Research Article

Gastroenterology, Hepatology & Digestive Disorders

Hepatocarcinoma in Instituto Guatemalteco de Seguridad Social Contrasting Global Epidemiology

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Received: 25 July 2018; **Accepted:** 20 August 2018

Citation: Sandoval G. Luis, Gatica Manuel. Hepatocarcinoma in Instituto Guatemalteco de Seguridad Social Contrasting Global Epidemiology. Gastroint Hepatol Dig Dis. 2018; 1(3): 1-4.

ABSTRACT

Background: *Guatemala has the highest incidence and mortality of hepatocellular carcinoma (HCC) in the entire American continent. This liver neoplasm is the 7th cause of cancer in Central America, and the 2nd cause of incidence and cancer mortality in Guatemala. There are many risk factors already identified, in the indisputable first place is cirrhosis, then hepatitis B virus (HBV), hepatitis C virus (HCV), alcoholism, nonalcoholic fatty liver disease (NAFLD), etc. Only about 10% of HCCs develop in non-cirrhotic livers. In every day medical practice, we have seen an increase in non-cirrhosis HCC, with no other traditional risk factors. It woke up our curiosity and interest to characterize our hepatic cancer.*

Methods: *Observational, retrospective and analytic study. All HCCs attended at Instituto Guatemalteco de Seguridad Social (IGSS) in 2015 – 2016 were analyzed, researching for epidemiological data, focusing in differences between cirrhotic vs. non-cirrhotic patients. Statistical analysis was performed with PSPP 2007. Categorical variables were presented with frequency and percentages, and analyzed by chi squared of homogeneity. Normality was tested with Kolmogorov-Smirnov. Numerical data were evaluated with t-student of independent samples. At relational level a bivariate study was made, then elevated to multivariate level.*

Result: *Total of 53 HCC cases were found, 15 cirrhotic and 38 non-cirrhotic (71.69%). Comparing both groups, there is no statistical difference between age, body mass index (BMI), sex, family history of cancer, alcoholism, tobacco, diabetes mellitus, obesity, HBV, HCV, alpha-fetoprotein (AFP), mass diameter, nor treatment (surgery, transarterial chemoembolization (TACE), radiofrequency ablation and sorafenib). There is difference in jaundice, ascites and encephalopathy, possibly due the same cirrhosis.*

Conclusions: *HCC in our medical center occurs in apparently healthy livers, contrasting global epidemiology. Staring with this new revealing knowledge we must analyze our medical approach to diagnose and manage HCC in Guatemala, and look for our nontraditional risk factors.*

Keywords

Aflatoxin, Guatemala, Hepatitis B, Hepatitis C, Liver cirrhosis, Liver neoplasm.

Introduction

HCC is the most common primary malignancy of the liver. There are over half a million new cases diagnosed annually, with a very high fatality rate [1]. Globally, the most common histology (approximately 80%) is hepatocellular carcinoma, a tumor of the parenchymal cells of the liver; then (approximately 15%) intrahepatic cholangiocarcinoma. The highest incidence rates of liver cancer in the world are in Asia and Africa. Approximately 75% of the liver cancer occurs in Asia, with China accounting for over 50% of the world´s burden. The country with the single highest incidence rate, however is Mongolia, with an age-standardized rate (ASR) per 100,000 person of 78.1 [2]. Guatemala has the highest incidence and mortality of hepatocarcinoma (HCC) in the entire American continent. This liver neoplasm is the 7th cause of cancer in Central America, and the 2nd cause, of incidence and cancer mortality in Guatemala [3]. Gender disparity in incidence

is notable in almost all countries, with rates among males being two to three-fold higher than females, High rates areas do not, however, have greater gender disparity than other areas [2]. There are many risk factors already identified, in the indisputable first place is cirrhosis, then hepatitis B virus (HBV), hepatitis C virus (HCV), alcoholism, nonalcoholic fatty liver disease (NAFLD), etc [4]. Only about 10% of HCCs develop in non-cirrhotic livers [5]. In every day medical practice between rounds, we have seen an increase in non-cirrhosis HCC, with no other traditional risk factors. It woke up our curiosity and interest to characterize our hepatic cancer.

Materials and Methods

We conducted 2 years observational, retrospective and analytic study. All cases of HCC attended at Hospital General de Enfermedades (HGE), Instituto Guatemalteco de Seguridad Social (IGSS) between 2015-2016 were analyzed, seeking for epidemiological, clinical, diagnosis algorithm, laboratory and treatment data, focusing in differences between cirrhotic vs. non-cirrhotic patients. Protocol was approved by the local research committee and by Internal Medicine Department of the hospital involved. Authors designed the study and analyzed the data, and all authors had access to the data and made the decision to submit the manuscript for publication.

Cases recruitment

The study included adults (>18 years old) hospitalized with HCC diagnosis by our medical staff, at HGE, IGSS. Within the discharged medical electronic record, the key words of hepatocarcinoma, hepatic neoplasia, hepatic / liver mass and hepatic cell carcinoma were searched. Then we accessed de electronic file and got the variables data.

End-points

The primary end-point was to characterize the epidemiological data of HCC in HGE. Secondary end-points was to compare the HCC in cirrhotic vs. non cirrhotic livers.

Statistical Analysis

Statistical analysis was performed with PSPP 2007. Categorical variables were presented with frequency and percentages, and analyzed by chi squared of homogeneity. Normality was tested with Kolmogorov-Smirnov. Numerical data were evaluated with t-student of independent samples. At relational level a bivariate study was made, then elevated to multivariate level.

Results

Total of 53 HCC cases were found, 15 cirrhotic and 38 non-cirrhotic (71.69%) (Figure 1). Variables distribution stratify by cirrhosis and no cirrhosis are shown in Tables 1 and 2. Median age was 66.31 (68.73 for cirrhosis and 63.89 for non-cirrhosis) years old, normal range of BMI, mass diameter media of 12.47 cm, male predominance (81.13%), high levels of AFP (2,502 in cirrhosis and 3,198 in non-cirrhosis), no differences between alcohol and tobacco consumption, diabetes, obesity, nor cancer family history. There were only two cases of viral hepatitis associated HCC (HCV and HBV). Cirrhotic cases had more portal hypertension symptoms (jaundice, encephalopathy, and ascites). The treatment was mainly palliative care with TACE, radiofrequency ablation and sorafenib, with the latter taking up the vast majority (Figure 1, Panel B).

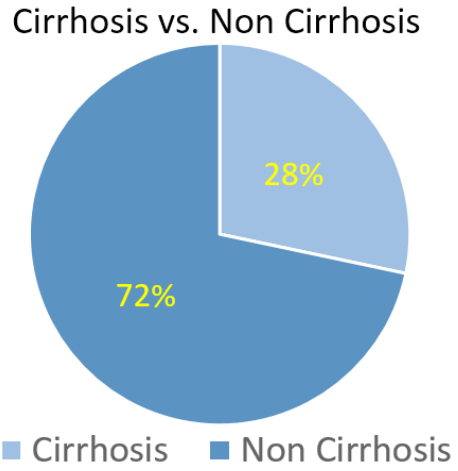

Figure 1: HCC: hepatocellular carcinoma.

	Cirrhosis	Non-Cirrhosis		
	X (SD)	X (SD)	CI 95%	p
Age	68.73 (9.11)	63.89 (12.30)	(-2.21 - 11.89)	0.174
BMI	24.46 (4.69)	23.68 (4.18)	(-2.39 - 3.92)	0.625
Diameter (cm)	13 (12.53)	11.94 (4.24)	(-2.16 - 3.33)	0.971
AFP	2502.49 (5196.8)	3198.16 (8951.53)	(-5853.7 - 4462.38)	0.787

Table 1: Numerical Variables Distribution.
Abbreviation: X: mean, SD: standard deviation, CI: confidence interval, BMI: body mass index and AFP: alpha-fetoprotein.

		Cirrhosis	Non-Cirrhosis	Total	p
Gender (f)	Female	2	8	10	0.706
	Male	13	30	43	
FHCa(f)	Yes	0	2	2	0.534
	No	15	35	50	
ETOH (f)	Present	10	19	29	0.489
	Absent	5	18	23	
Tobacco (f)	Present	7	8	15	0.157
	Absent	8	29	37	
DM (f)	Yes	3	5	8	0.687
	No	12	32	44	
Obesity (f)	Yes	4	6	10	0.442
	No	11	32	43	
AgsHBV (f)	Positive	1	0	1	0.283
	Negative	14	38	52	
HCV (f)	Positive	1	0	1	0.283
	Negative	14	38	52	
Jaundice (f)	Present	9	9	18	0.022
	Absent	6	29	35	
Ascites (f)	Present	12	15	27	0.014
	Absent	3	23	26	

Palpable Mass (f)	Yes	12	26	38	0.51
	No	3	12	15	
Weight Lost >10% (f)	Yes	9	27	36	0.322
	No	6	11	17	
Encephalopathy (f)	Yes	5	3	8	0.033
	No	10	35	45	
Imaging (f)	CT	6	10	16	0.597
	Three phase CT	7	23	30	
	MRI	2	5	7	
Biopsy (f)	Yes	6	27	33	0.058
	No	9	11	20	
Surgery (f)	Yes	1	5	6	0.662
	No	14	33	47	
TACE (f)	Yes	0	3	3	0.36
	No	15	35	50	
Radiofrequency (f)	Yes	0	1	1	0.717
	No	15	37	52	
Sorafenib (f)	Yes	6	20	26	0.544
	No	9	18	27	

Table 2: Categorical Variables Distribution.
Abbreviation: F: frequency, FHCa: family history of cancer, ETOH: ethyl alcohol, DM: diabetes mellitus, AgsHBV: hepatitis B surface antigen, HCV: hepatitis C virus, TACE: trans arterial chemoembolization.

Discussion

The risk factors for hepatocarcinoma are widely described, among which the most important is cirrhosis, also mentioned as important influences: HBV, HCV, metabolic syndrome, NAFLD, among others. Guatemala does not have any longitudinal studies to identify our risk factors. Reason why the first step is to epidemiologically characterize our liver cancer, and compare with de global data.

Around the world the gender disparity in incidence is notable in almost all countries. Male is the principal affected gender, being two to three-fold higher than rates among females [2]. These results match with our 81% males cases (Table 2). There are some untested hypothesis that this apparent risk factor could be due to hormonal factors and/or male predominance alcohol consumption, with related diseases. Globally cirrhosis is present >90% of HCC diagnosis [5], but after stratification we found one of the most relevant fact, HCC was present in 72% non-cirrhotic livers (Figure 1), with no other apparent risk factors, no HCV or HBV.

At the time of diagnosis liver lesions were 13 and 11.94 cm. (p=0.971) for cirrhotic and non-cirrhotic respectively (Table 1), which calls the attention that we are making the diagnosis in advanced stages. This is the result that there is no standardization of how hepatocellular carcinoma should be screened in the liver without risk factors.

International publications have disclosed their risk factors (Obesity, diabetes mellitus, alcohol consumption, tobacco, HCB and HVB), nevertheless the prevalence in our center is low (Table 2). There are not isolated risk factor for Guatemala, however there are new data aiming the new research guidelines to look for levels of mycotoxin (aflatoxin and fumonisin) contamination of cultivated products, specially maize (Zea mays) [6,7]. Another possibility would be intrinsic or environmental features, like proto-oncogenes or metabolic risk factors [8]. Simultaneously, low rates of HBV and HCV infection suggest that these viruses may not play a major etiological role in HCC in Guatemala.

Portal hypertension signs (encephalopathy, jaundice and ascites) were more prevalent in cirrhosis cohort (Table 2). We can infer that this result is not completely secondary to HCC but to cirrhosis per se.

Biopsy is indicated in population at high risk of HCC, who do not fully comply with the imaging criteria and in cases without risk factors for HCC [5,4,9]. Biopsy was performed in 62.26% of cases (6 in cirrhotic and 27 in non-cirrhotic) (Table 2). We still use the biopsy as a primordial diagnose, because our HCC occurs in apparently healthy livers. Linking with the mentioned result of the liver mass size at the time of the diagnosis, we can expect that the treatment is almost exclusively palliative, which is reflected in the distribution (Figure 2) and comparison (Table 1) of the therapeutic options.

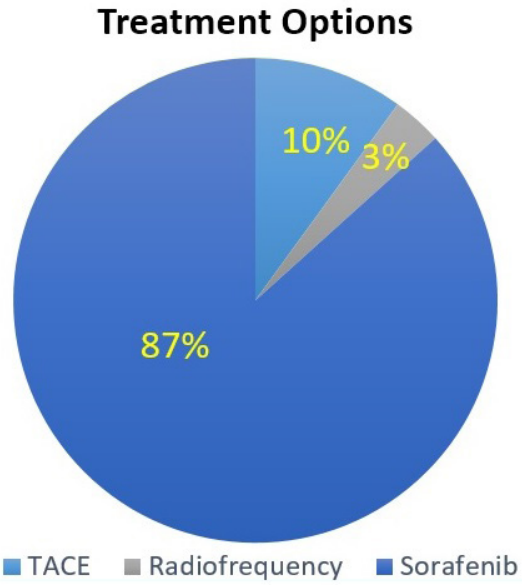

Figure 2: TACE: Trasn Asrterial Chemoembolization.

Guatemala has a unique profile of HCC risk factors, but there are no prospective, analytical or multivariate studies to determine and weigh the risk factors for primary hepatic neoplasia.

Staring with this new revealing knowledge we must analyze our medical approach to diagnose and manage HCC in Guatemala, and look for our nontraditional risk factors.

Limitations

The limitations of the study were that it was performed in a single hospital and the number of patients involved was small.

Conclusion

HCC in our center is in liver with no high risk factors (cirrhosis, HBV, HCV, etc.), male predominance, with hepatic mass considerably bulky (late diagnosis), with no portal hypertension signs, and most of them receive only palliative care. There is no difference between cirrhosis vs. non-cirrhosis in our variables studied, with exception in portal hypertension signs.

Acknowledgments

Presented in the 14th Annual Congress on Gastroenterology & Hepatology, on August 6th – 7th of 2018, Osaka, Japan.

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