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Changing in the etiologies and the presentation charactheristics in hepatocellular carcinoma. A single center experience in western Turkey

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INTRODUCTION: The primary aim of this retrospective study was to investigate the etiological distribution of hepatocellular carcinoma (HCC) patients who admitted Ege University Medical School Division of Gastroenterology between2005-2017 and the changes of this distribution among 5 years periods. Secondary aim was to investigate the changes of patients' characteristics during years when they admitted first time

METHODS: Patients folders were evaluated retrospectively. HCC diagnosed according to MRI, CT, Doppler findings and rarely histopathologically. The recorded parameters were patients' demographical and clinical characteristics, tumor characteristics, laboratuary findings, treatment modalities and prognostic scores. Etiological assessment was based on laboratuary tests like viral serology, autoantibodies, ceruloplasmin and alpha-1 antitrypsin levels, transferrin saturation, ferritin levels, risk factors for fatty liver and abdominal USG.

RESULTS: There were 474 patients who had HCC final diagnosis and enough data from 2005 to 2017. Five major etiology were Hepatitis B (n= 256; 63.8%), Hepatitis C (n= 83; 20.7%), alcohol (n=27; 6.7%), Hepatitis D (n=16; 4%) and non-alcoholic steatohepatitis (NASH) (n=19; 4.7%). The number of patients who had these 5 etiologies was 401. The mean age was 62.5 ± 9.9. There were 314 (78.3%) male, 87 (21.7%) female patients. There were newly diagnosed 124 patients between 2005-2009, 199 patients between 2010-2014, 99 patients between 2015-2017. Eighty three percent patients had cirrhosis previously. The etiology of HCC was not investigated adequately (n=48) or diagnosis was cryptogenic cirrhosis in 73 patients. There was more than one etiology in few patients. 219 (85.5%) of patients related to Hepatitis B, 44 (53%) of patients related to Hepatitis C, all patients related to alcohol, 11 (69%) of patients related to Hepatitis D, 13 (68%) of patients related to NASH were men (p<0,0001). The mean age of these groups were 61±10, 67±9, 63±9, 56±11, 68±12 respectively (p<0,0001). The distribution of these etiologies between periods of 2005-2009, 2010-2014, 2015-2017 was shown in Figure 1. (Chi square 16.5; p=0.036) (Linear by linear association p=0.019). Consistently changed basal parameters of HCC which were statistically significant were mean of age (60.5 ±10.5 [2005-2009]; 63.3 ±9.8 [2010-2014]; 63.7±9.1 [2015-2017] p=0.029) and, male gender 73.4% [2005-2009]; 77.4 [2010-2014]; 88.5% [2015-2017] p= 0.027).

CONCLUSION: HBV and HCV were less; alcohol, NASH and HDV were more effective as etiology of HCC

Keywords: hepatocellular carsinoma; HBV, HCV, alcohol, cirrhosis, Non-alcoholic steatohepatitis

Table 1. Patient demographics and clinical assessment	
Gender	Presence of portal hypertension
Age	Presence of ascites
Etiology	Encephalopathy
Presence of fatty liver	Esophageal variceal hemorrhage
Presence of Diabetes Mellitus	Hemodialysis treatment
Fibrosis level if liver biopsy presents	Follow-up duration before HCC diagnosis
Presence of cirrhosis	
Tumor characteristics	
Number of Tumors	Hepatic vein involvement
Largest tumor diameter	Lymph node metastasis
Total diameter	Presence of distant metastases
Portal vein involvement	Location of distant metastasis
Laboratory	
AST	INR
ALT	Urea
Alkaline phosphatase	Creatinine
GGT	Neutrophil count
Thrombocyte	Lymphocyte count
Na	Neutrophil/ Lymphocyte ratio
Total cholesterol	Thrombocyte / Lymphocyte ratio
Triglyceride	T. Bilirubin
Total protein	AFP
Albumin	
TREATMENT	
Transplantation	Radiofrequency ablation
TAKE	Resection
Prognostic scores	
MELD score	CLIP score
Child-Pugh score	OKUDA score
BCLC stage	ALBI score

The parameters recorded in the first presentation of the patients are shown in Table 1.

Table 2: The distribution of patients with five major etiologies		
Disease	Number	Percentage
HBV	256	63.8
HCV	83	20.7
Alcohol	27	6.7
Delta	16	4.0
NASH	19	4.7
Total	401	100.0

The distribution of most common etiologies between periods of 2005-2009, 2010-2014, 2015-2017

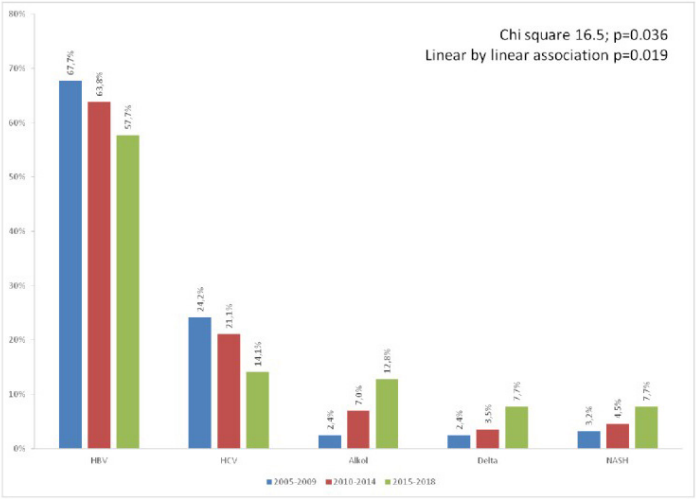

Table 3. Consistently changed basal parameters with statistical significance					
		2005-2009	2010-2014	2015-2017	p
Gender (M/F) Ratio	%	73.4/26.6 2.758	77.4/22.6 3.422	88.5/11.5 7.667	0.027
Age	Mean±SD	60.5±10.5	63.3±9.8	63.7±9.1	0.029
Neutrophil	Median	3020	3300	3715	0.007
GGT	Median	67	72	79	0.002
Total protein	Mean±SD	7.73±0.87	7.33±0.77	7.29±0.72	7.29±0.72 0.0001

Table 4. Variables changing consistently over years but having no statistical significance				
		2005-2009	2010-2014	2015-2017
NLR	Mean (95% CI)	2.82 (2.42 – 3.22)	3.30 (2.68 – 3.91)	5.05 (1.56 – 8.55)
INR	Mean (95% CI)	1.16 1.13 – 1.19	1.20 1.17 – 1.23	1.22 1.15 – 1.29
T. Bilirubin	Mean (95% CI)	1.41 1.24 – 1.58	1.73 1.33 – 2.12	2.42 1.00 – 3.83
Diagnosis during follow-up	%	71.4	67.7	63.6
Presence of ascites	%	28.5	29.1	29.9
Fatty liver	%	6.5	9.1	11.5