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Study of insulin like growth factor1 as a marker of severity of liver cirrhosis in upper Egypt patients

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Abstract
Purpose: To assess the severity of the liver cirrhosis by measuring the level of insulin like growth factor 1 in the serum of the upper Egypt patients and controls.
Design: Cross section design.
Methods: One hundred patients with liver cirrhosis selected from out patients clinic of internal medicine department, Al-Azhar Assuit University hospital, twenty healthy individuals were being selected as a control group.
Results: Reported 24 months Study Of Insulin like Growth Factor1 as a marker of severity of liver cirrhosis in upper Egypt patients there is IGF 1 was significantly lower in child class C than child class B; also IGF 1 was significantly lower in child class B than class A.
Conclusion: IGF-1 can be used as an index for evaluating the severity of cirrhosis.

Keywords: insulin like growth factor1, child A, chid B, chid C and liver cirrhosis

Introduction

Recent advances in the understanding of the natural history and pathophysiology of cirrhosis, and in treatment of its complications, have resulted in improved management, quality of life, and life expectancy of patients [1].

Insulin-like growth factor 1 (IGF-1) is a soluble protein produced by the liver that binds to a trans membrane receptor called IGF-1 receptor (IGF-1R). IGF-1R is expressed in the entire body but mainly in the cartilage, bone, liver, kidneys, lung, and central nervous system [2] and the liver is the main source of circulating insulin-like growth factor I, accounting for ~75% of circulating IGF-I levels secondary to the GH stimulation on hepatocytes [3]. As a reflection of decreased hepatic synthetic function, lower IGF-I serum levels have been demonstrated in patients with cirrhosis when compared to healthy controls. These markers also seem to be related to the degree of hepatic dysfunction, as decreased levels were reported in more advanced stages of cirrhosis. Therefore, these tests appear to represent promising tools for evaluating patients with liver cirrhosis. [4].

New markers of hepatic synthetic function would be especially useful in evaluating patients admitted to the hospital due to complications of cirrhosis, who have high mortality. In this regard, liver biopsy remains the most sensitive and specific means of providing important diagnostic and prognostic information. Nonetheless, given that liver biopsy is an invasive procedure, with occasional complications and poor patient acceptance [5].

IGF-1 can be used as an index for evaluating the severity of cirrhosis; also it can be used for determining the severity of the disease [6].

Subjects and Methods

This study was conducted on one hundred patients with liver cirrhosis. The patients were selected from out patient's clinic o f Internal Medicine Department, Al Azhar Assuit University Hospital, from June 2016 to April 2018.

Twenty healthy individuals were being selected as a control group.

Exclusion Criteria

1. Hepatorenal syndrome due to the probability of octreotide treatment that inhibite IGF 1.
2. Diabetes mellitus associated with increase in IGF 1
3. Gastrointestinal bleeding due to octreotide treatment that inhibit IGF 1.
4. Chronic renal disease due to IGF 1increase in chronic renal disease.
5. Hepatocellular carcinoma due to IGF 1 secreted as a part of Para neoplastic syndrome of HCC.
6. Body mass index > 30 due to hyperinsulinemia.

Methods

All patients and control were subjected to the following:

1. Full history taking.
2. Complete clinical examinations.
3. Laboratory tests:

- Serum ALT
- Serum AST
- Serum Bilirubin total and direct
- Serum Prothrombin time and activity and INR

- IGF 1 serum level
- Blood Urea and creatinine
- CBC
- Serum Albumin
- Fasting blood glucose level and postprandial

4. Abdominal ultrasound
5. Upper endoscopy
6. Child Pugh score
7. MELD score
8. AST / Platelets ratio.

Statistical Analysis

Analysis of data was performed with a personal computer usin g Graph Pad Prism version 5, as follows:

1. Description of quantitative variables using mean, standard deviation (SD) and range.
2. Unpaired t-test was used to determined significant differences of IGF 1in control and patient groups.
3. ANOVA test was used to determined significant differenc es within the patient child class and MELD subgroup.
4. Pearson correlation coefficient was used to determine corr elation between IGF 1 and all patient parameters the level of significance was ($p<0.05$).

Results

This case study included one hindered Patients with liver cirrhosis. Their ages ranged from 40to55years (mean of 50.07± 3.01 SD).They were 69 males (69%) and 31 females (31%)

In addition, twenty healthy age and sex matched volunteers served as controls were included in the study. Their ages ranged from 40 to 56 years (meanof51.12±4.71SD). They were 13 males (65%) and 7 females (35%) as shown in Table (1).

Table 1: Comparison between patients and controls regarding their demographic data.

		Groups			
		Patient		control	
Age	Range	40-55		40-56	
	Mean ±SD	50.07± 3.01		51.12±4.71	
BMI	Range	20-30		20-27	
	Mean ±SD	23.88±2.91		22.95±2.04	
		N	%	N	%
Sex	Male	69	69	13	65
	Female	31	31	7	35

Table 2: Comparison between patient and control regarding liver functions.

Liver functions	Groups		t test	P value
	Patient	Control		
AST(mg/dl)	39.23±8.69	23.25±2.63	3.749	0.001^{HS}
ALT(mg/dl)	27.92±6.43	17.05±5.08	2.922	0.001^{S}
BILT(mg/dl)	2.87±1.46	0.91±0.03	5.97	0.001^{HS}
BILD(mg/dl)	1.28±0.73	0.51±0.05	4.754	0.001^{HS}
Albumin(g/l)	3.05±0.54	4.10±0.57	7.850	0.001^{HS}
PA (%)	62.39±6.85	99.40±5.55	9.690	0.001^{HS}

S= significant at p value ≤ 0.05, HS= highly significant at p value ≤ 0.001
AST: Aspartate Aminotransferase ALT: Alanine Aminotransferase BILT: total bilirubin BIL D: direct bilirn
PA: prothrombine activity.

It revealed highly statistically significant difference between patient and control as regard AST, BILT, BILD, albumin and PA ($p \leq 0.001$). Also statistically significant difference between patient and control as regard ALT in table 2.

Table 3: Comparison between patients and controls as regard IGFI.

	Groups		t test	P value
	Patient	control		
IGFI (ng/ml)	73.57±41.13	257.55±34.49	18.712	0.001^{HS}

It revealed highly statistically significant difference between patient and control as regard IGFI ($p \leq 0.001$).

Table 4: Comparison among patients child class A, B and C as regard liver functions.

Liver functions	Child			F ratio	P value
	A	B	C		
AST(mg/dl)	31.06±6.47	62.50±9.95	24.50±3.34	325.18	0.001^{HS}
ALT(mg/dl)	17.81±2.79	48.72±7.39	15.69±2.51	509.55	0.001^{HS}
BILT(mg/dl)	0.98±0.12	1.82±0.40	4.29±0.51	515.70	0.001^{HS}
BILD(mg/dl)	0.45±0.06	0.84±0.05	1.90±0.59	105.401	0.001^{HS}
Albumin(g/l)	3.89±0.35	3.04±0.39	2.78±0.37	53.06	0.001^{HS}
PA %	93.75±3.94	66.94±4.45	48.52±5.58	522.07	0.001^{HS}

HS= highly significant at p value ≤ 0.001, AST: Aspartate Aminotransferase ALT: Alanine Aminotransferase BIL T: total bilirubin BIL D: direct bilirubin PA: prothrombine activity.

It revealed no statistically significant difference between patient's child class A, B and C as regard AST, ALT, BILT, BILD, albumin and PA (p≤0.001).

Table 5: Comparison among patients class A, B and C as regard IGFI.

	Child			F ratio	P value
	A	B	C		
IGFI (ng/ml)	157.81±38.17	68.83±6.02	49.04±4.68	286.217	0.001[HS]

It revealed highly statistically significant difference between patient's child class A, B and C as regard IGF1 (p≤ 0.001).

Table 6: Comparison among MELD score as regard IGFI.

	MELD score			F ratio	P value
	<9	10----19	20----29		
IGFI (ng/ml)	153.21±42.17	65.13±11.12	46.04±7.88	207.54	0.001 [HS]

It revealed highly statistically significant difference between mild score as regard IGFI (p≤ 0.001).

Table 7: Comparison among AST/Plat ratio as regard IGFI.

	AST/Platratio			F ratio	P value
	<0.5	0.5-----1.5	>1.5		
IGFI (ng/ml)	156.41±39.17	69.33±14.12	46.39±7.21	205.65	0.001 [HS]

It revealed highly statistically significant difference between AST/Plat ratioas regard IGFI (p≤ 0.001).

Discussion

In our study, we estimated the level of IGF1 in normal subject s (control group) (N=20) and in subjects with liver cirrhosis (patient group) (N=100**).** Most of the patients were in the fourth and fifth decades. We found that patients with cirrhosis had decreased levels of IGF1 compared healthy controls. The mean values for IGFI in 100 cirrhotic patients is 73. 10± 42.32 ng/ml which were significantly lower than those in 20 healthy subject. Several previous studies reported similar results [7].

On the same way found that the Mean IGF level was 92.95± 91.51. IGF1 level in 14 patients (14%) was \ with in the normal range while 86 patients (86%) had abnormal IGF-1 values [8].

In our study we found inverse correlation between IGF-1and the age. In other study found a significant inverse relationship with the increase in age of patients with cirrhosis, adecrease in IGF-1 level was observed [9].

Our study demonstrates a direct correlation between IGF1 and albumin and inverse correlation between IGF 1and INR and creatinine. Similar results were observed in a Turkish study that included 42patients with cirrhosis, in which IGFI levels Were positively correlated with albumin and negatively correlated with serum creatinine [10].

In another study investigating one seventy four patient admission due to complication of liver cirrhosis demonstrating IGF-I level was positively correlated with albumin and negatively correlated with Child-Pugh, MELD, creatinine, bilirubin and INR. This result is agreement with our result [11].

Conclusion

IGF-1 can be used as an index for evaluating the severity of cirrhosis. IGF 1 is correlated with variables related to liver dysfunctions like serum bilirubin, albumin and PT%. Moreover IGF1 is correlated with child Pugh score, MELD score.

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