

AIM OF THE WORK

The aim of this work is to study serum Glycated Albumin to whole blood HbA1c ratio in patients with liver cirrhosis in relation to severity of cirrhosis and risk of bleeding from esophageal varices.

SUBJECTS

To fulfill the aim of the study the following groups were compared:

- Group I:** 20 patients with liver cirrhosis and EV which have previously bled.
- Group II:** 20 patients with liver cirrhosis and EV which have not yet bled.
- Group III:** 20 patients with liver cirrhosis without EV.
- Group IV:** 20 normal healthy control subjects.

Inclusion criteria

Liver cirrhosis: diagnosis was based on clinical examination, biochemical investigation and ultrasonographic criteria.

Exclusion criteria

Any patient with malignancy, diabetes mellitus, endocrinal diseases, cardiovascular disease, pulmonary diseases, chronic kidney disease, collagenic diseases, on immunosuppressive therapy, also patient with EV band ligation, or sclerotherapy were excluded from this study. None of them had had primary prophylactic treatment for variceal bleeding or any surgical treatment for portal hypertension.

This is to avoid any hemodynamic changes and to avoid any other factor will affect risk of bleeding in patients with esophageal varices.

All selected patients will provide written informed consent before enrollment in the study.

METHODS

I. History taking

Thorough medical history will be taken from patients including history of hematemesis and/or melena and history of previous upper GIT endoscopies.

II. Physical examination

To detect signs of hepatic dysfunction including spider angiomas, palmer erythema, jaundice, flappy tremors, hepatic encephalopathy, ascites, and splenomegaly.

III. The patient will be scored according to Child-Pugh classification.⁽³³⁾

IV. Electrocardiogram and chest X- ray: to exclude chest or cardiac disorders.

V. **Laboratory investigations:** Laboratory investigations: including

1. Complete urine analysis to exclude protienurea.

2. Fasting whole venous blood samples divided as follows:

a) Whole EDTA blood for: Complete blood picture^(184,185)

b) Citrated plasma for measurement of prothrombin time, activity, and calculation of the international normalized ratio (INR).^(184,185)

c) Serum sample for determination of concentrations of glucose, urea, creatinine, total proteins, albumin, total and direct fractions of bilirubin concentrations, as well as activities of alanine and aspartate aminotransferases, alkaline phosphatase and gamma glutemyl transpeptidase.^(184,185)

d) Serum hepatitis-C virus antibodies detection using enzyme immunoassay. Screening for serum hepatitis-B virus surface antigen (HBsAg) using enzyme immunoassay.^(184,185)

e) Detection of autoimmune markers (antinuclear antibody (ANA), anti-smooth muscle antibody (SMA), liver/kidney microsomal antibody and anti-mitochondrial antibody (AMA) to diagnose autoimmune cirrhosis^(184,185)

VI. Special investigations

1- Serum HbA_{1c} measurement.^(184,185)

2- Serum GA determination: using an enzyme immunoassay, and calculation of the GA to HbA_{1c} ratio.^(184,185)

Sampling

Following an eight to ten hours fasting period, five milliliters of whole venous blood sample were obtained from every individual enrolled in the study. Portion of the blood was

collected in tripotassium EDTA coated vacutainer tubes for the determination of whole blood glycated hemoglobin, and complete blood count. Another portion of the blood was collected on sodium citrate for the determination of prothrombin time and calculation of the international normalized ratio (INR). The rest of the blood was collected in serum vacutainer tubes, left to clot at 37°C for 30 minutes, centrifuged at 3000 rpm for 15 minutes. The obtained serum sample was divided into 2 aliquots; one aliquot was used for the determination of serum levels and activities of some biochemical parameters, and the other aliquot was stored at -20°C till the time of assay of glycated albumin.

Glycated hemoglobin: ⁽¹⁸⁶⁾

It was determined using a column chromatographic separation technique (Biosystems SA, Barcelona Spain) according to the manufacturer's instructions. Lysis of whole EDTA blood was done to eliminate the labile fraction of hemoglobin. Hemoglobin fractions were retained by cationic exchange resin, where the hemoglobin-A_{1c} (HbA_{1c}) fraction was specifically eluted after washing away the hemoglobin A_{1a} and A_{1b} fractions, and were quantified by direct photometric reading at 405 nm. The total hemoglobin concentration was measured in the same lysate followed by direct photometric reading at 405nm. When determining the HbA_{1c} relative concentration in the sample, care was taken in correcting the volume of elution buffer used in HbA_{1c} fraction elution (4 mL) as well as the volume of elution buffer used in determination of total hemoglobin concentration (12 mL) as follows:

$$\% \text{HbA}_{1c} = \frac{\text{AHbA}_{1c} \times \text{VHbA}_{1c} (4 \text{ mL})}{\text{AHb}_{\text{total}} \times \text{VHb}_{\text{total}} (12 \text{ mL})} \times 100$$

Glycated albumin: ⁽¹⁸⁷⁾

Glycated albumin (GA) was determined using a competitive 2 site enzyme immunoassay (Cusabio Inc, Wuhan, Hubei Province 430206, P.R.China – Cat No. CSB-E09599h) according to the manufacturer's instructions.

Principle

This GA immunoassay used the competitive inhibition technique. The microtiter plate provided in this kit was pre-coated with GA. The competitive inhibition reaction was launched between pre-coated GA and GA in samples (or standards) for the same binding sites of the horseradish peroxidase (HRP) conjugated antibody. The tetramethylbenzidine substrate solution added to the wells generated a blue color that was inversely proportional to the amount of GA in the samples (or standards). Termination of the enzymatic reaction using the stop solution turned the blue color into a yellow one that was measured.

Reagents

1. **Assay plate (12 x 8 coated Microwells):** coated with GA.
2. **Standard (Freeze dried):** the standard vial was centrifuged at 6000-10000 rpm for 30 seconds prior to use. Reconstitution of the standard with 1.0 mL of the sample diluent produced a concentration of 1200 pmol/mL. The reconstituted standard was allowed to stand for 15 minutes with gentle agitation prior to making dilutions. Serial dilutions were carried out in a set of Wassermann tubes using the supplied sample diluent as follows:

Methods

STD (pmol/mL)	1200	600	300	150	75	37.5	18.75
STD (volume in μ L)	1.0	150	150	150	150	150	150
Diluent (volume in μ L)	-	150	150	150	150	150	150

The sample diluent served as the zero standard.

- HRP-conjugate (100x concentrate):** the conjugate vial was centrifuged at 6000-10000 rpm for 30 seconds prior to use. The supplied HRP-conjugate diluent was used in the 1:100 dilution of the HRP conjugate.
- Wash Buffer (20 mL) (25x concentrate):** It was diluted in 500 mL of distilled water prior to use.
- Tetramethyl benzedine (TMB) Substrate:** ready to use.
- Stop Solution:** ready to use.

Sample preparation

The serum samples were left at room temperature for 20 minutes till complete thawing. The samples were diluted in a set of Wassermann tubes 1000 times using the supplied sample diluent as follows; the first dilution was carried out using 8 μ L of the sample mixed with 152 μ L of the diluent. From the first dilution, 6 μ L were taken and mixed with 294 μ L of the sample diluent.

Procedure

- 50 μ L of the stock standard solution, serially diluted standards, sample diluent (zero standard) and diluted samples were dispensed in their designated wells. A blank well was left empty.
- 50 μ L of the diluted HRP conjugate (1x) were dispensed into each well except the blank well.
- Incubation was done in an incubator set at 37°C for 30 minutes.
- The plate contents were automatically aspirated and washed using 200 μ L / well of the diluted wash solution. A 2 minute soak period was advised by the manufacturer. Washing step was carried out using the Universal Elx50 microplate washer ((BioTek Instruments Inc, Canada). Blot drying of the plate was done to remove any traces of wash buffer.
- 90 μ L of substrate solution were dispensed into each well, followed by 20 minutes incubation at 37°C protected from light.
- 50 μ L of the stop solution were dispensed into each well, followed by reading the absorbance of the resulting yellow color in each well using the Universal ELx800 microplate reader (BioTek Instruments Inc, Canada) set at 450 nm (primary wavelength) and 540 nm (secondary wavelength used to correct for optical imperfections in the plate).

Calculation of GA concentration

The GA concentrations in the samples were deduced from a standard curve utilizing linear XY axis scale generated by the software of the microplate reader as shown in figure 10. The obtained GA concentrations were multiplied by the 1000 dilution factor used in sample dilution.

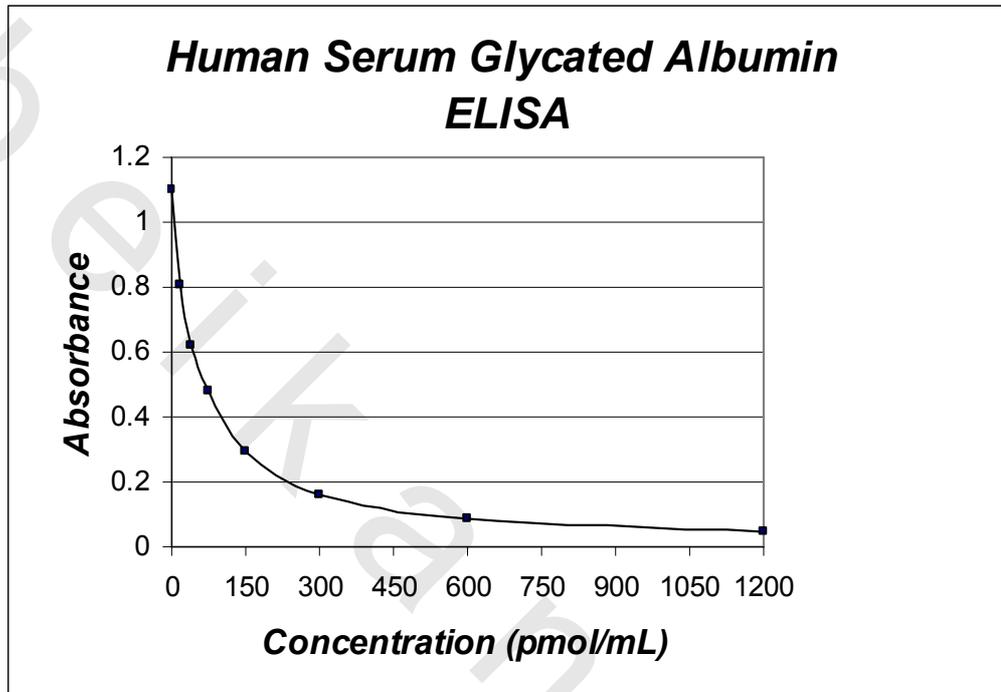


Figure (7): The GA concentrations curve by ELISA

Glycated albumin to glycated hemoglobin (HBA_{1c}) ratio

The serum total albumin expressed in gm/dL was converted to $\mu\text{mol/L}$ using the endmemo online calculator, with the following website link: (<http://www.endmemo.com/medical/unitconvert/Albumin.php>).

Next the total serum albumin expressed in $\mu\text{mol/L}$ was further converted to pmol/mL. GA concentration in pmol/mL was divided by serum total albumin expressed in pmol/mL and the final product was multiplied by 100 to obtain percent GA concentration.

The GA: HBA_{1c} ratio was obtained by dividing the percent GA value by the percent HBA_{1c} value.

VII Abdominal ultrasound

To evaluate the following liver parameters:

1. Presence of coarse parenchymal structure and irregular liver border indicating cirrhosis.
2. Longitudinal length of the right lobe of the liver.

3. Presence or absence of ascites and its grade.
4. Longitudinal diameter of the spleen.
5. Diameter of portal vein.

VIII. Upper gastrointestinal endoscopy examination was done for the patients groups using a video-endoscopy Olympus XQ 240 for the detection of:

1. Esophageal varices which were graded according to Beppu (Japanese) grading system as follow: ⁽¹⁰⁹⁾
 - F0 no varices
 - F1 (small) Small straight varices
 - F2 (medium) Enlarged tortuous varices occupying less than one third of the lumen
 - F3 (large) Large coil-shaped varices occupying more than one third of the lumen
2. Detection for presence or absence of gastric varices.
3. Detection and grading of portal hypertensive gastropathy according to NIEC ⁽¹⁰⁴⁾
 - a) Mild: mucosal mosaic pattern
 - b) Severe: mosaic mucosal pattern and any of the following red marks (red point lesions) or cherry red spots.
4. All patients with EV were scored according to the North Italian endoscopic club (NIEC) classification, ⁽¹⁰⁴⁾ estimating from it the NIEC index, which is calculated from size of varices, presence and extent of risk signs in varices, and Child-Pugh class as shown in table (6).

IX. Calculation of different noninvasive ratios to assess EV

1- Platelet count spleen parameter ratio:

This was calculated this ratio is calculated by dividing the platelet number/mm³ by the maximum spleen bipolar diameter in mm as estimated by abdominal ultrasound.

2. Right Lobe Liver Albumin Ratio:

This ratio is calculated by dividing the right liver lobe diameter (as assessed by abdominal ultrasound and measured in millimeters) by the serum albumin concentration (g/L).

3. Aspartate amino transferase to platelet ratio index (APRI):

$$\text{APRI} = \frac{\text{AST (times above upper limit of normal)}}{\text{platelet count}} \times 100$$

Statistical analysis of the data⁽¹⁸⁸⁾

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0.⁽¹⁸⁹⁾ Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells had expected count less than 5, correction for chi-square was conducted using Fisher's Exact test or Monte Carlo correction. The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agstino test, also Histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests were applied. If the data were abnormally distributed, non-parametric tests were used. For normally distributed data, comparison between two independent population was done using independent t-test. For abnormally distributed data comparison between two independent population was done using Mann Whitney test. Significance test results were quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

RESULTS

This study was carried out on sixty patients with liver cirrhosis and twenty normal control subjects. They were divided into four groups each group has twenty subjects. Group I included 20 cirrhotic patients which were with bleeding esophageal varices by endoscopy, group II included 20 cirrhotic patients with no history of bleeding, group III included cirrhotic patients with no esophageal varices, and group IV included normal control subjects. They were subjected to clinical, laboratory, ultrasonographic and endoscopic evaluation, Statistical analysis of data was performed for all groups in all parameters except for the control group (group IV) in whom only the GA, HbA1c and GA\HbA1c ratio results were analyzed, and the results of the study were as follows:

I. Demographic data: (table 8)

In our study, group I included 16 male and 4 female patients, their age ranged between 35 and 67 years with a mean of 52.9 ± 10.14 years. Group II included 13 male and 7 female patients, their age ranged between 40 and 71 years with a mean 51.70 ± 7.21 years. Group III included 15 male and 5 female subjects, their age ranged between 25 and 70 years with a mean 51.2 ± 11.11 years. Group IV included 13 male and 7 female patients, their age ranged between 39 and 61 years with a mean of 48.30 ± 6.43 years. There was no statistically significant difference between different studied groups regarding **age and gender**.

Table (8): Comparison between the studied groups according to demographic data

	Group I (n=20)		Group II (n=20)		Group III (n=20)		Group IV (n=20)		Test of sig.	P
	No.	%	No.	%	No.	%	No.	%		
Sex										
Male	16	80.0	13	65.0	15	75.0	13	65.0	$\chi^2=1.648$	0.649
Female	4	20.0	7	35.0	5	25.0	7	35.0		
Age										
Min. – Max.	35.0 – 67.0		40.0 – 71.0		25.0 – 70.0		39.0 – 61.0		F= 0.953	0.419
Mean \pm SD.	52.9 \pm 10.14		51.70 \pm 7.21		51.2 \pm 11.11		48.30 \pm 6.43			
Median	55.0		50.50		54.50		48.0			
Residence										
Rural	15	75.0	13	65.0	14	70.0	11	55.0	$\chi^2=1.957$	0.581
Urban	5	25.0	7	35.0	6	30.0	9	45.0		

p: p value for comparing between the studied groups

χ^2 : Chi square test

F: F test (ANOVA)

SD: standard deviation

II. Clinical data: (table 9), figure (8-13)

Jaundice was found in 80% & in 75% of patients in groups I & II respectively. There was no statistically significant difference between both groups. Also, it was found in 77.5% of patient with cirrhosis and esophageal varices (EV) namely group I and II and in 40% of patients with cirrhosis and with no EV namely group III. There was a statistically significant difference between both groups.

Splenomegaly was found in 100% of patients in groups I & II. There was no statistically significant difference between both groups. Also in patients with cirrhosis and EV, 100% had splenomegaly while in patients with cirrhosis but without EV only 60% had splenomegaly. There was a statistically significant difference between both groups.

Ascites was found in 95% & in 85% of patients in groups I & II respectively. There was no statistically significant difference between both groups. In patients with cirrhosis and EV 90% had ascites, while it was found in 30% of patients with cirrhosis without EV. There was a statistically significant difference between both groups.

Hepatic encephalopathy was found in 50% & in 15% of patients in groups I & II respectively. There was a statistically significant difference between both groups. In group of patients with cirrhosis and EV, 32.5% of patients had hepatic encephalopathy while it was found in 5% of patients with cirrhosis and no EV. There was a statistically significant difference between both groups.

Spider angiomata were found in 70.2% & in 45.0% of patients in groups I & II respectively. There was a statistically significant difference between both groups. In patients with cirrhosis and EV 60% were found to have spider angiomata while 25% of patients with cirrhosis and without EV were found to have spider angiomata. There was a statistically significant difference between both groups.

Palmar erythema was found in 65% & in 45% of patients in groups I & II respectively. There was no statistically significant difference between both groups. In group of patients with cirrhosis and without EV 55% were found to have palmar erythema while it was found in 25% of patients with cirrhosis and without EV. There was a statistically significant difference between both groups.

Table (9): Comparison between the studied groups according to clinical data

	Group I (n=20)		Group II (n=20)		Cirrhotic with EV (n=40)		Cirrhotic without EV (n=20)	
	No.	%	No.	%	No.	%	No.	%
Jaundice								
No	4	20.0	5	25.0	9	22.5	12	60.0
Yes	16	80.0	15	75.0	31	77.5	8	40.0
P	^{FE} p ₁ =1.000				^{FE} p ₂ =0.004*			
Splenomegaly								
No	0	00.0	0	00.0	0	00.0	8	30.0
Yes	20	100.0	20	100.0	40	100.0	12	60.0
P	-				^{FE} p ₂ <0.001*			
Ascites								
No	1	5.0	3	15.0	4	10.0	14	70.0
Yes	19	95	17	85.0	36	90	6	30.0
P	^{MW} p ₁ =0.700				^{MW} p ₂ <0.001*			
HE								
No	10	50.0	17	85.0	27	67.5	19	95.0
Yes	10	50.0	3	15.0	13	32.5	1	5.0
P	χ^2 p ₁ =0.018*				^{FE} p ₂ =0.023*			
Spider angiomata								
No	7	29.8	11	55.0	18	40.0	15	75.0
Yes	13	70.2	9	45.0	22	60.0	5	25.0
χ^2p	χ^2 p ₁ =0.022*				χ^2 p ₂ =0.025*			
Palmar Erythema								
No	7	35.0	11	55.0	18	45.0	15	75.0
Yes	13	65.0	9	45.0	22	55.0	5	25.0
χ^2p	χ^2 p ₁ =0.204				χ^2 p ₂ = 0.028*			

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

χ^2 : Chi square test

FE: Fisher Exact test

*: Statistically significant at p ≤ 0.05

HE = hepatic encephalopathy

SD: standard deviation

MW: Mann Whitney test

n: Number of patients per group

EV= esophageal varices

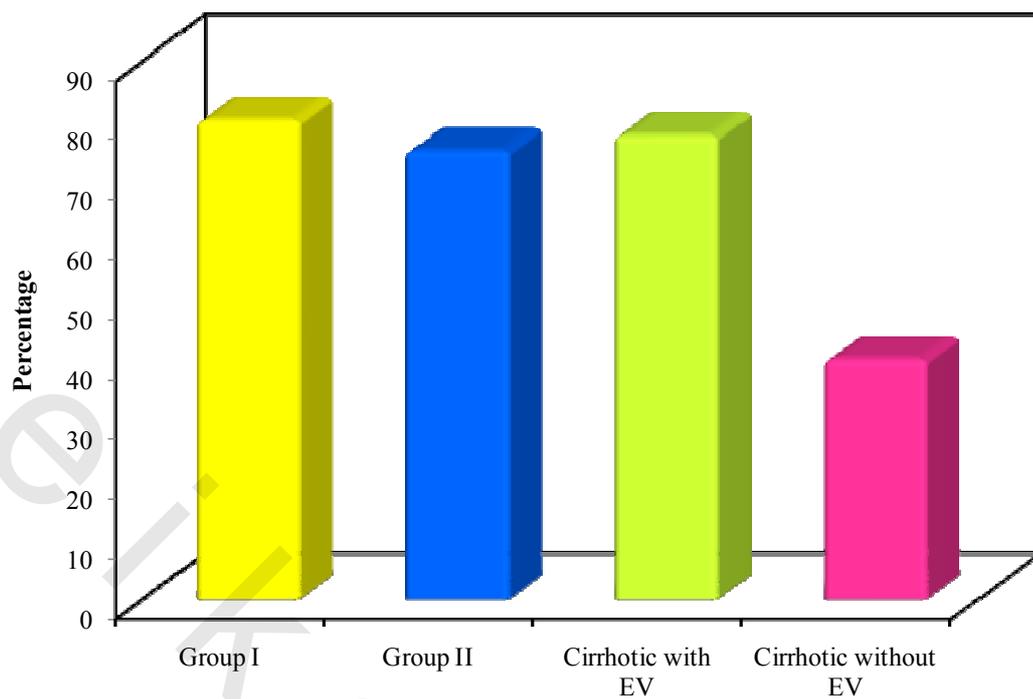


Figure (8): Comparison between the studied groups according to jaundice

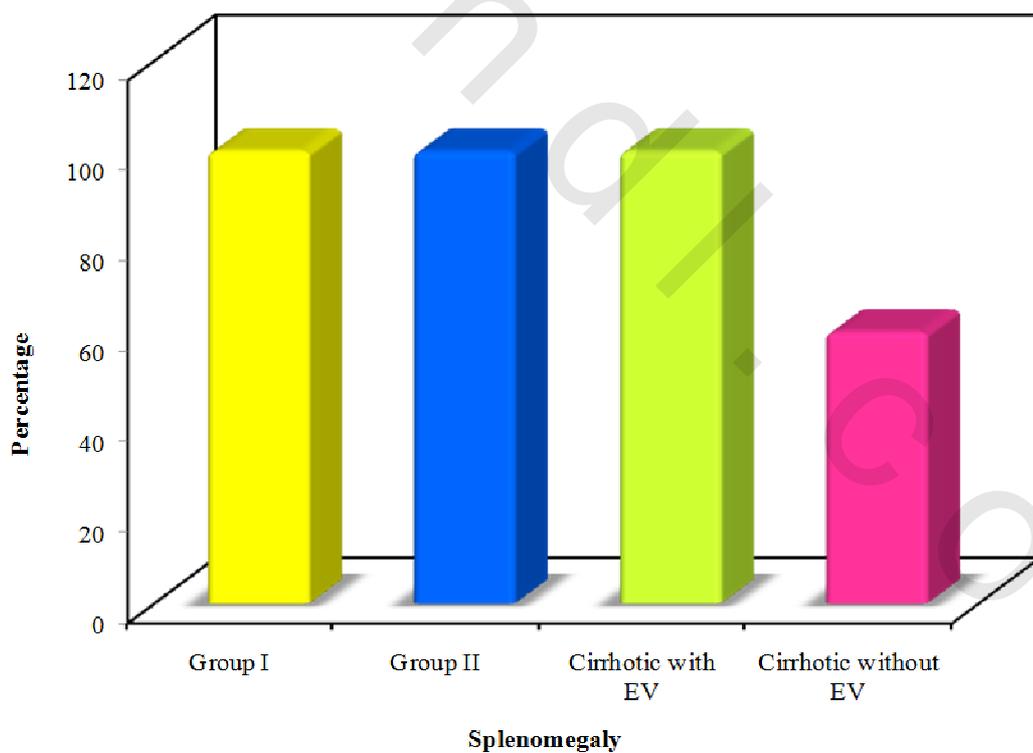


Figure (9): Comparison between the studied groups according to splenomegaly

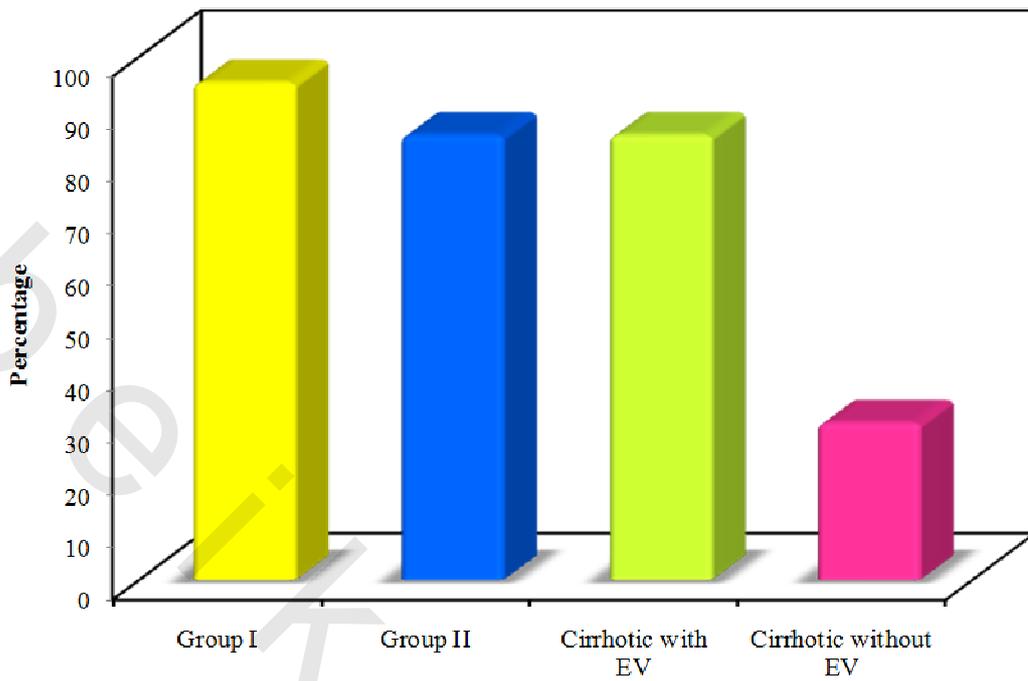


Figure (10): Comparison between the studied groups according to ascites

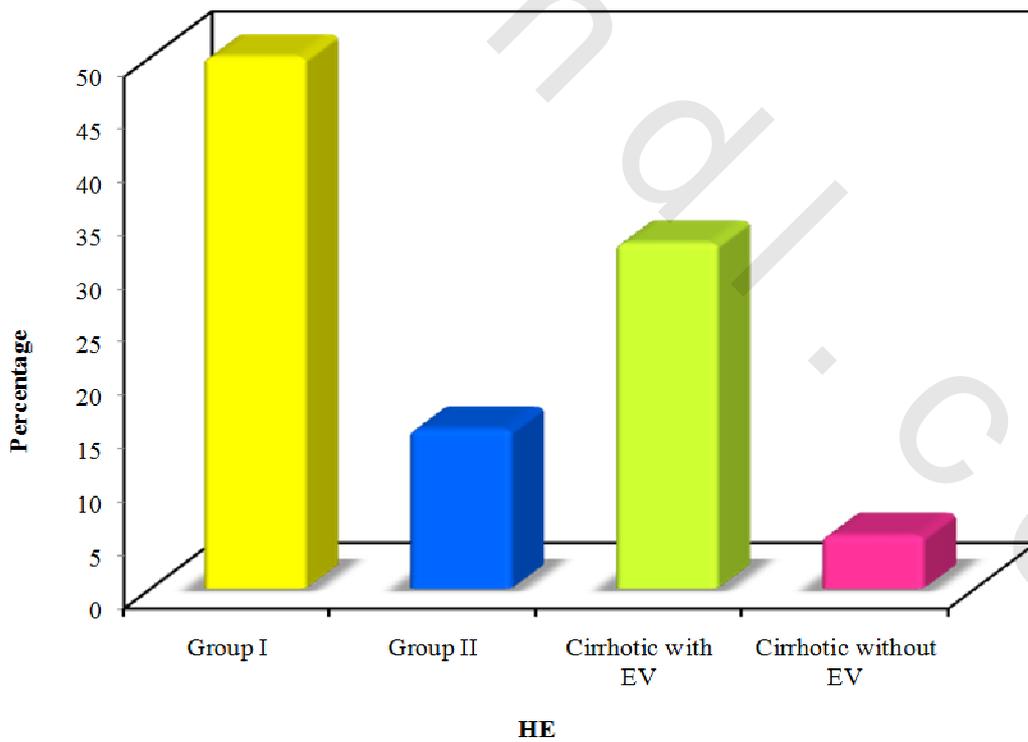


Figure (11): Comparison between the studied groups according to hepatic encephalopathy (HE).

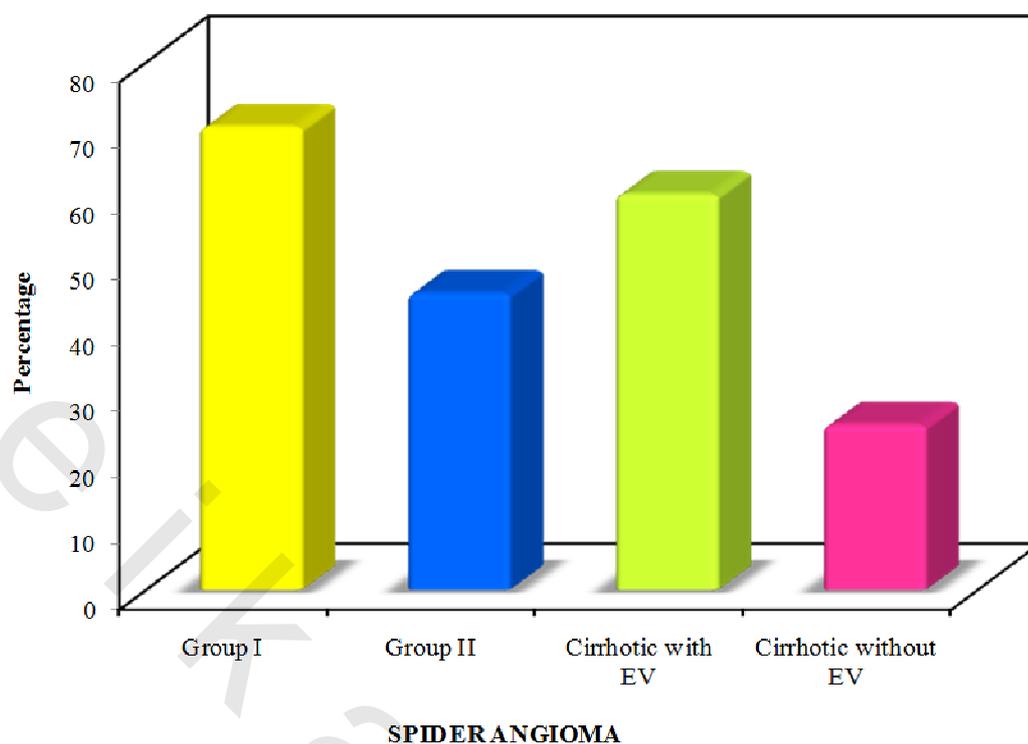


Figure (12): Comparison between the studied groups according to Spider angioma

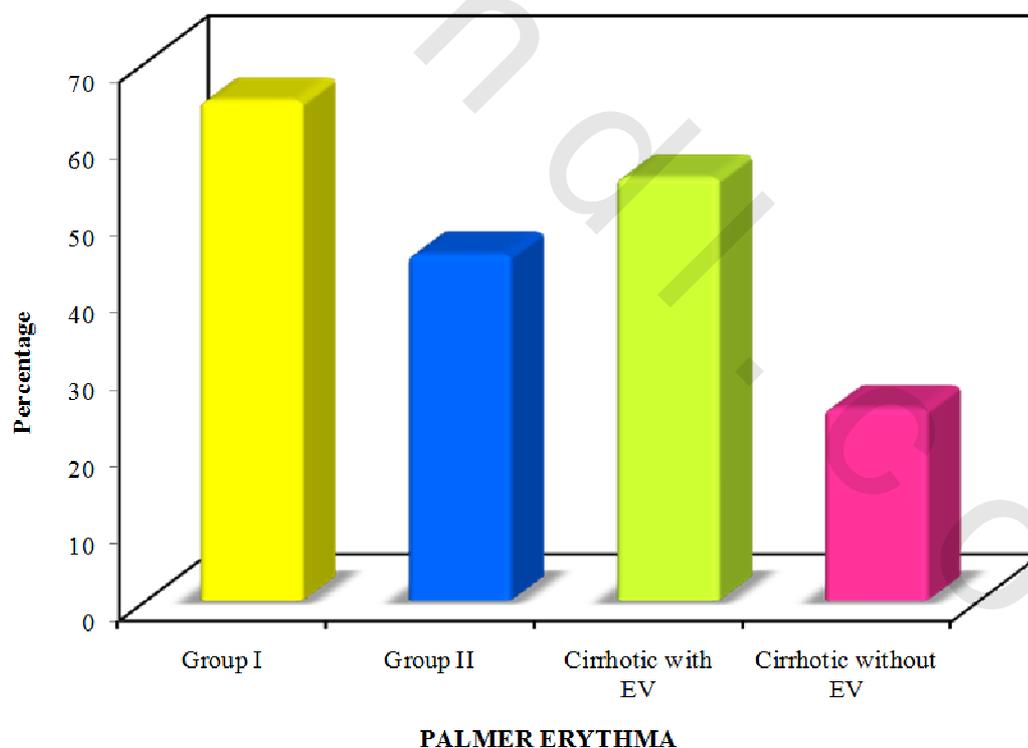


Figure (13): Comparison between the studied groups according to Palmar Erythema

III. Laboratory data

A. Complete blood count: (table 10), (figure 14)

Hemoglobin (Hb) level ranged between 6.7 and 12 g/dl with a mean of 10.13 ± 1.23 g/dl in group I. In patients of group II, hemoglobin level ranged between 6.50 – 15.80 g/dl with a mean of 10.27 ± 1.91 g/dl. There was no statistically significant difference between group I and II. In patients with cirrhosis and EV, it ranged between 6.50 – 15.80 g/dl with a mean of 10.20 ± 1.59 g/dl. In patients with cirrhosis and without EV it ranged between 8.80 – 16.0 g/dl with a mean of 12.27 ± 2.25 g/dl. There was a statistically significant difference between the two groups.

Platelets (PLT) count ranged between 10 and 134×10^3 cell/mm³ with a mean of $73.95 \pm 29.81 \times 10^3$ cell/mm³ in group I. In patients of group II, Platelets count ranged between 42 and 168×10^3 cell/mm³ with a mean of $93.10 \pm 27.44 \times 10^3$ cell/mm³. There was a statistically significant difference both groups. In patients with cirrhosis and EV, it ranged between 10 and 168×10^3 cell/mm³ with a mean of $83.53 \pm 28.32 \times 10^3$ cell/mm³. In patients with cirrhosis and without EV it ranged between 80 and 237×10^3 cell/mm³ with a mean of $145.7 \pm 45.4 \times 10^3$ cell/mm³. There was a statistically significant difference between the two groups.

White blood cells (WBC) count ranged between 1.70 and 11×10^3 cell/mm³ with a mean of $5.96 \pm 2.56 \times 10^3$ cell/mm³ in group I. In patients of group II, WBC count ranged between 1.26 and 10.50×10^3 cell/mm³ with a mean of $4.64 \pm 2.31 \times 10^3$ cell/mm³. There was no statistically significant difference both groups. In patients with cirrhosis and EV, it ranged between 1.26 and 11.0×10^3 cell/mm³ with a mean of $5.30 \pm 2.50 \times 10^3$ cell/mm³. In patients with cirrhosis and without EV it ranged between 2.0 and 11.0×10^3 cell/mm³ with a mean of $5.36 \pm 2.01 \times 10^3$ cell/mm³ with no statistically significant difference between the two groups.

Results

Table (10): Comparison between the studied groups according to CBC

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
HB(g/dl)				
Min. – Max.	6.70 – 12.0	6.50 – 15.80	6.50 – 15.80	8.80 – 16.0
Mean ± SD.	10.13 ± 1.23	10.27 ± 1.91	10.20 ± 1.59	12.27 ± 2.25
Median	10.50	10.05	10.10	12.10
t_p	p ₁ =0.777		p ₂ =0.001*	
PLT				
Min. – Max.	10.0 – 134.0	42.0 – 168.0	10.0 – 168.0	80.0 – 237.0
Mean ± SD.	73.95 ± 29.81	93.10 ± 27.44	83.53 ± 28.32	145.7±45.4
Median	72.0	90.50	80.50	152.0
t_p	p ₁ =0.041*		p ₂ <0.001*	
WBCs (x10³ /mm³)				
Min. – Max.	1.70 – 11.0	1.26 – 10.50	1.26 – 11.0	2.0 – 11.0
Mean ± SD.	5.96 ± 2.56	4.64 ± 2.31	5.30 ± 2.50	5.36 ± 2.01
Median	5.68	4.18	5.0	5.05
t_p	p ₁ = 0.096		p ₂ =0.918	

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

t: Student t-test

*: Statistically significant at p ≤ 0.05

Hb: hemoglobin WBCs: white blood cells PLTs: platelets

n :Number of patients per group

SD= standard deviation

EV: esophageal varices

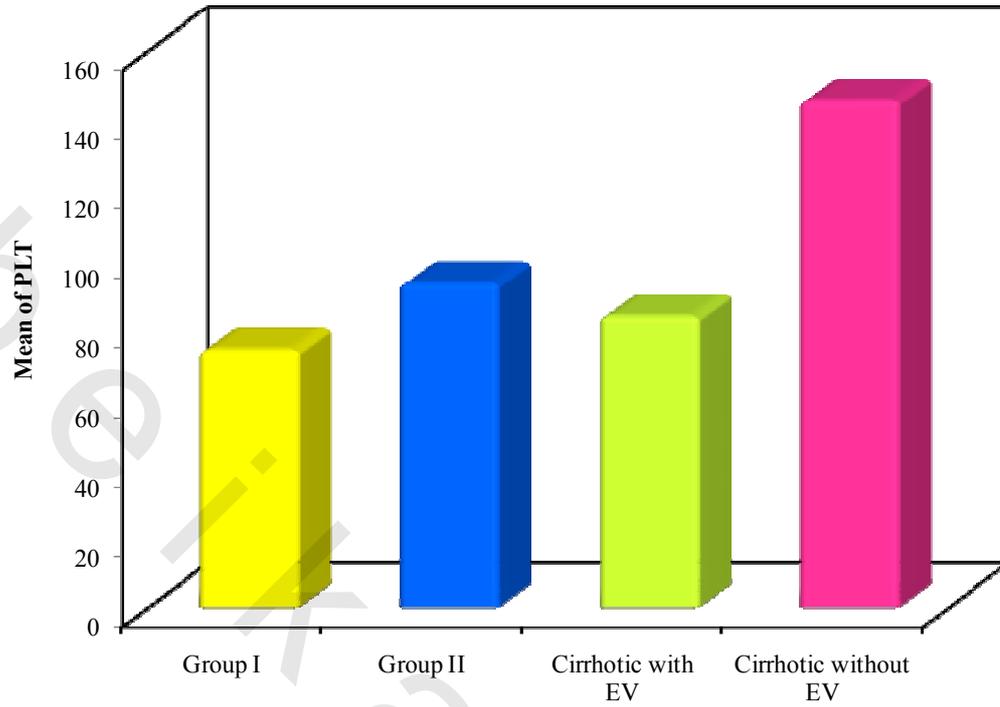


Figure (14): Comparison between the studied groups according to Platelet count

B. Biochemical data: table (11)

Fasting blood sugar level ranged between 66 and 116 mg/dl with a mean of 96.90 ± 13.40 mg/dl in group I patients. It ranged between 81.0 and 120 mg/dl with a mean of 67.60 ± 12.04 mg/dl in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 66 and 120 mg/dl with a mean of 97.25 ± 12.58 mg/dl.. In patients with cirrhosis and without EV it ranged between 80 and 120 mg/dl with a mean of 97.60 ± 11.63 mg/dl. There was no statistically significant difference between the two groups.

Serum urea level ranged between 22 and 51mg/dl with a mean of 36.48 ± 12.06 mg/dl in group I patients. It ranged between 24 and 40 mg/dl with a mean of 33.12 ± 4.92 mg/dl in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 22 and 51 mg/dl with a mean of 37.28 ± 10.42 mg/dl.. In patients with cirrhosis and without EV it ranged between 19 and 40 mg/dl with a mean of 31.40 ± 6.61 mg/dl. There was no statistically significant difference between the two groups.

Serum creatinine level ranged between 1.80 and 2.20mg/dl with a mean of 1.86 ± 0.45 mg/dl in group I patients. It ranged between 1.70 and 2.10 mg/dl with a mean of 1.82 ± 0.17 mg/dl in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 1.70 and 2.20 mg/dl with a mean of 1.8 ± 0.81 mg/dl.. In patients with cirrhosis and without EV it ranged between 0.8 and 1.20 mg/dl with a mean of 1.04 ± 0.14 mg/dl. There was no statistically significant difference between the two groups.

Total protein level ranged between 5.10 and 7.80 g/dl with a mean of 6.44 ± 0.81 g/dl in group I patients. It ranged between 5.30 and 8.60 g/dl with a mean of $1.6.66 \pm 0.90$ g/dl in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 5.10 and 8.60 g/dl with a mean of 6.55 ± 0.85 g/dl.. In patients with cirrhosis and without EV it ranged between 5.40 and 8.80 g/dl with a mean of 7.02 ± 0.91 g/dl. There was no statistically significant difference between the two groups.

C. Urine analysis

All subjects in all groups did urine analysis to detect proteinuria, any of them had proteinuria excluded from the study.

Results

Table (11): Comparison between the studied groups according to biochemical data

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
FBS(mg/dl)				
Min. – Max.	66.0 – 116.0	81.0 – 120.0	66.0 – 120.0	80.0 – 120.0
Mean ± SD.	96.90 ± 13.40	67.60 ± 12.04	97.25 ± 12.58	97.60 ± 11.63
Median	98.50	95.50	97.50	97.50
t_p	p ₁ =0.863		p ₂ =0.917	
Urea (mg/dl)				
Min. – Max.	22.0 – 51.0	24.0 – 40.0	22.0 – 51.0	19.0 – 40.0
Mean ± SD.	36.48 ± 12.06	33.12 ± 4.92	37.28 ± 10.42	31.40 ± 6.61
t_p	p ₁ =0.363		p ₂ =0.375	
Creatinine (mg/dl)				
Min. – Max.	1.80 – 2.20	1.70 – 2.10	1.70 – 2.20	0.80 – 1.20
Mean ± SD.	1.86 ± 0.45	1.82 ± 0.17	1.8 ± 0.81	1.04 ± 0.14
t_p	p ₁ =0.850		p ₂ = 0.655	
T.PTN (g/dl)				
Min. – Max.	5.10 – 7.80	5.30 – 8.60	5.10 – 8.60	5.40 – 8.80
Mean ± SD.	6.44 ± 0.81	6.66 ± 0.90	6.55 ± 0.85	7.02 ± 0.91
Median	6.55	6.55	6.55	7.0
t_p	p ₁ =0.420		p ₂ =0.053	

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

t: Student t-test

T.PTN = total protein

n :Number of patients per group

SD= standard deviation

EV: esophageal varices

D. Liver profile: table (12, 13) and figure (15, 16)

Total serum bilirubin level ranged between 2.7 and 18.10 mg/dl with a mean of 5.41 ± 4.34 mg/dl in group I patients. It ranged between 2.20 and 11.50 mg/dl with a mean of 4.11 ± 2.63 mg/dl in patients of group II. There was a no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 2.20 and 18.10 mg/dl with a mean of 5.76 ± 3.60 mg/dl. In patients with cirrhosis and without EV it ranged between 0.40 – 3.40 mg/dl with a mean of 1.26 ± 0.83 mg/dl. There was a statistically significant difference between the two groups.

Direct serum bilirubin level ranged between 1.5 and 11.10 mg/dl with a mean of 3.35 ± 2.73 mg/dl in group I patients. It ranged between 1.20 and 7.40 mg/dl with a mean of 2.36 ± 1.76 mg/dl in patients of group II. There was a no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 1.20 and 11.10 mg/dl with a mean of 3.20 ± 2.32 mg/dl. In patients with cirrhosis and without EV it ranged between 0.20 – 1.70 mg/dl with a mean of 0.65 ± 0.40 mg/dl. There was a statistically significant difference between the two groups.

Serum aspartate transaminase (AST) level ranged between 23 and 285 IU/L with a mean of 82.40 ± 65.79 IU/L in group I patients. It ranged between 13 and 390 with a mean of 72.05 ± 73.41 IU/L in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 13 and 390 IU/L with a mean of 72.05 ± 73.41 IU/L. In patients with cirrhosis and without EV it ranged between 6 and 100 IU/L with a mean of 44.35 ± 30.78 IU/L. There was a no statistically significant difference between the two groups..

Serum alanine transaminase (ALT) level ranged between 11 and 172 IU/L with a mean of 47.35 ± 37.67 IU/L in group I patients. It ranged between 9 and 249 IU/L with a mean of 38.40 ± 51.27 IU/L in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 9 and 249 IU/L with a mean of 42.88 ± 44.68 IU/L. In patients with cirrhosis and without EV it ranged between 9 and 110 IU/L with a mean of 42.88 ± 44.68 IU/L. There was a no statistically significant difference between the two groups

Gamma glutemyl transpeptidase (GGT) level ranged between 12 and 270 IU/L with a mean of 57.0 ± 70.24 IU/L in group I patients. It ranged between 13 and 337 IU/L with a mean of 48.72 ± 71.8 IU/L in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 12 and 337 IU/L with a mean of 52.86 ± 70.23 IU/L. In patients with cirrhosis and without EV it ranged between 15 and 134 IU/L with a mean of 43.0 ± 28.78 IU/L. There was a no statistically significant difference between the two groups.

Alkaline phosphatase (ALP) level ranged between 61 and 228 IU/L with a mean of 109.25 ± 45.05 IU/L in group I patients. It ranged between 51 and 173 IU/L with a mean of 112.05 ± 32.79 IU/L in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 51 and 228 IU/L with a mean of 110.65 ± 38.92 IU/L. In patients with cirrhosis and without EV it ranged between 53 and 150 IU/L with a mean of 93.85 ± 26.85 IU/L. There was no statistically significant difference between the two groups.

Serum albumin level ranged between 1.6 and 2.9 g/dl with a mean of 2.18 ± 0.32 g/dl in group I patients. It ranged between 1.70 and 2.90 g/dl with a mean of 2.19 ± 0.37 g/dl in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 1.6 and 2.9g/dl with a mean of 2.18 ± 0.32 . In patients with cirrhosis and without EV it ranged between 2.70 and 4.90 with a mean of 3.54 ± 0.97 . There was a statistically significant difference between the two groups.

Prothrombin time: (PT) ranged between 14.6 and 28 seconds with a mean of 20.26 ± 3.90 seconds in group I patients. It ranged between 14.0 and 25.30 seconds with a mean of 17.15 ± 2.77 seconds in patients of group II. There was a statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 14.0 and 28.0 seconds with a mean of 17.70 ± 3.38 seconds. In patients with cirrhosis and without EV it ranged between 11 and 19.70 seconds with a mean of 14.12 ± 2.58 seconds. There was a statistically significant difference between the two groups.

Prothrombin activity (PA) ranged between 28.0 and 77.0% with a mean of 52.48 ± 12.06 % in group I patients. It ranged between 28.0 and 61.0 % with a mean of 45.07 ± 8.73 % in patients of group II. There was a statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 28.0 and 77.0 %with a mean of 47.28 ± 10.42 %. In patients with cirrhosis and without EV it ranged between 40.0 and 100.0 % with a mean of 67.74 ± 19.94 %. There was a statistically significant difference between the two groups.

International normalized ratio (INR) ranged between 1.23 and 3 with a mean of 1.92 ± 0.54 in group I patients. It ranged between 1.24 and 2.20 with a mean of 1.55 ± 0.24 in patients of group II. There was a statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 1.23 and 3 with a mean of 1.74 ± 0.45 . In patients with cirrhosis and without EV it ranged between 1 – 2.79l with a mean of 1.36 ± 0.40 . There was a statistically significant difference between the two groups.

Results

Table (12): Comparison between the studied groups according to liver profile

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
Total Bilirubin (mg/dl)				
Min. – Max.	2.70 – 18.10	2.20 – 11.50	2.20 – 18.10	0.40 – 3.40
Mean ± SD.	5.41 ± 4.34	4.11 ± 2.63	5.76 ± 3.60	1.26 ± 0.83
Median	3.20	2.45	2.65	1.0
^{MW} p	p ₁ =0.372		p ₂ <0.001*	
Direct Bilirubin (mg/dl)				
Min. – Max.	1.50 – 11.0	1.20 – 7.40	1.20 – 11.0	0.20 – 1.70
Mean ± SD.	3.35 ± 2.73	2.36 ± 1.76	3.20 ± 2.32	0.65 ± 0.40
Median	1.45	1.35	1.40	0.50
^{MW} p	p ₁ =0.309		p ₂ <0.001*	
ALT (IU/L)				
Min. – Max.	11.0 – 172.0	9.0 – 249.0	9.0 – 249.0	9.0 – 110.0
Mean ± SD.	47.35 ± 37.67	38.40 ± 51.27	42.88 ± 44.68	42.88 ± 44.68
Median	39.0	25.0	28.50	31.50
^{MW} p	p ₁ =0.168		p ₂ =1.000	
AST (IU/L)				
Min. – Max.	23.0 – 285.0	13.0 – 390.0	13.0 – 390.0	6.0 – 100.0
Mean ± SD.	82.40 ± 65.79	61.70 ± 80.68	72.05 ± 73.41	44.35 ± 30.78
Median	66.0	44.50	48.50	32.50
^{MW} p	p ₁ =0.066		p ₂ =0.086	
S.ALB (g/dl)				
Min. – Max.	1.60 – 2.90	1.70 – 2.90	1.60 – 2.90	2.70 – 4.90
Mean ± SD.	2.18 ± 0.32	2.19 ± 0.37	2.18 ± 0.32	3.54 ± 0.97
Median	2.30	2.25	2.30	3.90
^t p	p ₁ =0.850		p ₂ <0.001*	
GGT (IU/L)				
Min. – Max.	12.0 – 270.0	13.0 – 337.0	12.0 – 337.0	15.0 – 134.00
Mean ± SD.	57.0 ± 70.24	48.72 ± 71.80	52.86 ± 70.23	43.0 ± 28.78
Median	34.50	25.0	31.50	34.50
^{MW} p	p ₁ =0.685		p ₂ =0.375	
ALP (IU/L)				
Min. – Max.	61.0 – 228.0	51.0 – 173.0	51.0 – 228.0	53.0 – 150.0
Mean ± SD.	109.25 ± 45.05	112.05 ± 32.79	110.65 ± 38.92	93.85 ± 26.85
Median	96.50	117.50	109.0	92.0
^t p	p ₁ =0.823		p ₂ =0.089	

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

t: Student t-test

MW: Mann Whitney test

*: Statistically significant at p ≤ 0.05

n :Number of patients per group

ALT = alanine aminotransferases

S.ALB= serum albumin

ALP=alkaline phosphatase

EV; esophageal varices

AST=aspartate aminotransferases

GGT=gamma glutemyl transpeptidase

SD= standard deviation

Table (13): Comparison between the studied groups according to prothrombin time, activity and INR

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
PT (seconds)				
Min. – Max.	14.60 – 28.0	14.0 – 25.30	14.00 – 28.0	11.0 – 19.70
Mean ± SD.	20.26 ± 3.90	17.15 ± 2.77	17.70 ± 3.38	14.12 ± 2.58
Median	19.0	16.55	16.75	13.25
^tp	p ₁ =0.006*		p ₂ <0.001*	
PA (%)				
Min. – Max.	28.0 – 77.0	28.0 – 61.0	28.0 – 77.0	40.0 – 100.0
Mean ± SD.	52.48 ± 12.06	45.07 ± 8.73	47.28 ± 10.42	67.74 ± 19.94
Median	53.40	44.50	47.50	63.65
^tp	p ₁ =0.032*		p ₂ <0.001*	
INR				
Min. – Max.	1.23 – 3.0	1.24 – 2.20	1.23 – 3.0	1.0 – 2.79
Mean ± SD.	1.92 ± 0.54	1.55 ± 0.24	1.74 ± 0.45	1.36 ± 0.40
Median	1.88	1.50	1.55	1.28
^{MW}p	p ₁ =0.042*		p ₂ <0.001*	

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

t: Student t-test

MW: Mann Whitney test

*: Statistically significant at p ≤ 0.05

INR: International Normalized Ratio

SD= Standard Deviation

PT: Prothrombin Time

PA: Prothrombin Activity

n: Number of patients per group

EV: Esophageal Varices

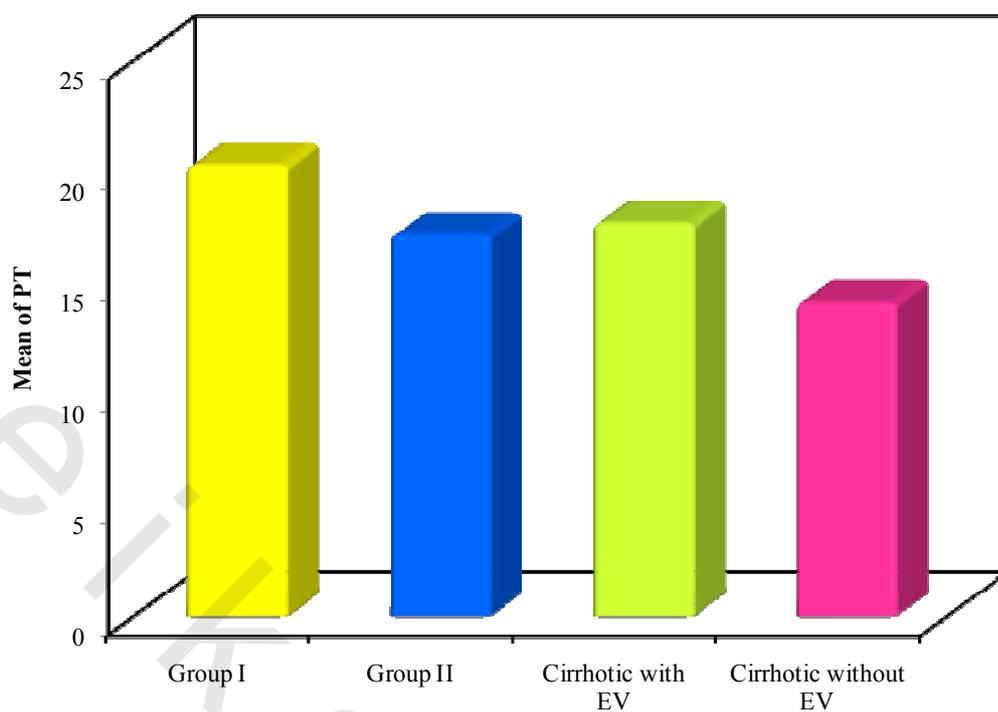


Figure (15): Comparison between the studied groups according to PT

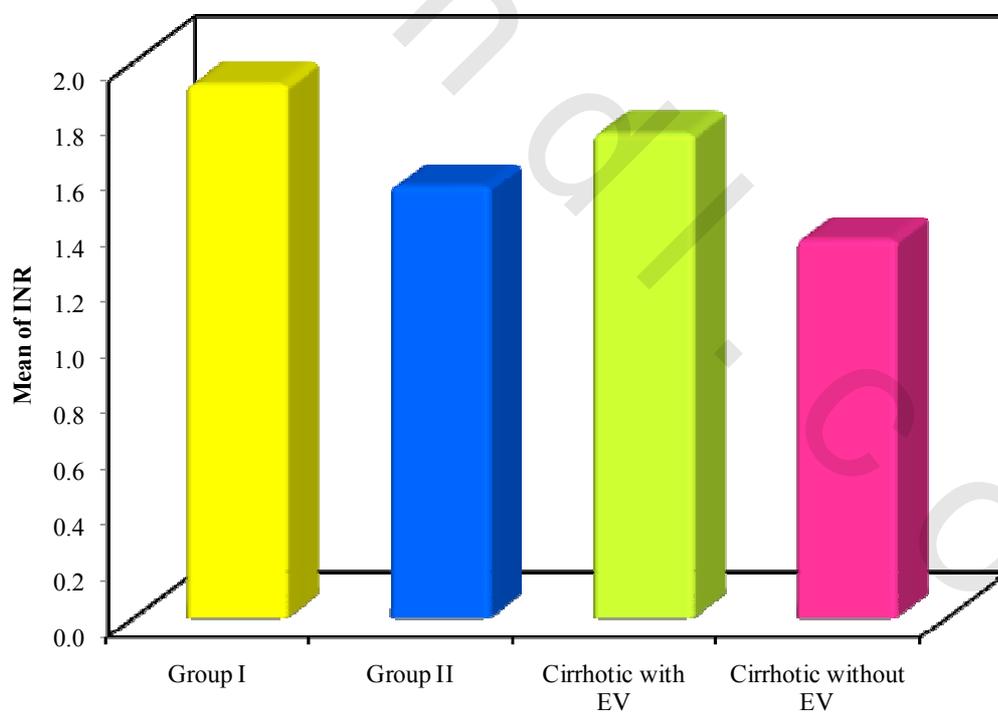


Figure (16): Comparison between the studied groups according to INR

IV. Viral and autoimmune markers: (table 14) and (figure 17).

Among the patient groups (I, II and III), there were 56 patients who tested positive for HCV antibodies, forming about 93% of the cases.

Two patients (3.3%) were positive for HBs Ag, while (3.3%) had positive markers for autoimmune liver cirrhosis.

Table (14):Distribution of studied cases according to Viral and autoimmune markers

	No.	%
The cause of cirrhosis		
HCV Abs	56	93.3
HBV Ag	2	3.3
Auto immune markers	2	3.3

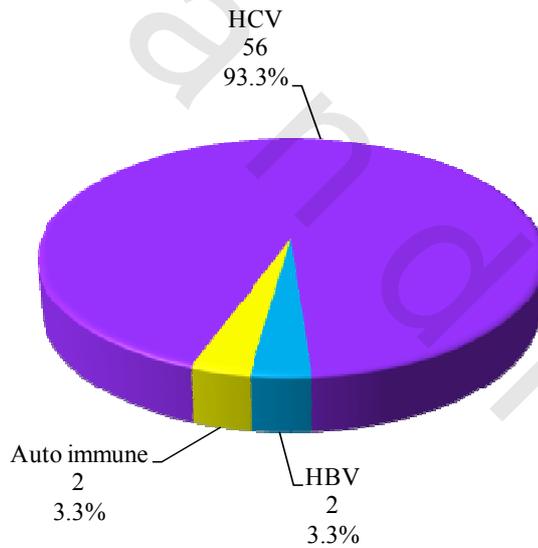


Figure (17): Distribution of studied cases according to viral and autoimmune markers

V. Child-Turcotte-Pugh classes and score: (table 15) and (figure 18, 19)

Child score was ranged between 8.0 and 15.0 with a mean of 10.95 ± 2.14 in group I patients. It ranged between 7.0 and 12.0 with a mean of 9.70 ± 1.53 in patients of group II. There was no statistically significant difference between groups I & II. In patients with cirrhosis and EV, it ranged between 7.0 and 15.0 with a mean of 10.33 ± 1.94 . In patients with cirrhosis and without EV it ranged between 5.0 and 9.0 with a mean of 6.45 ± 1.64 . There was a statistically significant difference between the two groups.

Among patient of group I there was 30% classified as child class B liver cirrhosis and 70% as child class C liver cirrhosis, while in group II there was 40% classified as child class B liver cirrhosis and 60% was classified as child class C liver cirrhosis. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, there was 35% classified as child class B liver cirrhosis and 65% classified as child class C liver cirrhosis. However, patients with cirrhosis and without EV were classified as 60% and 40% child class A and child class B liver cirrhosis respectively. There was a statistical significance difference between both groups.

Table (15): Comparison between the studied groups according to child score

	Group I (n=20)		Group II (n=20)		Cirrhotic with EV (n=40)		Cirrhotic without EV (n=20)	
	No	%	No	%	No	%	No	%
Child class								
A	0	0.0	0	0.0	0	0.0	12	60.0
B	6	30.0	8	40.0	14	35.0	8	40.0
C	14	70.0	12	60.0	26	65.0	0	0.0
MC p	p ₁ = 0.507				p ₂ = <0.001*			
Child score								
Min. – Max.	8.0 – 15.0		7.0 – 12.0		7.0 – 15.0		5.0 – 9.0	
Mean ± SD.	10.95 ± 2.14		9.70 ± 1.53		10.33 ± 1.94		6.45 ± 1.64	
Median	11.0		10.0		10.0		6.0	
t p	p ₁ = 0.040				p ₂ < 0.001*			

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

MC: Monte Carlo test

t: Student t-test

*: Statistically significant at $p \leq 0.05$

n :Number of patients per group

EV: esophageal varices

SD: standard deviation

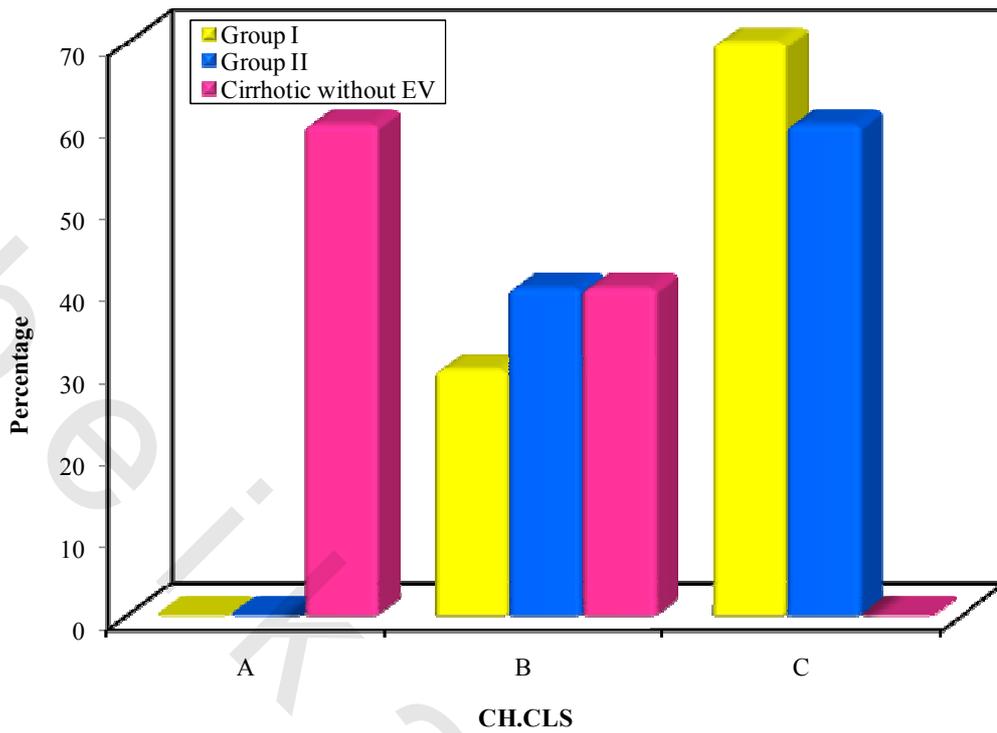


Figure (18): Comparison between the studied groups according to child class

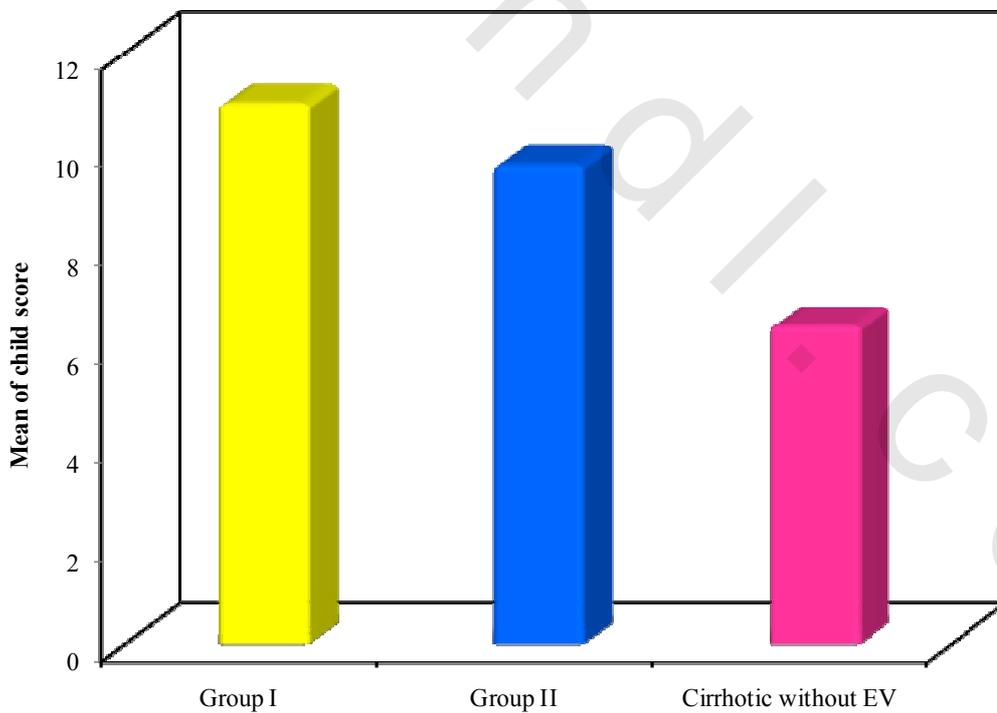


Figure (19): Comparison between the studied groups according to Child score

VI. Radiological data; abdominal ultrasonography: (table 16, 17) figure (20,21)

In group I, **portal vein (PV)** diameter ranged between 14.0 and 18.0 mm with a mean of 15.59 ± 1.18 mm. It ranged between 13.80 and 16.0 mm with a mean of 15.14 ± 0.77 mm in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 13.80 and 18.0 mm with a mean of 15.36 ± 1.01 mm. In patients with cirrhosis and without EV it ranged between 12.0 and 16.0 mm with a mean of 14.11 ± 1.36 mm. There was a statistically significant difference between the two groups.

In group I, longitudinal diameter of the **spleen** ranged between 17.0 cm and 22.0 cm with a mean of 19.04 ± 1.60 cm. It ranged between 14.0 – 21.60 cm with a mean of 17.37 ± 2.42 cm in group II. There was a statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 14.0 and 22.0 cm with a mean of 18.21 ± 2.19 cm. In patients with cirrhosis and without EV it ranged between 12.0 – 19.90 cm with a mean of 13.88 ± 2.18 cm. There was a statistically significant difference between the two groups.

In group I, longitudinal diameter of the **right lobe of the liver** ranged between 10.0 cm and 15.0 cm with a mean of 12.68 ± 1.55 cm. It ranged between 10.40 – 15.0 cm with a mean of 12.84 ± 1.36 cm in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 10.0 and 15.0 cm with a mean of 12.76 ± 1.44 cm. In patients with cirrhosis and without EV it ranged between 11.0 – 15.10 cm with a mean of 12.81 ± 1.08 cm. There was no statistically significant difference between the two groups.

No **ascites** was found in 5% versus 15% of patients in groups I & II respectively. Mild ascites was found in 5% versus 10 % of patients in groups I & II respectively. Moderate ascites was found in 30% versus 15% of patients in groups I & II respectively. Massive ascites was found in 60% versus 60% of patients in groups I & II respectively. There was no statistically significant difference between both groups. No ascites was found in 10% versus 70% of patients in cirrhotics with EV versus those without EV respectively. Mild ascites was found in 7.5% versus 10% of patients in cirrhotics with EV versus those without EV respectively. Moderate ascites was found in 22.5% versus 5% of patients in cirrhotics with EV versus those without EV respectively, and massive ascites was found in 60% versus 15% of patients in groups cirrhotics with EV versus those without EV respectively with a statistically significant difference between both groups.

Results

Table (16): Comparison between the studied groups according to abdominal ultrasound

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
PV diameter (mm)				
Min. – Max.	14.0 – 18.0	13.80 – 16.0	13.80 – 18.0	12.0 – 16.0
Mean ± SD.	15.59 ± 1.18	15.14 ± 0.77	15.36 ± 1.01	14.11 ± 1.36
Median	15.25	12.25	15.25	14.10
MW p	p ₁ =0.276		p ₂ = 0.002*	
Spleen (cm)				
Min. – Max.	17.0 – 22.0	14.0 – 21.60	14.0 – 22.0	12.0 – 19.90
Mean ± SD.	19.04 ± 1.60	17.37 ± 2.42	18.21 ± 2.19	13.88 ± 2.18
Median	18.50	17.50	18.0	13.10
t p	p ₁ =0.014*		p ₂ <0.001*	
Right Lobe (cm)				
Min. – Max.	10.0 – 15.0	10.40 – 15.0	10.0– 15.0	11.0 – 15.10
Mean ± SD.	12.68 ±1.55	12.84 ± 1.36	12.76 ±1.44	12.81 ± 1.08
Median	13.0	12.7	13.0	13.0
t p	0.731		p ₂ = 0.892	

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

t: Student t-test

MW: Mann Whitney test

*: Statistically significant at p ≤ 0.05

n :Number of patients per group

PV = portal vein

SD = standard deviation

EV: esophageal varices

Results

Table (17): Comparison between the studied groups according to ascites by ultrasound

	Group I (n=20)		Group II (n=20)		Cirrhotic with EV (no=40)		Cirrhotic without EV (no=20)	
	No.	%	No.	%	No.	%	No.	%
Ascites								
No	1	5.0	3	15.0	4	10.0	14	70.0
Mild	1	5.0	2	10.0	3	7.5	2	10.0
Moderate	6	30.0	3	15.0	9	22.5	1	5.0
Massive	12	60.0	12	60.0	24	60.0	3	15.0
P	MW $p_1=0.700$				MW $p_2<0.001^*$			

p_1 : p value for comparing between group I and group II

p_2 : p value for comparing between cirrhotic with EV and cirrhotic without EV group

χ^2 : Chi square test

FE: Fisher Exact test

MW: Mann Whitney test

*: Statistically significant at $p \leq 0.05$

n :Number of patients per group

SD = standard deviation

EV: esophageal varices



figure (20) ultrasonographic picture of portal vein



figure (21) ultrasonographic picture of splenomegaly

VII. Endoscopic data: (table 18), figure (22-23):

Esophageal varices were graded according to Beppu (Japanese) grading system. In group I, no patient had F1 esophageal varices (EV), while 55% of patients in groups II were found to have F1 EV. F2 EV were found in 80% versus 40% of patients in groups I & II respectively. F3 EV were found in 20% versus 5% of patients in groups I & II respectively. There was statistically significant difference between both groups.

In group I, 25% versus 20% of patients in group II respectively were found to have **gastric varices (GV)**. There was no statistically significant difference between both groups.

In group I, 100% versus 20% of patients in group II respectively were found to have **red colour signs**. There was a statistically significant difference between both groups.

Portal hypertensive gastropathy (PHG) was detected and graded according to NIEC. 5% versus 20% of patients in groups I & II respectively were found to have no PHG. Mild PHG was found in 45% of patients in both groups. Severe PHG was found in 50% versus 35% of patients in groups I & II respectively. There was no statistically significant difference between both groups.

North Italian Endoscopic Club (NIEC) index was calculated to estimate the esophageal variceal risk of bleeding. It ranged between 38.60 and 49.70 with a mean of 43.09 ± 3.74 in group I patients. In group II patients, it ranged between 24.90 and 43.30 with a mean of 32.80 ± 5.73 . There was a statistically significant difference between both groups, being higher in group I.

Table (18): Comparison between the studied groups according to EV, gastric varices, PHG and risk signs of bleeding

	Group I (n=20)		Group II (n=20)		Test of sig.	P
	No.	%	No.	%		
EV						
No	0	0.0	0	0.0	$\chi^2=15.467^*$ ^{FE} p<0.001*	
F1	0	0.0	11	55.0		
F2	16	80.0	8	40.0		
F3	4	20.0	1	5.0		
Gastric varices						
No	15	75.0	16	80.0	$\chi^2=0.143$ ^{FE} p=1.000	
Yes	5	25.0	4	20.0		
PHG						
No	1	5.0	4	20.0	Z=1.291	0.197
Mild	9	45.0	9	45.0		
Severe	10	50.0	7	35.0		
Red wale sign						
No	0	0.0	12	60.0	$\chi^2=17.143^*$	<0.001*
Yes	20	100.0	8	20.0		
NIEC						
Min. – Max.	38.60 – 49.70		24.90 – 43.30		t=6.718*	<0.001*
Mean ± SD.	43.09 ± 3.74		32.80 ± 5.73			
Median	42.10		31.70			

p: p value for comparing between group I and group II

χ^2 : value for Chi square

FE: Fisher Exact test

Z: Z for Mann Whitney test

t: Student t-test

*: Statistically significant at $p \leq 0.05$

N: Number of patients per group

EV: Esophageal Varices

PHG: Portal Hypertensive Gastropathy

NIEC: North Italian Endoscopic Club

SD: Standard Deviation

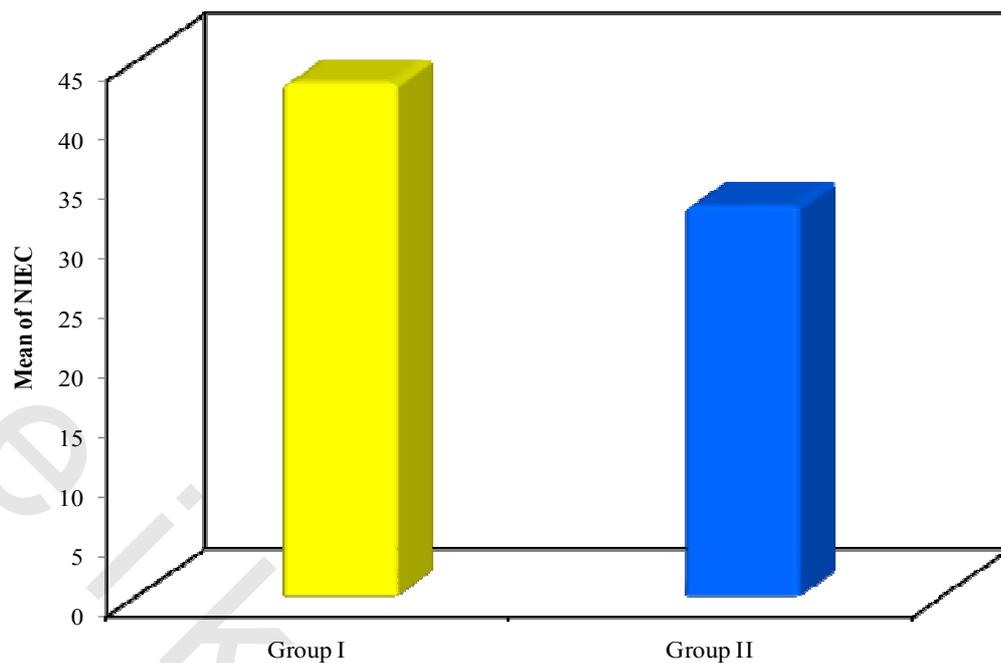


Figure (22): Comparison between the studied groups according to NIEC

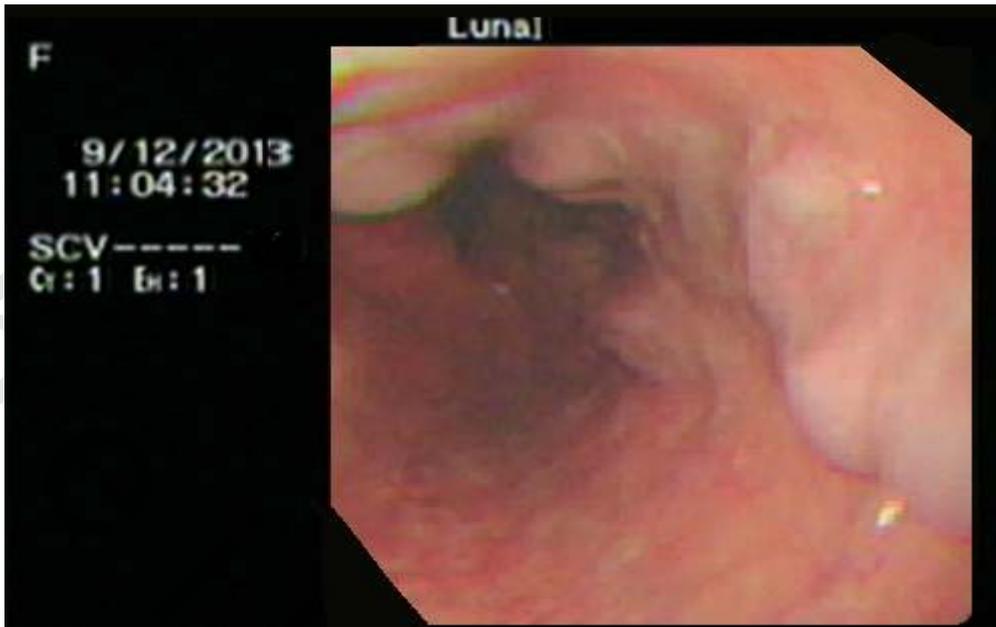


Figure (23): Endoscopic picture of F1 esophageal varices



Figure (24): Endoscopic picture of F2 esophageal varices with red spots

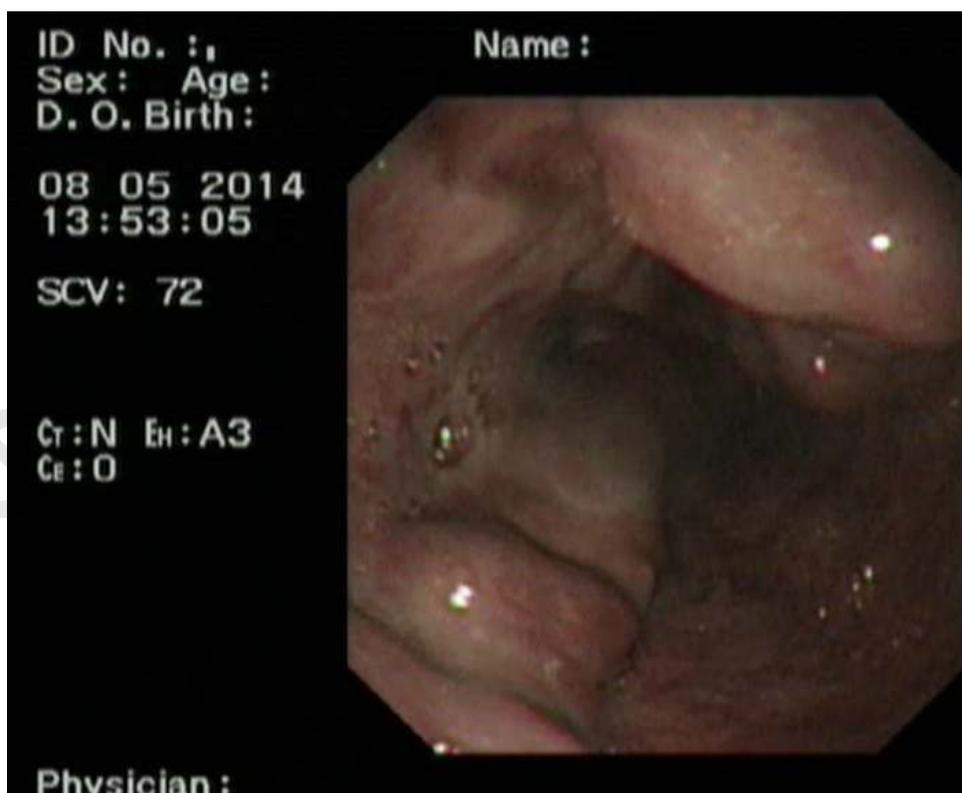


Figure (25): Endoscopic picture of F3 esophageal varices



Figure (26): Endoscopic picture of portal hypertensive gastropathy

VIII. Comparison between the studied groups according to other non-invasive ratios for assessment of EV (table 19)

In group I, **Platelet /spleen ratio** ranged between 154.6 and 800.0 with a mean of 475.0 ± 147.9 . It ranged between 84.5 and 945.7 with a mean of 521.6 ± 221.4 in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 84.5 and 945.7 with a mean of 498.9 ± 188.3 . In group of patients with cirrhosis and without EV it ranged between 410.4 and 1339.13 with a mean of 776.39 ± 296.96 . There was a statistically significant difference between the two groups.

In group I, **right lobe albumin ratio** ranged between 4.24 and 8.35 with a mean of 5.53 ± 9.58 . It ranged between 3.32 and 7.68 with a mean of 5.62 ± 1.11 in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 3.32 and 8.35 with a mean of 5.58 ± 1.03 . In patients with cirrhosis and without EV it ranged between 2.39 and 8.0 with a mean of 4.03 ± 1.53 . There was a statistically significant difference between the two groups.

In group I, **Aspartate amino transferase -to- platelet ratio index (APRI)** ranged between 0.67 and 8.48 with a mean of 2.68 ± 2.37 . It ranged between 0.29 and 17.37 with a mean of 2.36 ± 3.76 in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 0.29 and 17.73 with a mean of 2.52 ± 0.310 . In patients with cirrhosis and without EV it ranged between 0.08 and 2.36 with a mean of 0.88 ± 0.69 . There was a statistically significant difference between the two groups.

Results

Table (19): Comparison between the studied groups according to noninvasive ratios for assessment of EV

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
Platelet /spleen ratio				
Min. – Max.	154.6-800.0	84.5-945.7	84.5 - 945.7	410.4-1339.13
Mean ± SD.	475.0±147.9	521.6±221.4	498.9±188.3	776.39±296.96
Median	476.5	513.5	478.6	1000.0
P	p ₁ =0.555		p ₂ <0.001*	
RT lobe/ Alb. ratio				
Min. – Max.	4.24– 8.35	3.3– 7.68	3.32 – 8.3	2.39– 8.0
Mean ± SD.	5.5 ± 0.95	5.62 ± 1.1	5.5 ± 1.0	4.0 ± 1.5
Median	5.4	5.8	5.57	3.5
P	p ₁ =0.792		p ₂ <0.001*	
APRI				
Min. – Max.	0.67 – 8.48	0.29 – 17.73	0.29 – 17.73	0.08 – 2.36
Mean ± SD.	2.68 ± 2.37	2.36 ± 3.76	2.52 ± 0.310	0.88 ± 0.69
Median	1.94	1.32	1.59	0.63
t_p	p ₁ =0.204		p ₂ <<0.001*	

p₁: p value for comparing between group I and group II

p₂: p value for comparing between cirrhotic with EV and cirrhotic without EV group

t: Student t-test

MW: Mann Whitney test

*: Statistically significant at p ≤ 0.05

N= Number of patients per group

SD = standard deviation

RT lobe: right lobe of the liver

Alb.=albumin

APRI =Aspartate amino transferase -to- platelet ratio index

EV: esophageal varices

IX. Comparison between the studied groups according to GA, HbA1c and GA/HbA1c ratio (table 20-21) figures (figures 27-38).

In group I, **GA** ranged between 12.61 and 40.76 with a mean of 29.53 ± 7.93 . It ranged between 12.78 and 41.43 with a mean of 28.06 ± 9.20 in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 12.61 and 41.43 with a mean of 28.79 ± 8.51 . In patients with cirrhosis and without EV it ranged between 1.21 and 38.01 with a mean of 23.0 ± 9.13 . There was a statistically significant difference between the two groups. When comparing between the cirrhotic patients and control group; the GA ranged from 12.1 to 41.43 with a mean of 26.86 ± 9.07 in cirrhotic patients while it ranged from 0.73 to 34.41 with a mean of 21.47 ± 10.07 in control group. There was a statistically significant difference between the two groups.

In group I, **HbA1c** ranged between 3.10 and 6.50 with a mean of 4.48 ± 0.80 . It ranged between 3.10 and 6.20 with a mean of 4.13 ± 0.70 in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 3.10 and 6.50 with a mean of 4.30 ± 0.76 . In patients with cirrhosis and without EV it ranged between 3.50 and 5.60 with a mean of 4.65 ± 0.58 . There was no statistically significant difference between the two groups. When comparing between the cirrhotic patients and control group; the HbA1c ranged from 3.10 to 6.50 with a mean of 4.42 ± 0.72 in cirrhotic patients while it ranged from 3.77 to 5.84 with a mean of 4.63 ± 0.48 in control group. There was no statistically significant difference between the two groups.

In group I, **GA/HbA1c ratio** ranged between 3.07 and 11.0 with a mean of 6.82 ± 2.39 . It ranged between 3.55 and 13.37 with a mean of 6.94 ± 2.67 in group II. There was no statistically significant difference between both groups. In patients with cirrhosis and EV, it ranged between 3.07 and 13.37 with a mean of 6.88 ± 2.50 . In patients with cirrhosis and without EV it ranged between 0.25 and 7.69 with a mean of 4.98 ± 1.91 . There was a statistically significant difference between the two groups. When comparing between the cirrhotic patients and control group; the GA/HbA1c ratio ranged from 0.25 to 13.37 with a mean of 6.25 ± 2.48 in cirrhotic patients while it ranged from 0.14 to 7.82 with a mean of 4.73 ± 2.28 in control group. There was a statistically significant difference between the two groups.

There was a significant positive correlation between GA/HbA1c ratio and Child score.

There was no correlation between NIEC index and GA/HbA1c ratio, ($r_s = 0.090$, $p = 0.582$).

Table (20) Comparison between the studied groups according to GA, HbA1c and GA/HbA1c ratio

	Group I (n=20)	Group II (n=20)	Cirrhotic with EV (n=40)	Cirrhotic without EV (n=20)
HbA1c				
Min. – Max.	3.10 – 6.50	3.10 – 6.20	3.10 – 6.50	3.50 – 5.60
Mean ± SD.	4.48 ± 0.80	4.13 ± 0.70	4.30 ± 0.76	4.65 ± 0.58
Median	4.30	4.20	4.30	4.55
P	p ₁ = 0.142		p ₂ =0.080	
GA				
Min. – Max.	12.61 – 40.76	12.78 - 41.43	12.61 – 41.43	12.1 - 38.01
Mean ± SD.	29.53 ± 7.93	28.06 ± 9.20	28.79 ± 8.51	23.0 ± 9.13
Median	30.20	28.24	29.13	23.09
P	p ₁ = 0.592		p ₂ =0.019*	
GA/HbA1c ratio				
Min. – Max.	3.07 – 11.0	3.55 – 13.37	3.07 – 13.37	0.25 – 7.69
Mean ± SD.	6.82 ± 2.39	6.94 ± 2.67	6.88 ± 2.50	4.98 ± 1.91
Median	6.46	6.56	6.50	5.44
P	p ₁ =0.871		p ₂ =0.008*	

p₁: p value for Mann Whitney test for comparing between group I and group II

p₂: p value for Mann Whitney test for comparing between cirrhotic with EV and cirrhotic without EV group

*: Statistically significant at p ≤ 0.05

N: Number of patients per group

HbA1c = Glycated Hemoglobin

GA= Glycated Albumin

EV= Esophageal Varices

SD= Standard Deviation

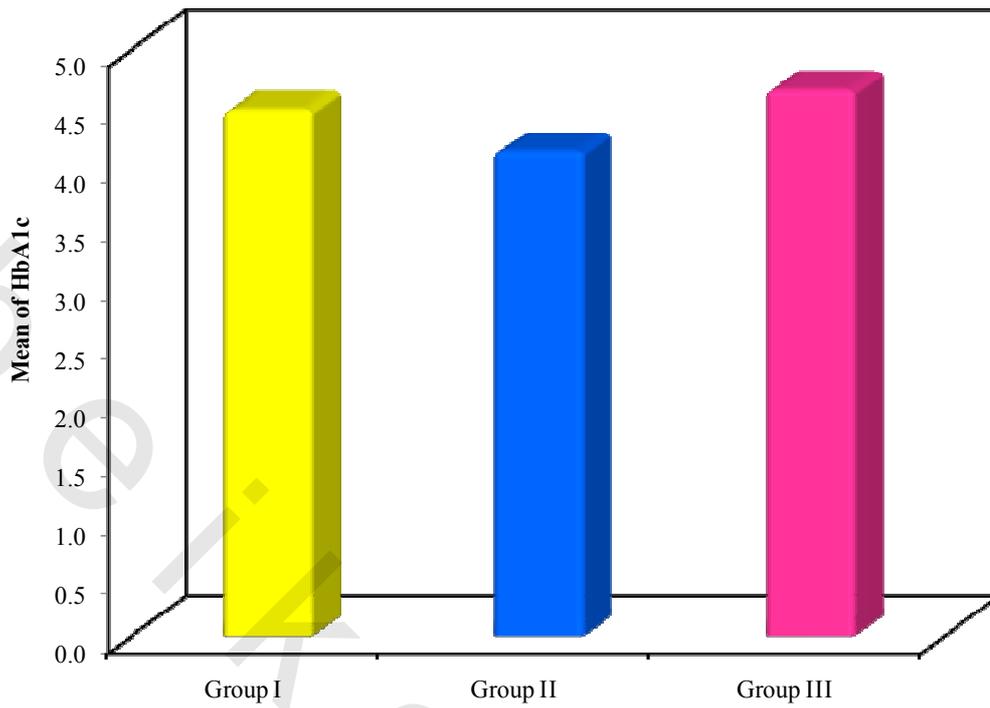


Figure (27): Comparison between the studied groups (group I, II and III) according to HbA1c

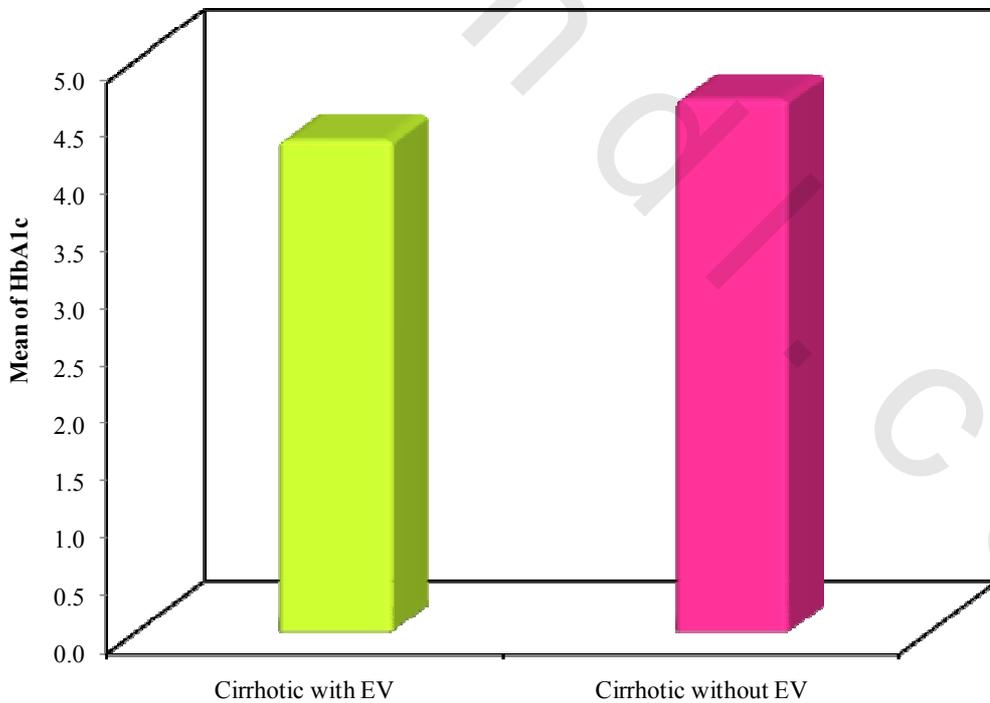


Figure (28): Comparison between the cirrhotic with EV and cirrhotic without EV according to HbA1c

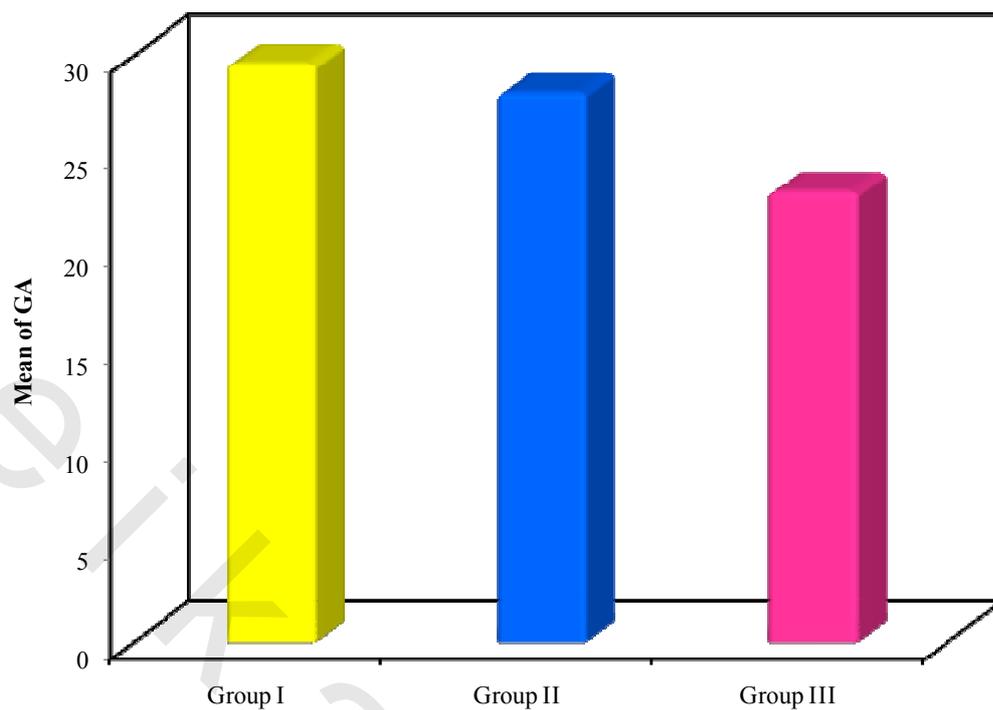


Figure (29): Comparison between the studied groups (group I, II and III) according to GA

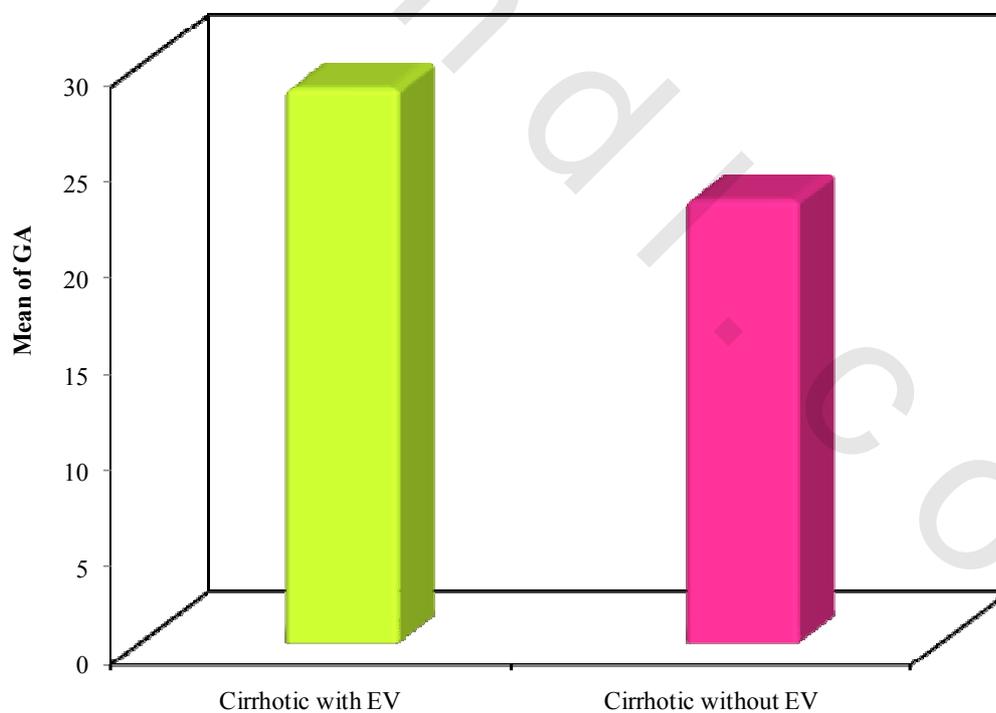


Figure (30): Comparison between cirrhotic with EV and cirrhotic without EV according to GA

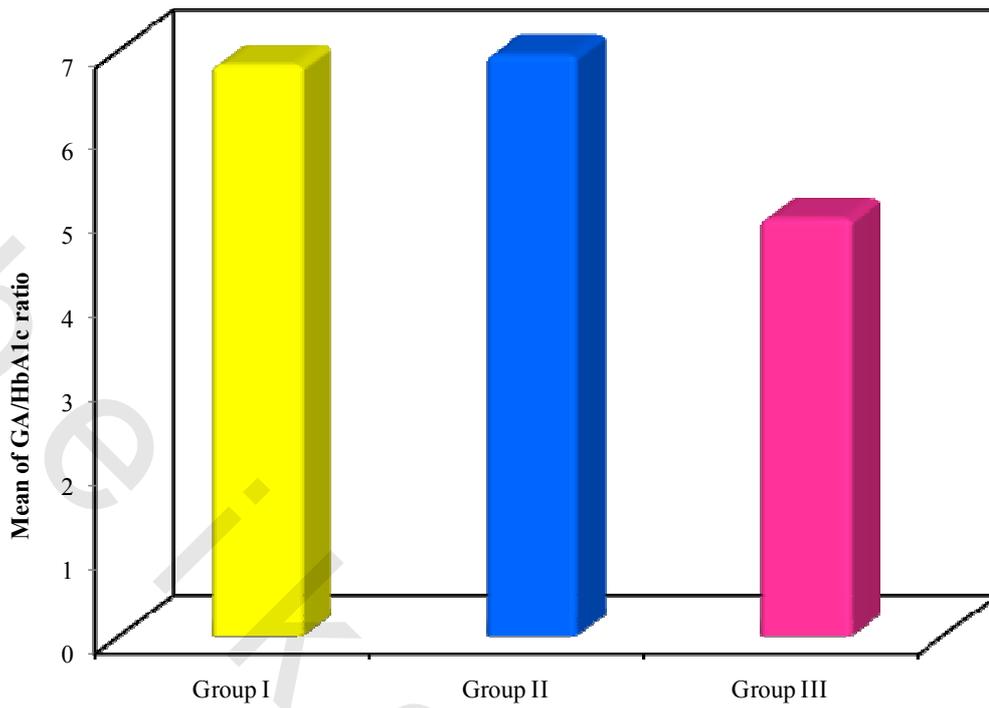


Figure (31): Comparison between the studied groups(group I, II and III) according to GA/HbA1c ratio

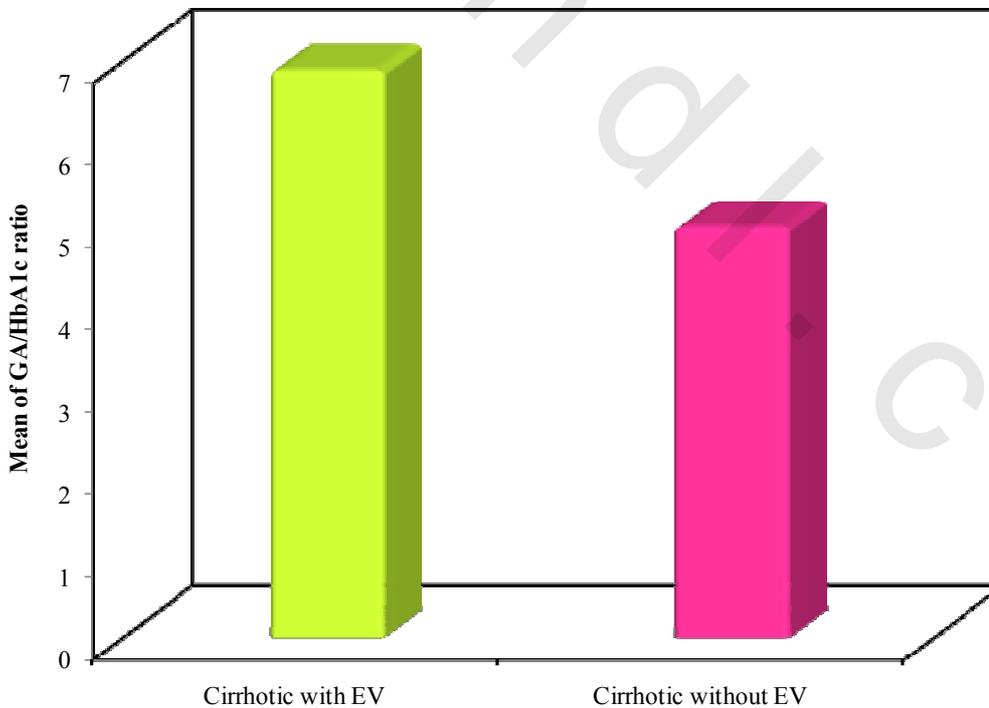


Figure (32): Comparison between cirrhotic with EV and cirrhotic without EV according to GA/HbA1c ratio

Results

Table (21): Comparison between cirrhotic patients and control group according to GA, HbA1c and GA/HbA1c ratio

	Cirrhotic patients (n=60)	Control (n=20)	Test of sig.	P
HbA1c				
Min. – Max.	3.10 – 6.50	3.77 – 5.84		
Mean ± SD.	4.42 ± 0.72	4.63 ± 0.48	t= 1.253	0.214
Median	4.40	4.69		
GA				
Min. – Max.	1.21 – 41.43	0.73 – 34.41		
Mean ± SD.	26.86 ± 9.07	21.47 ± 10.07	t= 2.241 *	0.028*
Median	27.94	24.01		
GA/HbA1c ratio				
Min. – Max.	0.25 – 13.37	0.14 – 7.82		
Mean ± SD.	6.25 ± 2.48	4.73 ± 2.28	Z= 2.039*	0.041*
Median	6.29	5.24		

Z: Z for Mann Whitney test

t: Student t-test

*: Statistically significant at $p \leq 0.05$

N Number of patients per group

SD: standard deviation

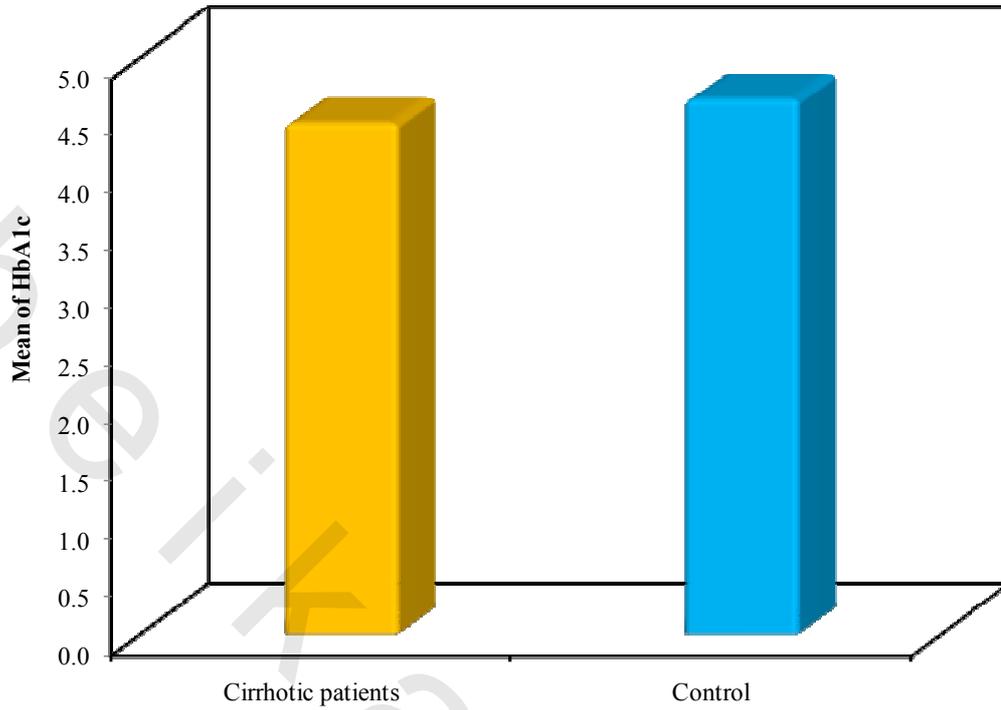


Figure (33): Comparison between cirrhotic patients and control group according to HbA1c

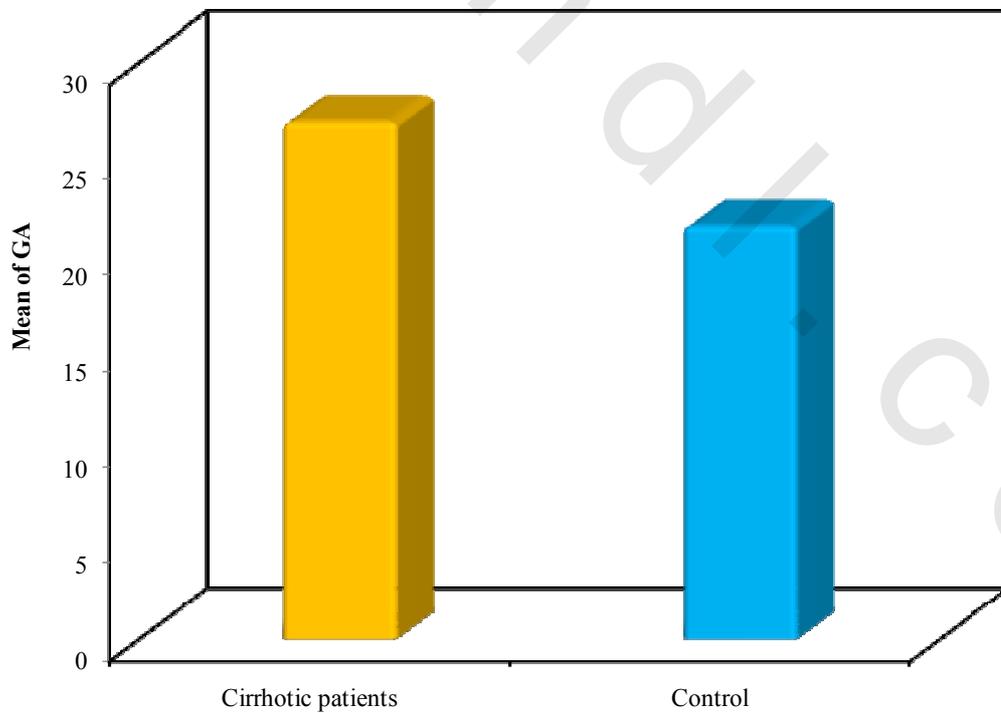


Figure (34): Comparison between cirrhotic patients and control group according to GA

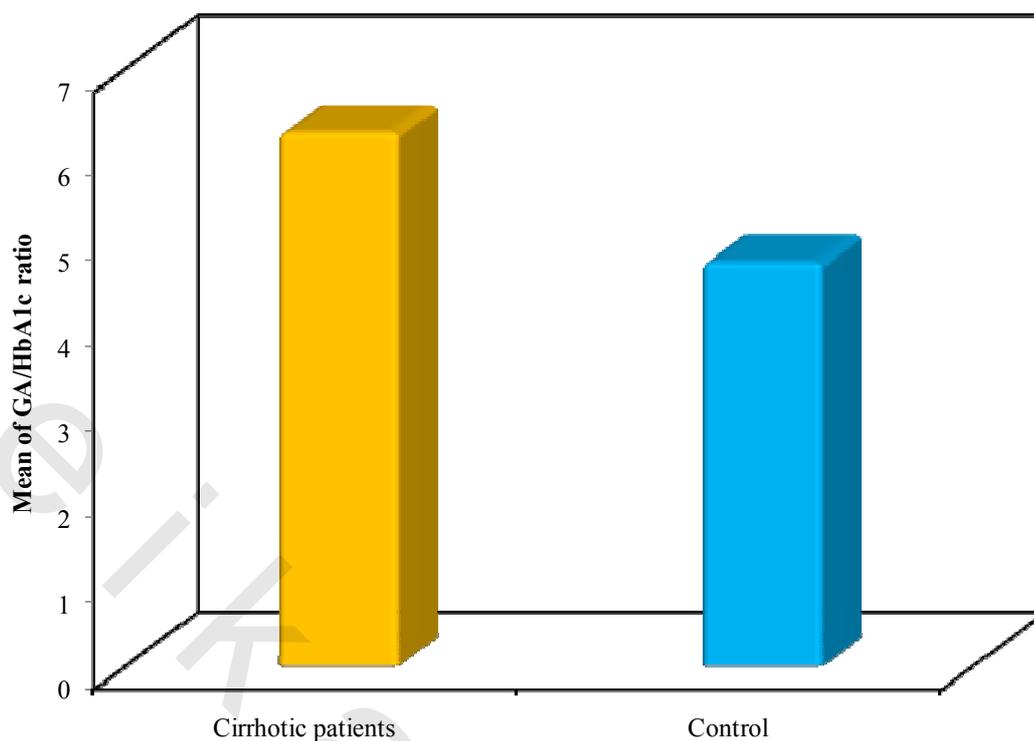


Figure (35): Comparison between cirrhotic patients and control group according to GA/HbA1c ratio

Table (22): Correlation between GA/HbA1c ratio and child score in Cirrhotic patients group

	GA/HbA1c ratio (n = 60)	
	r_s	P
Child score	0.263*	0.042

r_s : Spearman coefficient

*: Statistically significant at $p \leq 0.05$

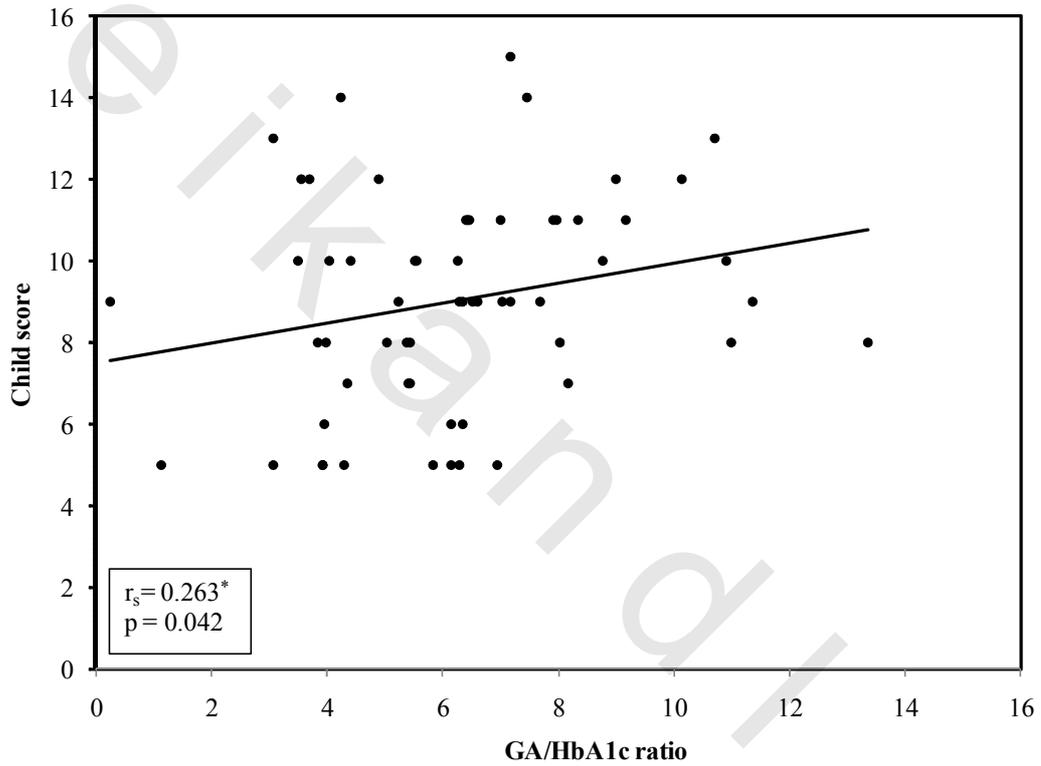


Figure (36): Correlation between GA/HbA1c ratio and Child score in cirrhotic patients group

Results

The diagnostic performance of GA/HbA1c ratio was compared to that of endoscopy, considered the gold standard, in patients presenting with esophageal varices. The receiver operator characteristic (ROC) curve analysis generated a ratio cut off value (COV) of 6.35 that could discriminate esophageal varices cirrhotic patients from non variceal cirrhotic patients, with an area under the curve of 0.711 ($p=0.008$). The ratio COV of 6.35 gave a diagnostic specificity of 85% , a sensitivity of 60%, and predictive values (positive and negative) of 89% and 52% respectively, making this method a rather specific one capable of detecting esophageal varices in cirrhotic patients (85%), than estimating the degree of its severity among such patients (60%).

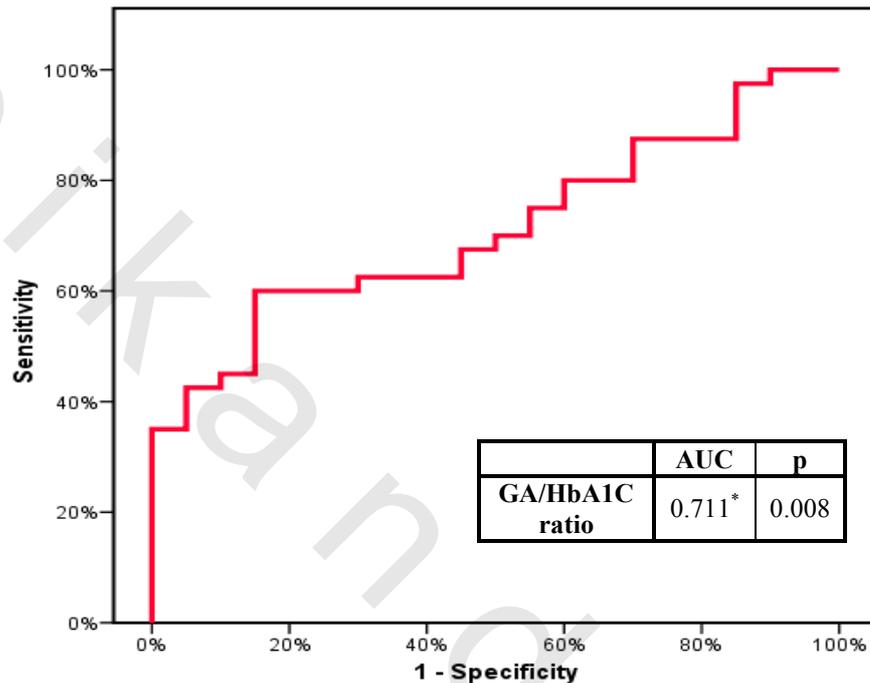


Figure (37): ROC curve for GA/HbA1c ratio to differentiate between cirrhotics with no varices [Group 3] and cirrhotics with EV [Group 1 and 2].

Table (23): Agreement (sensitivity, specificity and accuracy) for GA/HbA1c ratio with cirrhotic with EV

	COV	Cirrhotic without OV	Cirrhotic with OV	Sensitivity	Specificity	PPV	NPV	Accuracy
GA/Hb A1c ratio	≤6.35	17	16	60.0	85.0	88.89	51.52	68.33
	>6.35	3	24					

AUC; Area under the curve,
PPV; Positive predictive value

COV; Cut-off value,
NPV; Negative predictive value

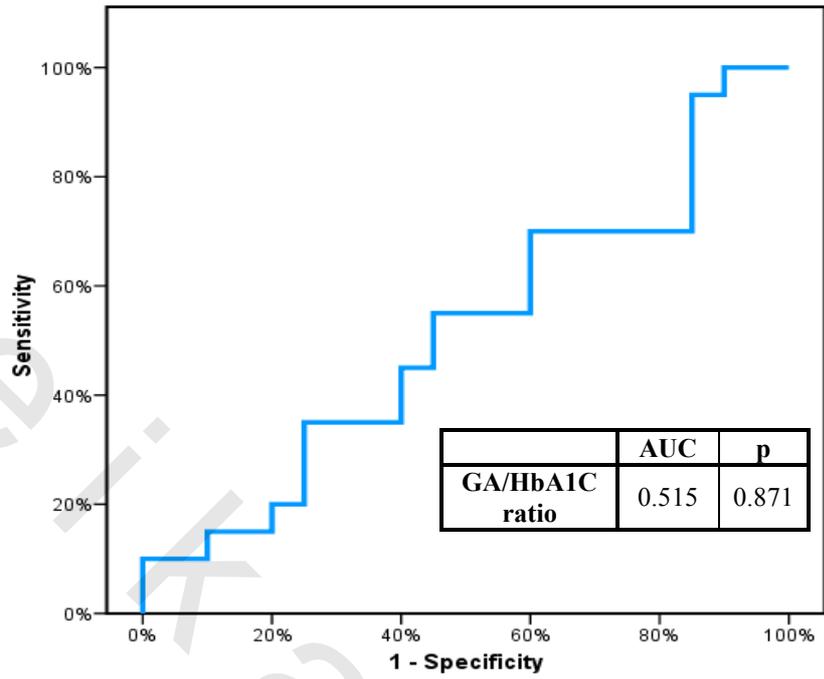


Figure (38): ROC curve for GA/HbA1C ratio to differentiate between cirrhotics with bleeding EV [Group 1] and cirrhotics with non bleeding EV [Group 2].