Original Research Article

Clinical Characteristics and Etiology of Chronic Liver Disease among Egyptian Patients in Nile Delta: A Clinical Study

Abstract

Background: Chronic liver disease (CLD) is an extremely common clinical condition that causes significant morbidity and mortality and was responsible for 1.3 million deaths worldwide. There had been a 46% increase in CLD mortality in the world between 1980 and 2013 and most of this increase has been reported in low-income countries in Asia and Africa including Egypt. These countries are experiencing a demographic and epidemiologic transition in disease burden and Egypt is one of the epicenters of this change. Previously, CLD in Egypt was traditionally attributed to schistosomiasis mainly in the region of the Nile Delta until the mid-1980s.

Aims: To capture the modes of clinical presentation and at which stage CLD patients seek clinical care, as well as the dramatic change in the etiological profile of CLD in this area of the Nile Delta

Methods: 1013 newly diagnosed CLD patients were selected and identified from the Tanta Liver Center (TLC) across the middle of the Nile Delta. After informed or written consent, all consecutive patients (18 years and above) referred to TLC with suspected or overt chronic liver disease were subjected to full history taking, clinical examination searching for stigmata of chronic liver disease, and laboratory studies including urine, blood sugar, liver biochemical tests (bilirubin, ALT, AST& serum albumin), prothrombin, viral markers (HCV Ab & HBS Ag) and AFP. Imaging studies including the abdominal US for all patients and triphasic CT and liver biopsy in selected patients.

Results: About 50% of our CLD patients present at a relatively advanced stage of decompensated cirrhosis (ascites in 39.2%, bleeding in 22.8%, and HCC in 9.3%).

CLD patients of schistosomal etiology presented mainly with manifestations of portal hypertension (splenomegaly, UGI Bleed & thrombocytopenia) that was significantly higher than the other 2 groups.

The vast majority of our CLD patients (83.5%) have viral etiology, while only 11.1% have schistosomal etiology and the remaining 5.4% have non-identified etiology.

Conclusion: based on the results of the present study, it is evident that HCV had replaced schistosomiasis as the predominant cause of CLD in Egypt particularly in the region of the Nile Delta. The late presentation of a good percentage of our CLD patients raises the importance of screening programs for CLD in this endemic area of the Nile Delta.

Key words: Chronic Liver Disease, Clinical Characteristics, Etiology

Introduction

Chronic liver disease (CLD) represents a major health problem worldwide, particularly, in Egypt. Cirrhosis is one of the significant causes of morbidity and mortality and it was the twelfth leading cause of death in the United States in 2013, accounting for 66.000 deaths annually. (1)

While compensated cirrhosis is often asymptomatic and unsuspected in 30-40% of cases, decompensated cirrhosis usually presents with ascites, portal hypertension, variceal bleeding, and hepatic encephalopathy. (2)

CLD results from a wide spectrum of disorders such as viral hepatitis, schistosomiasis, alcohol abuse, and genetic and metabolic disorders that ultimately result in hepatic dysfunction and cirrhosis. (3)

The prevalence of different etiologies and common causes of CLD and cirrhosis show variations in different geographical locations. Little is known about the distribution of CLD etiologies in these different populations. (4)

All published data on the prevalence, incidence, and natural history of CLD, are based on retrospective studies. (5)

Previously, CLD in Egypt was attributed to schistosomiasis which was hyperendemic in Nile Delta. Currently, about 15% of the population are seropositive for HCV. Moreover, a frequent association between schistosomiasis and HCV infection has been reported in Egypt (6). Thus, it is important to re-evaluate the etiology and clinical features of CLD in this country, particularly in this endemic area of the Nile Delta.

Therefore, this prospective study was conducted to explore the underlying etiologies, mode of clinical presentation, the scope of morbidity, and the changing pattern of different etiologies of CLD among Egyptian patients in this area of the Nile Delta.

Patients and Methods

In the period from February 2012 to February 2014, all consecutive patients (18 years and above) referred to Tanta liver Center (TLC) with suspected or overt CLD were enrolled in the study after informed or written consent.

All the study groups (1013) were subjected to full history, clinical examination searching for stigmata of CLD, laboratory studies including urine analysis, blood sugar, liver biochemical tests (serum bilirubin, ALT, AST & serum albumin), prothrombin, viral markers (HCVAb and HBSAg), urea and serum creatinine and alfa fetoprotein (AFP). Imaging studies include abdominal ultrasound (US) scan for all patients and triphasic CT and liver biopsy in selected patients.

Exclusion criteria:

- Patient less than 18 years old.
- The patient refused to give consent.
- Comatose patients.

Results

A total of 1013 CLD patients attending TLC from February 2012 to February 2014 were the subject of the present analysis.

Table (1): represents the different etiologies of the studied chronic liver disease patients n =1013.

CLD etiology	Frequencies	
	No.	**%**
Viral hepatitis	**846**	**83.5**
▪ HCV	834	80.3
▪ HBV	32	3.2
▪ HCV + HBV	4	0.4
Schistosomal etiology:	**112**	**11.1**
Pure schistosomal	(96)	(9.5)
Schistosomal + viral infection	(16)	(1.6**)**
▪ Schisto + HCV	15	1.5
▪ Schisto + HBV	1	0.1
Other etiologies (Non identified)	**55**	**5.4**
Total	**1013**	**100**

The vast majority of the analyzed 1013 CLD patients (846= 83.5%) have viral etiology, while only 112 (11.1%) have schistosomal etiology and the remaining 55 (5.4%) have non –identified

etiology. On further subanalysis 814(96.2%) out of 846 CLD patients of viral etiology were HCV-related, 32(3.8%) were HBV-related and 4(0.5%) were due to mixed infection. Therefore, currently, HCV had replaced schistosomiasis as the predominant etiology of CLD in Egypt, particularly in this area of the Nile Delta.

Importantly, the underlying etiology of CLD remains unknown in 5.4% of our study group. Since 90% of these patients (49/55) have also type 2 diabetes mellitus (DM), thus they may represent NAFLD/NASH which will be the most important CLD in the near future (table, 8).

Table (2): represents the demographic characteristics of the studied CLD patients (n=1013).

Demographic characteristics / Etiology		Viral etiology (n=846)	Schistosomal etiology (n=112)	Other etiologies (n=55)	Total (n=1013)	Significance test
Age	**Range**	19 – 84	34 – 62	21 – 83	19 – 84	F= **1.033**
	Mean ± SD	52.10 ± 11.26	48.0 ± 8.54	50.85 ± 12.53	51.85 ± 11.39	P= **0.356**
Gender	**Male (%)**	674 (79.7%)	98 (87.5%)	45 (81.8%)	810 (80%)	**X2: 3.938**
	Female (%)	172 (20.3%)	14 (12.5%)	10 (18.2%)	203 (20%)	P= **0.140**
Residence	**Rural (%)**	512 (60.5%)	84 (75%)	40 (72.7%)	630 (62.2%)	**X2: 11.341**
	Urban (%)	334 (39.5%)	28 (25%)	15 (27.3%)	383 (37.8%)	P= **0.003***

** Fisher exact test

This table reveals that CLD in this area of Nile Delta predominantly affects males, from rural areas of relatively younger age (50 years) irrespective of the etiology.

Table (3,A): Represents the clinical presentation of the studied chronic liver disease patients according to etiology (n=1013).

Etiology / Clinical presentation	Viral Hepatitis (n=846)		Schistosomal etiology(n=112)		Other etiology (n=55)		Total (n=1013)		P-value
	N0	%	No.	%	No	%	No.	%	
Splenomegaly	176	20.8	62	55.4	8	14.5	246	24.3	0.001*
UGIB	131	15.5	70	62.5	30	54.5	231	22.8	0.001*
Ascites	143	17	75	67	9	16	227	22.4	0.001*
Routine check-up	86	10.2	23	20.5	14	25.5	123	12.1	0.256
Edema of the lower limb	52	6.1	17	15.2	3	5.5	72	7.1	0.731
Jaundice	23	2.7	12	10.7	10	18.2	45	4.4	0.906
Hepatic encephalopathy	29	3.4	8	7.1	0	0	37	3.7	0.403
Fever	18	2.1	3	2.7	1	1.8	22	2.2	0.056
Coagulopathy	3	0.4	2	1.8	0	0	5	0.5	0.808
Itching	1	0.1	1	0.9	0	0	2	0.2	0.783
Fatigue	1	0.1	1	0.9	0	0	2	0.2	0.821
Limpping	1	0.1	0	0	0	0	1	0.1	0.837

Table (3,B): Clinical presentation of the studied group irrespective to the etiology (n=1013).

Clinical presentation	No.	%
Splenomegaly	246	24.3
UGIB	231	22.8
Ascites	227	22.4
Routine check-up	123	12.1
Edema of the lower limb	72	7.1
Jaundice	45	4.4
Hepatic encephalopathy	37	3.7
Fever	22	2.2
Coagulopathy	5	0.5
Itching	2	0.2
Fatigue	2	0.2
Limping	1	0.1

Figure (1): Frequencies of different clinical presentations among all patients in the studied groups.

Figure (2): Frequencies of different clinical presentations among patients with viral etiology.

Figure (3): Frequencies of different clinical presentations among patients with schistosomal etiology(n= 112).

About 50% of our CLD patients present at a relatively advanced stage of decompensated cirrhosis (ascites in 39.2% , GI bleeding in 22.8% and HCC in 9.3%).On further subanalysis, CLD patients of schistosomal etiology present mainly with manifestations of portal hypertension (splenomegaly& UGI Bleeding) that were significantly higher in these patients than in the other 2 groups (p=0.001).

Table (4): Represents ultrasonographic findings in the studied CLD patients (n=1013).

Ultrasonographic findings / Etiology		Viral Hepatitis (n=846)		Schistosomal etiology (n=112)		Other etiologies (n=55)		Total (n=1013)		P-value
		No.	%	No.	%	No.	%	No.	%	
Liver	**Normal**	129	15.2	35	31.2	9	15.9	158	15.6	**0.001***
• **Size**	**Enlarged**	414	48.9	56	50.0	36	66.2	522	51.5	
	Shrunken	303	35.8	21	18.8	10	17.9	333	32.9	
• **Echo pattern**	**Fibrosis**	16	1.9	96	85.7	0	0	112	11.1	0.001*
	Cirrhotic pattern	398	47.1	2	1.8	15	27.3	415	40.9	
	Bright echo	432	51	14	12.5	40	20.5	486	48	
• **Hepatic focal lesion**		87	10.3	4	3.6	9	16.4	100	9.9	0.021*
• **Dilated portal vein**		215	25.4	56	50	10	17.9	250	24.7	0.009*
Spleen	**Normal**	335	39.6	10	9	34	62	379	37.4	0.001*
	Enlarged	406	48	74	66	16	29	496	49	
	Splenectomy	105	12.4	28	25	5	9	138	13.6	
Ascites	**No**	569	67.3	14	12.5	33	60	616	61	0.001*
	Mild	122	14.4	18	16.1	14	25.5	154	15.2	
	Moderate	100	11.8	70	62.5	16	29.1	186	18.2	
	Massive	46	5.4	10	8.9	1	1.8	57	5.6	
Others	**Gall stones**	79	9.3	14	12.5	1	2	84	8.3	0.009*
	Hamangioma	2	0.2	0	0	0	0	2	0.2	0.821

Periportal fibrosis (PPF) was detected in 85.7% of CLD patients with schistosomal etiology and once again, manifestations of portal hypertension (splenomegaly &dilated portal vein were significantly higher among these patients than in the other 2 groups.

Additionally, US examination of our CLD patients revealed that 100 patients (9.9%) of them presents with HFL which was proved to be HCC by a triphasic liver study in 94 patients (9.3%) cases.

Table (5): Different etiologies of our HCC patients (n=94) .

HCC	N	%
Viral etiology	**81**	**86.2**
▪ HCV	(78)	(96.3)
▪ HBV	(3)	(3.7)
Non-viral etiology	**13**	**13.8**

Table (6): Demographic characteristics of our HCC patients (n=94).

		Hepatocellular carcinoma			P-value
		Viral	Non-viral	Total	
Age	**Range**	22 – 76	23 – 78	22 – 78	**0.337**
	Mean ± SD	52.04 ± 10.64	47.89 ± 18.20	51.44 ± 11.90	
Sex	**Male (%)**	71 (75.5%)	8 (61.5%)	79 (84%)	**0.602**
	Female (%)	13 (13.8%)	2 (15.4%)	15 (16%)	
Residence	**Rural (%)**	52 (55.3%)	6 (46.2%)	58 (61%)	**0.645**
	Urban (%)	32 (34%)	4 (30.7%)	36 (38.3%)	

Table (7): Clinical presentation of our HCC cases (n=94).

Clinical presentation of HCC	N	%
UGIB	40	43
Rapidly developing ascites	24	26
Accidentally discovered	23	24
Prolonged fever	4	4
Metastases	2	2
Itching	1	1

The last 3 tables revealed that our HCC patients are predominantly males (84%), from rural areas (61%), and of relatively younger age (51.44-+11.90). 86.2% of our HCC cases have viral etiology and 13.8% of them have non- viral etiology. HCV is the leading viral cause of our HCC cases (96.3%) while HBV plays a minor role (3.7%).

Table (8): Incidence of type 2 DM among the studied CLD patients (n=1013).

	Viral etiology N= 846		Schistosomal Etiology N=112		Unknown Etiology N=55		Total	
	No	%	No	%	No	%	No	%
2h plasma glucose > 200	171	(20.2%)	11	(9.8%)	49	(89%)	231	(22.8%)

Table (9): Liver biochemical tests in the studied groups n=(1013)

Liver function tests		Cut off point	Normal		Impaired	
			No	%	No	%
Bilirubin		1.2 mg/dl	546	53.9	467	**46.1**
ALT		40 U/L	603	59.5	410	40.5
AST		38 U/L	603	59.5	410	40.5
Albumin		4.5 g/dl	381	37.6	632	62.2
Prothrombine	time	12.5 sec	624	61.4	389	38.4
	INR	1.2	624	61.4	389	38.4

Table (10): Haematological findings in the studied chronic liver disease patients according to etiology (n=1013).

	Schistosomal etiology (Mean ± SD)	Viral Hepatitis (Mean ± SD)	Other etiologies (Mean ± SD)	Total (Mean ± SD)	p. value
Hb	13.21 ± 2.25	11.92 ± 1.89	10.18 ± 1.27	11.56 ± 1.31	0.358
WCC	4683.57 ± 1621.46	5669.71 ± 1850.36	5871.65 ± 516.28	5683.81 ± 3653.44	0.498
PLT	113957.14 ± 2714.57	122691.10 ± 8476.48	157420.63 ± 1839.04	127773.1 ± 63438.07	0.001*

Tables (8,9,10) represent laboratory findings in our studied CLD patients. The synthetic functions of the liver (serum albumin &prothrombin) were impaired in 62.2% and 38.4% of our CLD patients respectively. Once again denoting that about 50% of our CLD patients present with an advanced stage of cirrhosis.

The main hematologic abnormality detected in our study group was decreased, platelets count that was significantly lower in our CLD of schistosomal etiology than in the other 2 groups.

The incidence of type 2 DM among the studied CLD patients, out of the studied 1013 CLD patients 231(22.8%) have DM type 2. Out of the studied 231 CLD patients, 171 (20.2%) were due to viral etiology while 11(9.8%) were due to schistosomal etiology and 49(89%) were due to unknown or other etiology.

Discussion

Previously, CLD in Egypt was traditionally attributed to schistosomiasis, with an estimated 10% of 200 million persons infected with schistosomiasis being Egyptians in 1980, mainly in the region of the Nile Delta.

The objectives of the present analysis were to capture the modes of clinical presentation and at which stage CLD patients seek clinical care, as well as the dramatic change in the etiological profile of CLD in this area of the Nile Delta. This analysis was based on 1013 newly diagnosed CLD patients over 2 years (2012 to 2014) from a tertiary care center (TLC) across the middle of the Nile Delta.

Analysis of the demographic data of our study group revealed that CLD predominantly affects males, from rural areas, of relatively younger age (~50 years) during their productive period, a finding that was supported by other studies (7-8).

The increased prevalence of CLD among males in rural areas of the Nile Delta might be related to their unique lifestyle subjecting them more to both schistosomal and viral liver disease.

Regarding the mode of clinical presentation of the analyzed 1013 CLD patients in this study, our results revealed that a large segment of our CLD patients (~ 50%) present at a relatively advanced stage of decompensated cirrhosis (ascites in 22.4% and UGIB in 22.8%), a finding that highlights the importance of screening and building awareness about liver disease in this endemic area of Nile Delta.

In this regard, Egypt conducted a successful HCV screening program that covered 50 million residents and treated more than 4 million making Egypt probably the first in the world to eliminate HCV within it,s border. (9)

The late presentation of a large segment of our CLD patients was also supported by results of US examination that also revealed that 50%of them present with late complications of cirrhosis (ascites in 39.2% and HCC in 9.3%).

Moreover, our laboratory studies revealed that the synthetic functions of the liver (S.albumin and prothrombin) were also impaired in 62.2% and 38.4% of our CLD patients at presentation.

Importantly, CLD patients of schistosomal etiology presented mainly with manifestations of portal hypertension (splenomegaly and UGI Bleed) that was significantly more frequent than in the other 2 groups. Also, platelet count was significantly lower in this group of patients which could be attributed to hypersplenism which is another manifestation of portal hypertension.

Previously, CLD in Egypt was traditionally attributed to schistosomiasis with schistosoma mansoni being the main cause of liver disease mainly in the region of the Nile Delta until the mid-1980s. (10)

This could be attributed to contact with canal water during farming-related water activities in Nile Delta. (11)

Strikingly, our results highlighted the dramatic change in the etiological profile of CLD in this area of the Nile Delta. Among the analyzed 1013 CLD patients in our center, the vast majority of them (846=83.5%) have viral etiology, while only 112(11.1%) of them have schistosomal etiology and the remaining 55(5.4%) have non-identified etiology.

On further subanalysis, 814(96.2%) out of the 846 CLD patients of viral etiology are HCV-related, 32(3.8%) are HBV-related and the remaining 4(0.5%) are due to mixed infection.

Therefore, currently it is evident that HCV had replaced schistosomisis as the predominant cause of CLD in Egypt since the diagnostic serology for HCV become available in 1990s, our results are supported by the results of 4 other studies conducted in Egypt[11,12,13,14].

This was previously attributed solely to parenteral antischistosomal therapy between the 1950s and1980s. However, our results revealed that many other risk factors of HCV infection contribute to the increased prevalence of HCV among our CLD patients in the Nile Delta. 48.1% of them underwent dental procedures, 28.1% underwent surgical procedures, while a history of parenteral antischistosomal therapy was obtained only in 13% (table 3).

Additionally, our results revealed that HBV plays a minor role in the etiopathogenesis of CLD in this endemic area of Nile Delta being detected in only 3.2% of the analyzed 1013 CLD patients.

By contrast, another Egyptian study conducted at National Liver Institute (NLI) reported a much higher incidence of HBS Ag seropositivity (16.4%) among outpatients attending NLI.(15)

Importantly, the underlying etiology of CLD remains unknown in 5.4% of our study group. Since 90% of these CLD patients of unknown etiology (49/55) have also type 2 DM, this support our assumption that they may represent NAFLD/NASH which will be the most important CLD in the near future.

Moreover, we may not be able to recognize other uncommon causes of CLD in this group of patients that may also need other confirmatory tests including histology.

Surprisingly, 100 (9.9%) of the analyzed 1013 CLD have HFL at the presentation that was proved to be HCC by a triphasic liver study in 94(9.3%).81 (86.2%) of them have viral etiology and the remaining13 (14.8%) were due to non-viral etiology. Therefore, HCV is by far the

dominant viral cause of HCC among our CLD in the Nile Delta(96.3%), while HBV is still a minor risk factor(3.7%)

Finally, based on the result of the present study, it is evident that HCV had replaced schistosomiasis as the predominant cause of CLD in Egypt particularly in the region of the Nile Delta. The late presentation of a good percentage of our CLD raises the importance of screening programs for CLD in this endemic area of the Nile Delta.

Conclusion: Based on the result of the present study, it is evident that HCV had replaced schistosomiasis as the predominant cause of CLD in Egypt particularly in the region of the Nile Delta. The late presentation of a good percentage of our CLD raises the importance of a screening program for CLD in this endemic area of the Nile Delta.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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