetic resonance (MRI) with contrasts are some of the most popular radiological techniques used for surveillance.[12]

The liver sinusoidal endothelial cells (LSECs) construct the wall of the sinusoids. They lack organised basement membranes and have cytoplasm pierced by open fenestrae, resulting in a fragmented hepatic microvascular endothelium. LSECs have critical functions in maintaining hepatic homeostasis, particularly modulation of vascular tone, inflammation, and thrombosis, as well as controlling the liver's immune response.

LSECs change their phenotype in response to acute or chronic liver injury, negatively affecting adjacent cells and the pathogenesis of liver disease. The primary functions and phenotypical imbalances of LSECs in liver disorders, explicitly acute injuries like ischemia-reperfusion injuries, drug-induced hepatic injury and bacterial or viral infection, chronic liver diseases like metabolism-associated hepatic disorder and alcoholic steatohepatitis, and HCC, and provides an in-depth review on the role of LSECs as potential therapeutic targets for hepatic disorders.

Our study included 126 participants who met the study's inclusion criteria. There were 85 (67.5%) male and 41 (32.5%) female patients among the total 126 study cases. A survey from Lahore by Nadeem et al.[13] observed male gender preponderance in 68% of patients, which is comparable to our findings. Farooqi et al.[14] additionally observed that male gender pervasiveness in HCC is consistent with our results. Alam et al.[15] kept a 64% male gender dominance in HCC, which concurs with our findings.

The mean age of our research cases was 54.18 ± 9.13 years, with a minimum age of 39 years and a maximum age of 70 years. Male patients had a mean age of 53.88 ± 9.54 years, while female patients had a mean age of 54.80 ± 8.28 years. According to our findings, 79 (62.7%) of our research cases were over 50 years old. Nadeem et al.[13] found similar results in a study conducted in Lahore. Naheed et al.[16] also, in a study conducted in Lahore, reported a mean age of 45 ± 10.95 years for the individuals they studied, which is consistent with our findings. Farooqi et al.[14] also reported a mean age of 47.4 ± 4.2 years, comparable to our results. Alam et al.[15] also observed that 64% of the participants were between 45 and 60, which aligns with our findings.

54 (42.9%) of the 126 research cases were from rural, whereas 72 (57.1%) were from metropolitan regions. Smoking was found in 10 (7.9%) cases in our investigation. The more significant percentage of patients in urban areas can be ascribed to increased exposure to environmental toxins. The mean BMI was 25.43 ± 2.13 kg/m2, and obesity was observed in 18 (14.3%) of our study cases.

Only 5 (4%) of the research's individuals had a family history of HCC. Diabetes was identified in 43 (34.1%) of the individuals in our research. A study conducted in the Netherlands by Wlazlo et al.[17] revealed 37% diabetes, comparable to our observations. A survey carried out by Zein et al.[18] from the United States reported 25% diabetes, which correlates with our findings. In the study we conducted, hypertension was present in 74 (58.7%) of the cases. Almani et al.[19] reported 42% hypertension, per our findings.

Enhanced cd34 expression of sinusoid-like vascular endothelial cells in HCC was noted in 106 (84.1%) of our study cases. Cui et al.[20] reported 80 % enhanced cd34 expression in HCC, comparable to our study results.

CONCLUSION

Our study found a substantial prevalence of Enhanced cd34 expression of sinusoid-like vascular endothelial cells in HCC. Increasing age, diabetes, hypertension, and a family history of

HCC were all linked with increased cd34 expression in HCC. The increased cd34 expression can aid in the early diagnosis of HCC and the proper care of these patients to improve their quality of life.

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