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Prevalence of arterial hypertension in liver cirrhosis and correlation with the severity of liver disease

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Abstract---Background and aim: Metabolic diseases and hypertension have increased dramatically in recent years, so the prevalence of hypertension in patients with cirrhosis is expected to increase. The aim of the study was to estimate the prevalence of hypertension in patients with liver cirrhosis and to determine its association with the severity of the liver disease. Patients and methods: This was a descriptive, cross-sectional, analytical study conducted at the Tropical Medicine and Infectious Diseases Department, Tanta University Hospital, Egypt. A total of 2051 patients with liver cirrhosis of various etiology were screened for participation in this study. 2014 patients were enrolled. They underwent blood pressure evaluation, blood tests and abdominal ultrasonography. Patients were classified into hypertensive and non-hypertensive groups. Results: The prevalence of arterial hypertension in patients with liver cirrhosis was 30.8%. As regards Child-Pugh class, hypertensive patients in class A were

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significantly increased (72.9 versus 48.7% respectively) while patients in class B and C were significantly decreased when compared with non- hypertensive patients (25.5,1.6 versus 33.29,17.93% respectively) (P <0.001). Conclusions: The prevalence of arterial hypertension in Egyptian cirrhotic patients is 30.7%, lower than that of the general population. Arterial hypertension is inversely associated with the severity of liver disease.

Keywords---Arterial hypertension, liver cirrhosis, severity.

Introduction

Arterial hypertension is one of the worldwide pathologies. World Health Organization (WHO) reported that 40% of the adult population aged 30-79 years have hypertension defined as a systolic blood pressure greater than 140 mmHg or a diastolic blood pressure greater than 90 mmHg [1]. However, Centers for Disease Control and Prevention reported that 47% of population in the United States have hypertension, defined as a systolic blood pressure greater than 130 mmHg or a diastolic blood pressure greater than 80 mmHg [2]. Variety of hypertension guidelines resulted in different prevalence around the world [3,4,5].

In Egypt, the prevalence of hypertension is markedly increased. In 2020, WHO reported that 50.3% of Egyptian adult population (age group 45-59ys) have hypertension [6]. Most of hypertensive patients had essential hypertension which occur mainly after 40 years. However, less than 15% of hypertension are due to secondary causes as renal, cardiac and endocrinal diseases [5]. Prabhu et al, 2009 stated the prevalence of hypertension in cirrhotic patients is very low (7%). However, their study included a higher proportion of decompensated patients, in whom hypotension is common, and excluded patients under antihypertensive therapies[7]. Obesity and hypertension have been increased dramatically in the past few years [8]. With the presence of these adjuvant factors in Egypt, hepatitis C and obesity leading to non-alcoholic fatty liver (NAFLD) and hypertension, the prevalence of liver cirrhosis with hypertension has increased. The higher prevalence of NAFLD in non-obese hypertensive patients with normal liver enzymes was reported[9]. NAFLD and hypertension are both manifestations of metabolic syndrome and a specific contribution of NAFLD to increased cardiovascular diseases risk is difficult to discern from the combination of shared risk factors[10]. The aim of the study was to estimate the prevalence of hypertension in patients with liver cirrhosis and to determine its association with the severity of the liver disease.

Patients and Methods

Study design and patients

This was a descriptive, cross-sectional, analytical study conducted at the Tropical Medicine and Infectious Diseases Department, Tanta University Hospital, Egypt from October 2018 to October 2020. A total of 2051 patients with liver cirrhosis of various etiology were screened for participation in this study. Of these, 2014

patients fulfilling the inclusion criteria were enrolled. Inclusion criteria included patients with liver cirrhosis and aged >18 years. Patients on drugs affecting blood pressure (beta blockers, nitrates), pregnancy and lactation were excluded from the study. Liver cirrhosis was diagnosed on the basis of clinical and laboratory findings as well as abdomino-pelvic ultrasound. The severity of liver disease was assessed by Child-Pugh class [11]. Hypertension is defined according to American college of cardiology [5] as a systolic blood pressure (SBP) of 130 mm Hg or more, or a diastolic blood pressure (DBP) of 80 mm Hg or more. Institutional ethical committee approval was obtained before the start of the study and informed consent was signed by every patient before enrolment in the study.

Assessments

All cirrhotic patients underwent blood pressure evaluation (for systolic and diastolic BP), blood tests and abdominal ultrasonography. Blood pressure was measured with a mercury sphygmomanometer, with the patient seated for at least 10 minutes. All the measurements were performed by the same investigator, using the same equipment. Laboratory investigations including: complete blood picture, liver biochemical tests, coagulation profile, blood glucose, HbA1C, renal function tests, and viral markers (HBsAg, HBcAb, HCVAb, PCR for HCV), and echocardiography were done. Patients were classified into hypertensive and non-hypertensive groups.

Statistical analysis

The statistical data are reported as the mean ± standard deviation (SD), frequencies (number) and percentages when appropriate. A comparison of numerical variables between the study groups was performed using Student's t-test to compare independent samples from two groups when the samples were normally distributed. To compare categorical data, chi square test was performed. Values of p less than 0.05 (two-tailed) were considered statistically significant. All statistical calculations were performed using the computer program SPSS (Statistical Package for the Social Science; SPSS, Chicago, Illinois, USA) version15 for Microsoft Windows.

Results

A total of 2051 cirrhotic patients of various etiology were screened for study participation. Of these, 37 patients were excluded and subsequently 2014 were enrolled in this study (Fig. 1). Out of 2014 cirrhotic patients, arterial hypertension was detected in 620 (30.8%) patients and 1394 (69.2%) were non-hypertensive. The prevalence of arterial hypertension in our patients with liver cirrhosis was 30.8%. The baseline characteristics of patients of the studied groups are summarized in Table 1. The mean age of hypertensive patients was significantly younger than non-hypertensives (54.79 versus 56.03 years respectively) (P <0.001). Out of 620 hypertensive patients 389(62.47%) were smokers which was significantly higher than non-hypertensive group (42.57%) (P <0.001). HCV, as a cause of cirrhosis, was significantly higher in hypertensive group when compared with non-hypertensives (81.45 versus76.32% respectively) (P <0.001).

In the hypertensive patients, the mean serum bilirubin, ALT and INR was significantly decreased (P <0.001) while the mean serum albumin and platelets count was significantly increased when compared with non-hypertensives (P <0.05). The mean Child-Pugh score was significantly lower in hypertensive patients when compared with non-hypertensives (6.13 versus 8.11 respectively) (P <0.001). As regards Child-Pugh class, patients in class A were significantly increased in hypertensive group when compared with non-hypertensives (72.9 versus 48.7% respectively) (P <0.001). However, patients in Child-Pugh class B and C were significantly decreased in hypertensive group than those without hypertension (25.5,1.6 versus 33.29,17.93% respectively) (P <0.001), as shown in Table 1. Arterial hypertension is inversely associated with the severity of liver disease in terms of Child-Pugh class.

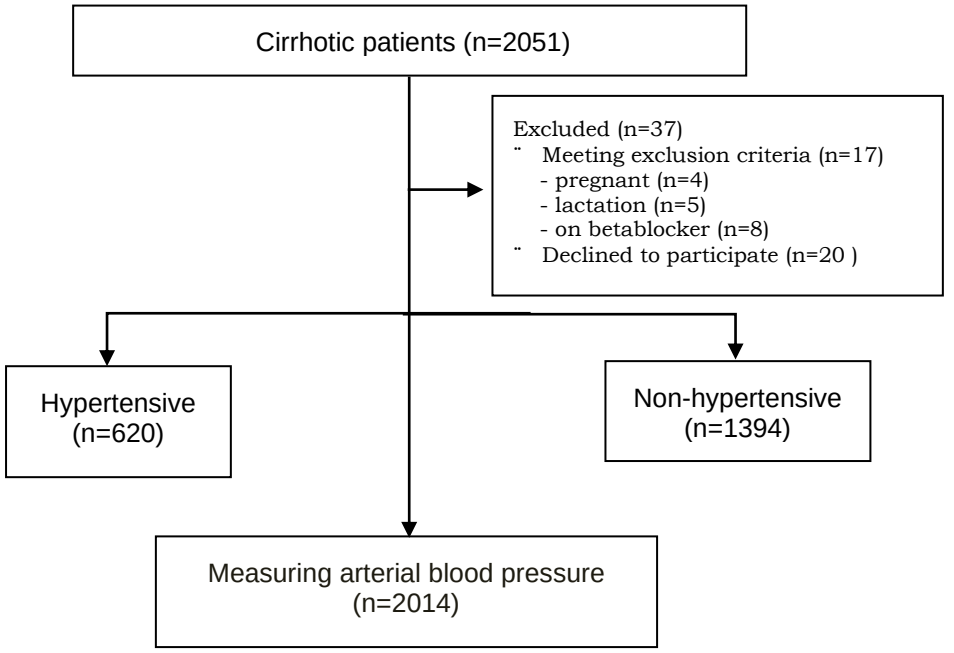

Figure 1. Study flow chart. n, number of patients

Table 1
Patient baseline characteristics

		Group						T-Test or Chi-square	
		Hypertensive (n=620)			Non-hypertensive (n=1394)			t / X^2	P-value
Age	Range	39	-	71	45	-	72	-4.087	<0.001*
	Mean ±SD	54.79	±	6.24	56.03	±	6.32		
Child score	Range	5	-	10	5	-	10	-29.694	<0.001*
	Mean ±SD	6.13	±	1.02	8.11	±	1.52		

Mean arterial pressure(mm Hg)	Range	65	-	125	55	-	70	178.961	<0.001*
	Mean ±SD	111.88	±	5.57	64	±	5.53		
Systolic Blood pressure	Range	135	-	180	60	-	120	166.198	<0.001*
	Mean ±SD	152.95	±	9.38	92.5	±	6.55		
Diastolic Blood pressure	Range	85	-	110	65	-	80	123.142	<0.001*
	Mean ±SD	91.83	±	5.22	70.5	±	2.55		
Ejection fraction	Range	47	-	67	38	-	66	34.991	<0.001*
	Mean ±SD	58	±	5.33	45	±	8.54		
ALT (Up. Nor. 40 IU/L)	Range	11	-	120	12	-	198	-10.391	<0.001*
	Mean ±SD	48.22	±	18.89	66.72	±	42.5		
AST (Up. Nor. 37 IU/L)	Range	10	-	132	18	-	112	-0.165	0.869
	Mean ±SD	45.32	±	18.75	45.52	±	27.46		
Serum Albumin (gm/dl)	Range	2.6	-	4.5	2.5	-	4	21.478	<0.001*
	Mean ±SD	3.49	±	0.39	2.91	±	0.62		
Total bilirubin (mg/dl)	Range	1	-	2.2	1	-	4	-22.667	<0.001*
	Mean ±SD	1.48	±	0.36	2.13	±	0.67		
INR	Range	1	-	2.5	1	-	2.6	-10.642	<0.001*
	Mean ±SD	1.43	±	0.6	1.82	±	0.82		
Hb (gm/dl)	Range	8.5	-	14	7	-	14	-0.696	0.487
	Mean ±SD	11.26	±	1.14	11.31	±	1.62		
WBC ($x10^3/mm^3$)	Range	2.8	-	10.4	3	-	10	1.891	0.059
	Mean ±SD	5.86	±	2.82	5.6	±	2.86		
Platelets ($x10^3/mm^3$)	Range	73	-	289	56	-	268	2.451	0.014*
	Mean ±SD	104.3	±	29.65	99.26	±	47.23		
		N		%	N		%		
Gender	Male	415		67	940		67.43	0.028	0.867
	Female	205		33	454		32.57		
Etiology of cirrhosis	HCV	505		81.45	1064		76.32	6.253	0.012*
	HBV	113		18.22	250		17.93	0.009	0.925
	Others	2		1.31	80		5.74	30.861	<0.001*
Diabetes mellitus	Yes	375		60.48	856		61.41	0.117	0.732
	No	245		39.51	538		38.59		

Child class	Child A	452	72.9	680	48.7	141.434	<0.001*
	Child B	158	25.5	464	33.29		
	Child C	10	1.6	250	17.93		
Ascites	YES	80	13%	710	29.8%	258.748	<0.001*
	NO	540	87%	684	70.2%		
Smoking	YES	389	62.47	596	42.57	67.810	<0.001*
	NO	231	37.25	798	57.25		
HCC	YES	53	8.5	164	11.8	0.574	0.449
	NO	567	91.5	1230	88.2		

N, number; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio;
Hb, hemoglobin; WBCs, white blood cells; SD, standard deviation; HCC, hepatocellular carcinoma; significant P ≤0.05*.

Discussion

In the current study, the prevalence of arterial hypertension in patients with liver cirrhosis was 30.8%. In contrast to our result, Prabhu et al.,2009 reported that the prevalence of arterial hypertension in patients with liver cirrhosis was 7%, which is less than that among the Indian general population (10-15%) [7]. This may be explained by that the prevalence of hypertension in Egyptian adult population in that age group (45-59ys) is 50.6% [6] which is higher than Indian population. The prevalence of arterial hypertension in our patients with liver cirrhosis was still lower than general population. This goes with Henriksen & Moller, 2006 and Prabhu, et al.,2009 studies which reported the relatively low prevalence of hypertension among the patients with cirrhosis[7,13].

Thereby postulating the possible protective effects of cirrhosis on the cardiovascular system, patients with cirrhosis exhibit profound and progressive derangements in systemic and regional hemodynamics. Cirrhosis is a state of hyperdynamic circulation with increased cardiac output, low overall systemic vascular resistance, high arterial compliance and low normal or low arterial blood pressure. This is mainly due to abnormal distribution of increased blood volume with a decrease in effective circulatory blood volume, neurohormonal activation and abnormal sodium and water handling. These factors probably account for the relatively low incidence of hypertension among cirrhotic patients[7,12]. Subjects with established arterial hypertension (essential, secondary) may become normotensive along with the development of chronic liver disease, and in patients with cirrhosis. Cirrhosis may have protective effects on the cardiovascular system and guard against the development of arterial hypertension[13]. It has been suggested that arterial hypertension, which is characterized by increased systemic vascular resistance, can counteract the peripheral vasodilation in cirrhotic patients and protect against complications ascribable to circulatory dysfunction[14].

The mean age of hypertensive patients was significantly younger than non-hypertensives (54.79 versus 56.03 years respectively) (P <0.001). The mean age of cirrhotic patients in this study was is in agreement with Moon, et al., 2019 who reported that, in Egypt and Middle East the age of cirrhotic patients ranged from 50 -60 years. This finding could be explained by the fact that most of our patients had HCV-related cirrhosis that occurs in adulthood and later life [15]. However, the hypertensive patients were significantly younger than non-hypertensives, this may be explained by that, patients with hypertension had early stage of cirrhosis as 72.9% of patients had Child A and only 1.6% had Child C cirrhosis. The main cause of cirrhosis in our results was HCV which was in accordance with Kamal ,2017 report in Egypt [16] and with EASL-HCV, 2018 who stated the prevalence of HCV infection is the most common cause of liver disease worldwide[17]. However, HCV, as a cause of cirrhosis, was significantly higher in our hypertensive group when compared with non-hypertensives (81.45 versus76.32% respectively) (P <0.001).

Many studies shown a relation between HCV infection and arterial hypertension [18,19,20]. HCV infection is associated with increased arterial stiffness, by two main pathways. First, HCV infection promotes NAFLD, which creates a pro-inflammatory state and associates increased arterial stiffness[18,19]. Secondly, HCV itself is linked independently to arterial stiffness. The current supposition is that inflammation induced by HCV cannot be characterized by general markers (such as C-reactive protein) and requires determination of more specific serologic markers (such as interleukins)[19].

Besides liver damage, the HCV virus has a series of extra-hepatic manifestations, including cryoglobulinemic vasculitis, lymphoma, type 2 diabetes mellitus and also cardiovascular disorders. Due to a proinflammatory state involving primarily tumor necrosis factor alpha, HCV promotes hepatic and systemic insulin resistance and contributes to the development of diabetes mellitus in chronically infected patients. This may lead to increased peripheral resistance and arterial hypertension[20]. Furthermore, HCV infection has been associated with the production of carotid artery plaques and coronary heart disease, as well as an increased risk for death caused by coronary artery disease proportional to the serum values of HCV- RNA. Also, HCV cure reduces the cumulative incidence of death, end-stage renal disease, ischemic stroke and acute coronary syndromes [18,19].

The majority of hypertensive patients in our study were Child-Pugh class A (72.9%) and patients in Child-Pugh class B and C were significantly decreased in hypertensive group than those without hypertension (P <0.001) which could explain that, the biochemical laboratory investigations are better in hypertensive patients when compared with non-hypertensives (P <0.05). These results are in consistent with Henriksen & Moller,2006 and Prabhu, et al.,2009 who found majority of hypertensive patients in their studies were Child A [7,13]. In addition to Gomez, et al., 2014 who found the frequency of arterial hypertension in cirrhotic patients is substantially reduced in advanced cirrhosis. The clinical course of arterial hypertension in patients with liver disease often shows decreased arterial blood pressure with the progression of liver cirrhosis [14].

Conclusions

The prevalence of arterial hypertension in Egyptian cirrhotic patients is 30.7%, lower than that of the general population. Arterial hypertension is inversely associated with the severity of liver disease in terms of Child-Pugh class.

Limitations

There was insufficient diversity of cirrhosis etiology.

Conflicts of interest

There are no conflicts of interest.

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