

# Mean Platelet Volume as a Fibrosis Marker in Patients with Chronic Hepatitis C

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**Background and study aim:** Liver biopsy limitations push us to search for new non invasive methods to detect liver fibrosis such as serum markers. The aim of this study is to evaluate mean platelet volume (MPV) as a fibrosis marker in patient with chronic hepatitis C.

**Patients and methods:** 150 patients diagnosed with chronic hepatitis C infection referred to Tanta Fever Hospital in period from May 2013 to January 2014 and 20 healthy volunteers as a control were included. All of them were tested for Mean Platelet Volume (MPV) in comparison with who done liver biopsy as standard.

**Results:** Statistically significant differences in MPV and Platelet Count were seen in patients with chronic hepatitis C (CHC) compared to healthy controls (MPV:  $8.95 \pm 1.39$  fL vs.  $7.57 \pm 0.68$  fl, P-value = 0.043; PC  $226.03 \pm 68.36$  vs.  $188.9 \pm 46.49$ , P-value = 0.02)

Multi-variate Logistic regression analysis shows only 5 variables remained as independent risk factors for fibrosis progression: (MPV, Schistosomiasis, ALT, AST and Prothrombin time).

AST (OR 1.11, 95% CI 1.02 to 1.21), ALT (OR 0.92, 95% CI 0.86 to 0.99), PT (OR 2.11, 95% CI 1.15 to 3.88), and MPV (OR 2.28, 95% CI 1.22 to 4.25).

Cut-off values were calculated for diagnostic performance, and the cut-off value for MPV was 9.22 fl., sensitivity 75.5%, specificity 62%, PPV 40.3%, NPPV 93.4% and Accuracy rate 61.8%

**Conclusion:** We suggest that high MPV levels (especially those over 9.22 fl) may help to predict advanced fibrosis in patients with CHC. However, it should not be forgotten that MPV is not a specific marker for fibrosis, and the negative predictive rate seems more valuable to exclude a high fibrosis ratio in patients with CHC.

## INTRODUCTION

Hepatitis C virus infection, with an estimated prevalence of more than 170 million people infected worldwide, is a major health problem [1]. Prevalence rates reach up to 10-20% in parts of central Africa and Egypt [2] [3].

HCV infection and its complications represent major public health problem in Egypt, where 10%- 15% (about 9 million) of the general population is infected [4].

Monitoring of liver fibrosis progression is important in patients with chronic hepatitis C, not only because it prompts screening for HCC, but also those patients have the most urgent need for antiviral therapy [5].

Liver biopsy has been considered the gold standard and an indispensable reference method for therapeutic decisions regarding CHC, as treatment indication is based on histological findings including inflammatory grading and staging [6].

However, liver biopsy problems can limit its application as diagnostic procedure such as sampling errors and intra and inter observer variabilities [7]. In addition; liver biopsy is an invasive and painful procedure, bleeding, biliary peritonitis, and pneumothorax and mortality range from 0.01% - 0.1%. In additional liver biopsy is contraindicated in the presence of coagulopathy, thrombocytopenia, and ascites [8].

These limitations push us to search for new non-invasive approaches such as serum markers of hepatic fibrosis examples are: AST/ALT Ratio, AST to Platelet Ratio Index (APRI score), Fibrotest and Actitest, PGA Index, Forns Index and Hepascore [9] and new imaging techniques (fibrosan) [10].

Platelet volume and its mean (MPV) is an indicator of platelet function, activity and aggregation capacity [11].

High Mean platelet volume levels (especially those over 8.4 fL) may help to predict advanced fibrosis in patients with chronic hepatitis C [12].

## PATIENTS AND METHODS

This study was conducted on about 150 patients selected from 172 patients diagnosed with chronic hepatitis C infection who were referred to Tanta Fever Hospital in period from May 2013 to January 2014. They were 87 males (58%) and 63 females (42%) and their age ranged from 18 years to 59 years with mean age of  $(41.61 \pm 7.79)$  and 20 healthy volunteers as a control.

They were categorized into 2 main groups: Group 1 (patients group): 150 patients with CHC which subdivided according to liver biopsy METAVIR system into 4 subgroups: F0/F1: no fibrosis/portal fibrosis without septa (17 patients), F2: portal fibrosis with rare septa (82 patients), F3: numerous septa without cirrhosis (33 patients) and F4: cirrhosis (18 patients). Group 2 (control group): 20 healthy volunteers as a control group. An informed consent was obtained before patients enter the study.

Chronic HCV infection was confirmed by detectable HCV-Ab by ELISA  $\geq 6$  months and serum HCV-RNA positivity by PCR.

With the following inclusion criteria: Age: 18-60 years, Proven HCV infection by HCV Ab and HCV RNA  $\geq 6$  months, compensated liver disease, BMI  $< 30$ .

About 22 patients were excluded from the study because they had one or more of the following exclusion criteria: Co-infection with hepatitis B virus, other causes of liver disease, pregnancy for female, decompensated liver disease, diabetes mellitus, arthritis or any collagen disease, chest disease namely sarcoidosis and suppurative lung disease, liver transplantation, anticoagulant treatment and patients who had received specific antiviral therapy prior to study.

All patients will be subjected to the following: Full history taking, complete clinical examinations, laboratory tests (complete blood count, liver function tests, prothrombin time, renal function tests, schistosomal ab by ELISA, autoimmune markers (ANA), alpha-feto-protein and TSH), abdominal-pelvic ultrasound, HCV RNA by quantitative PCR, liver biopsy for histological examination and quantification of liver fibrosis and inflammation and measuring the mean platelet volume: is calculated by the following formula:  $MPV (fL) = [(platelet (\%)/ Platelet count (x10^9/L) or computerized calculation by complete blood counters (histogram) .$

## Statistical analysis

Data were collected, tabulated and statistically analyzed by computer using SPSS version 16. The following tests; arithmetic mean, standard deviation (SD), standard student "t test", Chi square Test ( $X^2$ ), sensitivity, specificity, accuracy, positive predictive value, negative predictive value, linear correlation coefficient (r), Roc curve (Receiver operating characteristic curve), significance of results (P value) to evaluate mean platelet volume as a fibrosis marker in patient with chronic hepatitis C.

## RESULTS

Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) shows no significant differences as regard age and the gender as shown in table (1). Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) shows no significant differences as regard HB%, RBCS and WBCS, but it showed significant differences regarding MPV and Platelet count as shown in table (2). Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) shows no significant differences as regard total bilirubin, direct bilirubin, ALT, AST, alkaline phosphate and serum albumin but it showed significant differences regarding Prothrombin time as shown in table (3). Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) shows no significant differences as regard creatinine and urea as shown in table (4). Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) shows no significant differences as regarding random blood sugar (RBS), alpha feto protein (AFP), anti nuclear antibody titre (ANA) and thyroid

stimulating hormone (TSH) as shown in table (5). Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) showed significant differences as regarding presence of the schistosomal antibodies as shown in table (6). Statistical comparison between the HCV patients GI (Patients group) and G II (Control group) showed significant differences as regarding ultrasound findings of the liver shown in table (7). Statistical analysis between HCV patients (group I) with different degrees of fibrosis (F0/F1-F2-F3-F4) regarding age, sex and PCR level of HCV RNA shows no significant differences between them., but show significant differences with MPV-platelets counts-schistosomiasis-ultra sounds findings- ALT- AST- prothrombin time as shown table (8). Uni-variate Logistic regression analysis shows association between different degrees of the fibrosis (F0/F1-F2-F3-F4) with MPV- platelets counts- schistosomiasis -ultra sounds findings- ALT- AST- prothrombin time.

Multi-variate Logistic regression analysis shows only 5 variables remained as independent risk factors: (MPV, schistosomiasis, ALT, AST and prothrombin time.) as shown in table (9). As shown in the table, where 5 independent risk factors to of fibrosis are observed from all aspect of Area Under the Curve (AUC) , Cut Off Point (COP), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy rate (AR). As shown in table (10) Comparison of Receiver Operator Characteristic Curves (ROC) for the diagnostic performance of ALT, AST, P.T and MPV in identifying fibrosis in chronic hepatitis C as shown in figure (1). A plot to obtain cut off value of MPV that displays sensitivity and specificity variation for each MPV value as shown in figure (2). A dot diagram that plots the distribution of CHC samples with different degrees of fibrosis (F0/F1-F2-F3-F4) around an 9.22 FL cut off value as shown in figure (3).

**Table (1):** Statistical comparison of the age and the gender between the studied groups

		GI (Patients group)		G II (Control group)		Total		X <sup>2</sup> test	P value
		No	%	No	%	No	%		
Age (years)	>40y	86	57.3	7	35	93	55	1.06	0.14 NS
	≤ 40y	64	42.7	13	65	77	45		
	Total	150	100	20	100	170	100		
Sex	Male	87	58	15	75.0	102	60	1.97	0.16 NS
	Female	63	42	5	25.0	68	40		
	Total	150	100	20	100	170	100		

NS, non significant

**Table (2):** Statistical comparison of the results of complete blood picture between studied groups (HB%-RBCS-WBCS-MPV- Platelets)

Variable	GI ( Patients group)		G II (Control group)		Student t test	P value
	Mean	± SD	Mean	± SD		
HB% ( N= 12-16 gm/dL)	14.096	1.73	13.23	1.62	2.112	0.076 NS
RBCs ( $N = 4.5 - 6.5 \times 10^6$ /mm)	5.19	0.65	5.2	0.88	0.05	0.96 NS
WBCs ( $N = 4 - 11 \times 10^3$ /mm)	6.9	1.81	6.91	1.47	0.011	0.99 NS
MPV(6.5- 11.5 Femtolitre (F.L) *femtolitre = $10^{-15}$ litres	8.95	1.39	7.57	0.68	4.38	0.043 S
Platelets count ( $150 - 450 \times 10^3$ /mm)	188.9	46.49	226.03	68.36	2.36	0.020 S

S, significant, NS, non significant

**Table (3):** Statistical comparison of the results of liver function tests between studied groups (T.BIL-D.BIL-ALT-AST- Alk. Ph-S.alb- P.T)

Variable	GI ( Patients group)		G II (Control group)		Student t test	P value
	Mean	± SD	Mean	± SD		
Total bilirubin(mg/dl) (N=0.2-1.2mg/dl)	0.67	0.26	0.64	0.26	0.491	0.624 NS
Direct bilirubin(mg/dl) (N = upto 0.25 mg/dl)	0.222	0.11	0.226	0.14	0.127	0.899 NS
ALT (U/L) (up to 35)	56.59	46.8	42.8	12.75	1.31	0.048 NS
AST (U/L) (up to 41)	44.69	28.39	38.35	8.22	0.99	0.035 NS
Alkaline phosphate(U/L) (40-129 male /35-104 female)	102.49	58.13	129.1	85.74	1.81	0.073 NS
S. Albumin gm/dl (N=3.5-5.4)	4.36	0.36	4.33	0.39	0.397	0.692 NS
Prothrombin time (N=11:14 sec.)	12.77	0.60	12.83	0.55	0.43	0.037 S

S, significant, NS, non significant

**Table (4):** Statistical comparison of the results of renal function tests between studied groups (creatinine- urea)

Variable	GI ( Patients group)		G II (Control group)		Student t test	P value
	Mean	± SD	Mean	± SD		
Creatinine (n=0.5-1.5) mg/dl	0.795	0.15	0.74	0.14	1.64	0.103 NS
Urea (n=15-45) mg/dl	24.54	5.5	22.0	4.14	1.43	0.155 NS

NS, non significant

**Table (5):** Statistical comparison of the results of (RBS-AFP-ANA-TSH) between studied groups

Variable	GI ( Patients group)		G II (Control group)		Student t test	P value
	Mean	± SD	Mean	± SD		
Random blood sugar(RBS) (N= up to 140mg/dl)	101.21	37.3	103.2	27.21	0.231	0.818 NS
AlphaFetoProteins (AFP) (Up to 10 ng/ml)	5.22	9.76	3.18	4.16	1.79	0.074 NS
AntiNuclear Antibody titre(ANA) (Up to 14 u/ml)	8.58	2.49	7.96	2.17	1.07	0.285 NS
Thyroid Stimulating Hormone (N=0.27-4.2 uIU/ml)	2.67	10.85	1.52	0.77	1.41	0.16 NS

NS, non significant

**Table (6):** Statistical comparison of the results of Schistosomal antibodies between studied groups

Schistosomal antibodies	GI ( Patients group)		G II (Control group)		Total		X <sup>2</sup> test	P value
	No	%	No	%	No	%		
Present	99	66%	9	45%	111	65.3	4.12	0.042 S
Absent	51	34%	11	55%	59	34.7		
Total	150	100	20	100	170	100		

S, significant

**Table (7):** Statistical comparison of the ultrasonographic findings of the liver between the studied groups

Ultra sound finding of liver	GI ( Patients group)		G II (Control group)		Total		X <sup>2</sup> test	P value
	No	%	No	%	No	%		
Normal	53	35.3%	9	45%	61	35.90%	4.12	0.027 S
Fine periportal fibrosis	52	34.7%	8	40%	56	32.90%		
Coarse periportal fibrosis	22	14.7%	1	5%	24	14.10%		
Bright fatty liver	23	15.3%	2	10%	27	15.90%		
Total	150	100	20	100%	170	100%		

S, significant

**Table (8):** Statistical comparison between case groups regarding the different degrees of fibrosis (f0/f1-f2-f3-f4)

		F0-F1 N=17	%	F2 N=82	%	F3 N=33	%	F4 N=18	%	X <sup>2</sup>	P value
Age	>40y	13	76.47	43	52.43	22	66.66	10	55.55	1.325	0.362
	≤40y	4	23.52	39	47.56	11	33.33	8	44.44		
sex	Male	11	64.70	45	54.87	18	54.54	13	72.22	1.693	0.421
	Female	6	35.29	37	45.12	15	45.45	5	27.77		
MPV	> 8.5 FL	6	35.29	44	53.65	20	60.60	14	77.77	5.626	0.001
	≤ 8.5FL	11	64.70	38	46.34	13	39.39	4	22.22		
Plateets counts Normal (150-450) × 10 <sup>3</sup> cmm	Normal	15	88.23	76	92.6	20	60.60	10	55.55	2.325	0.014
	<150 × 10 <sup>3</sup> cmm	2	11.76	4	4.87	4	12.12	7	38.88		
	>450 × 10 <sup>3</sup> cmm	0	0	2	2.43	0	0	1	5.55		
Schistos omiasis	Positive	9	52.94	55	67.07	21	63.63	14	77.77	3.325	0.013
	Negative	8	47.05	27	32.92	12	36.36	4	22.22		
Ultra sounds finding	Normal	5	29.41	33	40.2	11	33.33	3	16.66	4.526	0.024
	Fine periportal fibrosis	7	41.17	28	34.14	15	45.45	5	27.77		
	Coarse periportal fibrosis	3	17.64	9	10.97	5	15.15	9	50		
	Bright fatty liver	2	11.76	12	14.63	3	9.09	1	5.55		
ALT	>39.5	9	52.94	51	62.19	22	66.66	11	61.11	3.258	0.022
	≤39.5	8	47.05	31	37.80	11	33.33	7	38.88		
AST	>38.5	8	47.05	49	59.7	23	69.69	8	44.44	4.619	0.035
	≤38.5	9	52.94	33	40.2	10	30.30	10	55.55		
Prothro mbin time	>12.65	10	58.82	35	42.68	19	57.57	9	50	6.253	0.001
	≤12.65	17	100	47	57.31	14	42.42	9	50		
PCR OF HCV RNA	>MILLION	8	47.05	36	43.90	18	54.54	12	66.66	0.247	0.526
	≤MILLION	9	52.94	46	56.09	15	45.45	6	33.33		

**Table (9):** Correlation of variable data with degree of fibrosis and Logistic (Univariate and multivariate) regression analysis

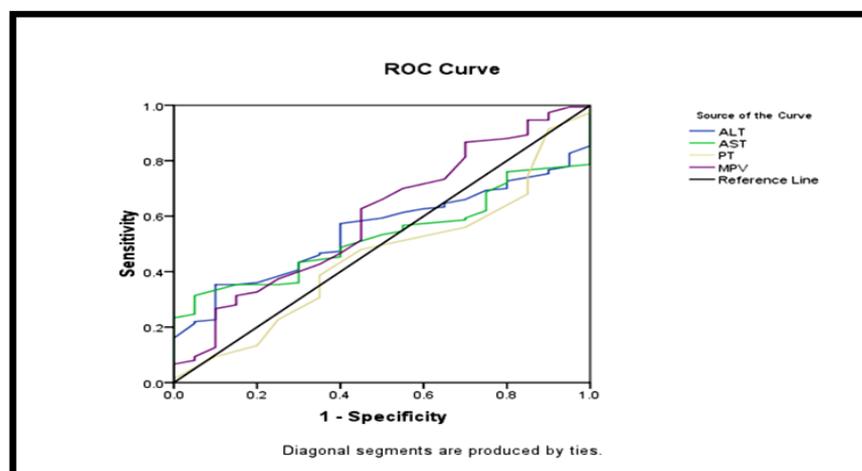
Variables	Fibrosis degree (f0/f1-f2-f3-F4)		
	P- VALUE	Logistic regression analysis	
		Univariate OR* (95% CI**)	Multivariate OR (95 %CI)
Age	0.362 NS	1.02 (0.97-1.07)	-----
Sex	0.421 NS	1.75 (0.67-4.59)	-----
MPV	0.001 S	1.56 (1.07-2.27)	2.28 (1.22-4.25)
Platelets counts	0.014 S	0.98 (0.97-0.99)	-----
Schistosomiasis	0.013 S	1.04 (0.99-1.08)	1.30 (1.15:2.20)
Ultra sounds finding	0.024 S	0.98 (0.93-1.03)	-----
ALT	0.022 S	1.02 (1.00-1.03)	0.92 (0.86-0.99)
AST	0.035 S	1.03 (1.01-1.05)	1.11 (1.02-1.21)
Prothrombin time	0.001 S	1.97 (1.28-3.04)	2.11 (1.15-3.88)
PCR OF HCV RNA	0.526 NS	0.58 (0.31-1.09)	-----

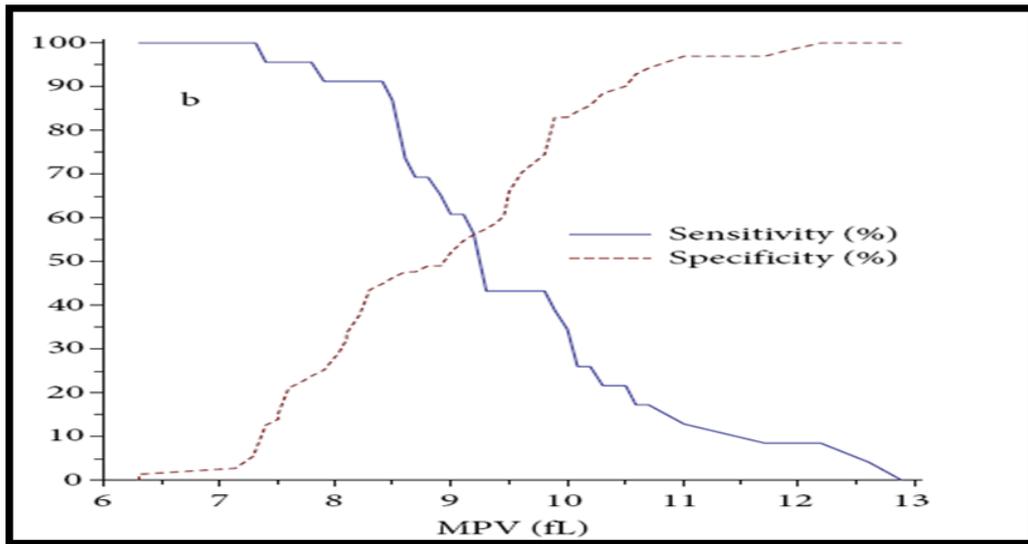
\*OR: Odd Ratio

\*\*CI: Confidence interval

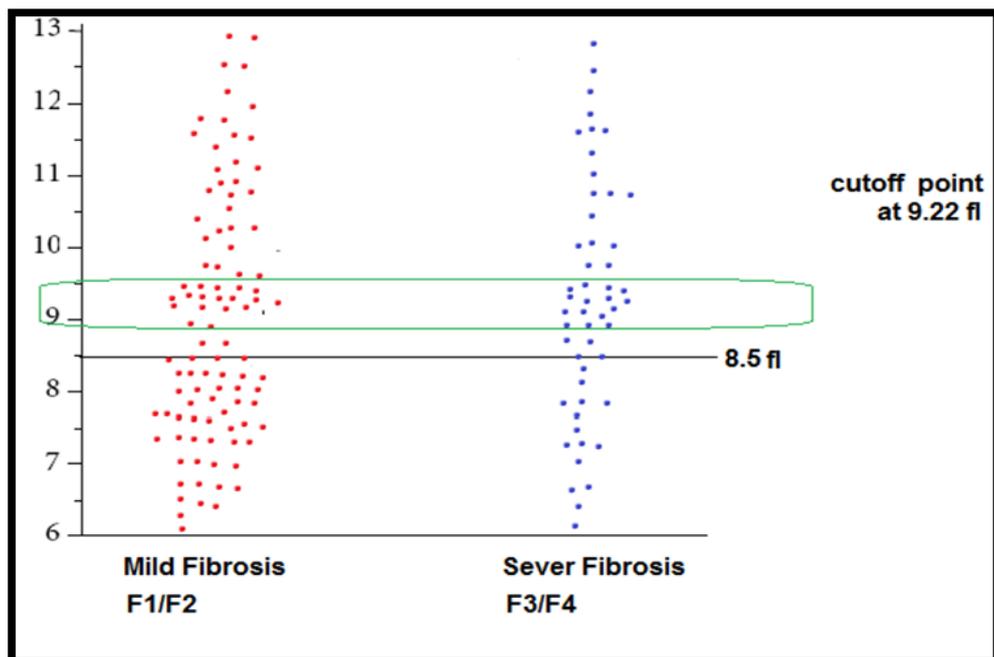
**Table (10):** Diagnostic measures of parameters in detection of liver fibrosis

Parameters	Diagnostic measures						
	Area Under Curve (AUC) %	Cut Off Point (COP) %	Sensitivity (Sen.) %	Specificity (Spec.) %	Positive Predictive Value (PPV) %	Negative Predictive Value (NPV) %	Accuracy Rate (AR) %
ALT	0.547	39.5	59.3	75.0	40.9	87.1	68.2
AST	0.528	38.5	53.3	66.0	44.9	88.5	72.9
P.T	0.454	12.65	50.0	80.0	52.9	83.4	76.8
MPV	0.598	9.22	75.7	62.0	40.3	93.4	61.8

**Figure (1):** Comparison of Receiver Operator Characteristic curves (ROC) for the diagnostic performance of ALT, AST, P.T and MPV in identifying fibrosis in chronic hepatitis C.



**Figure (2):** A plot to obtain cut off value of MPV that displays Sensitivity and specificity variation for each MPV value.



**Figure (3):** A dot diagram that plots the distribution of CHC samples with different degrees of fibrosis (F0/F1-F2-F3-F4) around an 9.22 FL cut off value.

## DISCUSSION

Monitoring of liver fibrosis progression is important in patients with chronic hepatitis C, not only because it prompts screening for HCC, but also those patients have the most urgent need for antiviral therapy [5]

In this study, statistical analysis revealed no significant difference between the studied groups as regard age and sex and that disagrees with Poynard et al. [13] who found an increased rate of fibrosis if the age at infection was > 40 years and if sex was male and also with Ahmad et al. [14] who found that liver fibrosis stages increase with age increasing.

The present study showed non-significant differences between studied groups as regarding HB%-RBCS-WBCS-RBS where p-value >0.05 while it showed significant differences regarding platelets count (where p-value <0.05)

In this study, statistical comparison of studied groups showed no significant differences regarding total bilirubin, direct bilirubin and alkaline phosphate (where p-value >0.05), but showing significant differences regarding ALT and AST, (where p-value <0.05). This is in agreement with Ahmad et al. [14] who found that ALT and HB % were not significant, while AST levels were good to differentiate liver fibrosis stages, they also found that viral load, bilirubin, ALP, AST, serum albumin and platelet count were significantly associated with various fibrosis stages. They concluded that as the fibrosis increased to cirrhosis, bilirubin and serum ALP level also increased, while platelet count and serum albumin level gradually reduced so, construction of a new index for the prediction of fibrosis stage based on the relationship four-biochemical markers, ALP, bilirubin, albumin and platelet count, they developed a new fibrosis-cirrhosis index for the prediction of HCV disease progression from initial fibrosis stage to end stage cirrhosis., it can be represented as:  $FCI = (ALP \times Bilirubin) / (Albumin \times Platelet\ count)$  [14]

Peck-Radoslavljevic [15] showed that low platelet count (thrombocytopenia) is a valuable marker of advanced liver disease, but it may be related to many mechanisms : hypersplenism, myelo-suppression by HCV, decreased thrombopoetin production, autoimmune.

Chun et al. [16] Showed that severity of liver fibrosis was correlated significantly with a gradual

increase in AST level as well as a decrease in platelet count, and that is called AST to platelet ratio index (APRI):

$$APRI = \frac{AST\ level\ (/ULN)}{Platelet\ counts\ (10^9/L)} \times 100$$

Muzzi et al. [17] found that patients with fibrosis were older, had higher levels of fasting glucose, higher levels of fasting insulinemia, a higher HOMA score and had higher Metavir activity score and more steatosis than patients without fibrosis.

Gordon et al. [18] found that assay of AST levels had a stronger correlation than ALT with hepatic fibrosis.

Giannini et al. [19] found that the increase in AST levels is related to mitochondrial dysfunction and to reduced clearance of AST by hepatic sinusoidal cells. Reversal of AST/ALT was reported in patients who progress from chronic hepatitis to liver cirrhosis and the AST/ALT ratio of more than 1 had a good predictive value for advanced fibrosis.

Giannini et al. [19] found that an AST/ALT ratio had also a predictive value with ratio greater than 1.16 in identifying cirrhotic patients who died within 1 year follow up and had 81.3% sensitivity and 55.3% specificity.

Mustafa et al. [20] found that an inverse relationship between indirect bilirubin levels and advanced liver fibrosis caused by CHC genotype 1b.

Imbert-Bismut et al. [21] concluded that bilirubin may be used as marker of liver injury, while a change in ALP levels greater than 120 U/L can be indicative of advanced disease progression., These findings suggest that serum ALP and bilirubin may be used as serum markers to assess the disease progression and fibrosis stages in chronic HCV patients.

Murawaki et al. [22] and Lackner et al. [23] concluded that platelets not only predict fibrosis but also correlate with fibrotic stages .

Many studies supported that platelet count alone may be clinically valuable as a non-invasive serum marker for liver fibrosis and cirrhosis [24,25].

In this study statistical comparison between the studied groups showed no significant differences regarding serum Albumin, AFP, ANA and TSH (where p-value >0.005), but it showed significant differences regarding Prothrombin time ( p-value

<0.05). This is in agreement with Croquet et al. [26] who noted that Prothrombin time (PT) as an index that reflects the synthesis capacity of the liver is one of the earliest indicators of liver cirrhosis and advanced fibrosis.

Hu et al. [27] showed that in patients with chronic hepatitis C, 23% of them had elevated serum AFP that is independently associated with stage III/IV hepatic fibrosis, elevated level of AST, and prolonged INR, where also serum AFP level of 15.0 µg/L was 22.8% sensitive and 94.5% specific for stage III/IV fibrosis.

In this study, statistical analysis revealed no significant differences between cases group and control group regarding serum creatinine and blood urea (where  $p$ -value > 0.05). Serra et al. [28] and Giannini et al. [29] found that Serum creatinine is increasingly being incorporated into prognostic models for patients with decompensated cirrhosis. In general, Creatinine and urea clearance are used to estimate glomerular filtration rate. using Creatinine based methods to estimate GFR in advanced liver disease patients is problematic for multiple reasons. Decline in hepatic functional capacity results in decreased creatine production and lower serum creatinine levels. Advanced liver disease patients are known to have less skeletal muscle mass, resulting in diminished creatine storage and less conversion of creatine to creatinine. All of these factors lead to a decreased serum creatinine level in advanced liver disease patients, making creatinine an unreliable factor in estimating GFR [30].

In this study statistical comparison between studied groups showed significant differences regarding schistosomiasis ( $p$ -value <0.05). Andrade [31] showed that schistosomiasis invariably results in liver fibrosis of the host. This fibrosis may be represented by small focal areas of chronic inflammation and excess extracellular matrix deposited in periportal granulomas, distributed in variable numbers at the periphery of the portal vein system. This is the outcome of 90% of the infected population in endemic areas. Thus, host-parasite interactions in schistosomiasis help us to understand a number of important features of liver fibrosis: its initiation and regulation, the significance of accompanying vascular changes, the dynamics of fibrosis formation and regression with anti-parasitic treatment; host genetic and immunological contributions.

Kamal et al. [32] reported that HCV/schistosomiasis co-infected patients have more rapid progression of hepatic fibrosis than those with HCV mono-infection.

In contrast Ahmad et al. [33] showed that schistosomiasis co-infection with HCV and/or non-alcoholic steatohepatitis had no significant impact on fibrosis stage. Mahasen et al. [34] showed that positive schistosomal serology has no effect on fibrosis stage but it is significantly associated with failure of response to HCV treatment despite anti-schistosomal therapy.

Andrade [35] and Blanton et al. [36] showed that several clinical and pathological studies have shown that schistosomal hepatopathy is a reversible condition and that resolution of the schistosomiasis disease is accompanied by subsequent fibrosis resorption.

In this study statistical comparison between studied groups showed significant sensitivity of ultrasound ( $p$ -value <0.05). Chih-Ching et al. [37] concluded that routine clinical ultrasound is not a sensitive predictor of early fibrosis in chronic viral hepatitis. Surface nodularity is the most sensitive sonographic feature for the detection of significant fibrosis and routine clinical ultrasound is the most useful for the detection of cirrhosis.

Bonekamp et al. [38] and Fontana and Lok [39] reported that Ultrasound is easily accessible in most health-care centers, making it the most commonly used imaging technique to evaluate chronic liver disease. Previous studies have demonstrated that ultrasound can predict liver cirrhosis or significant fibrosis.

Mathiesen et al. [40] and Nishiura et al. [41] concluded that the reasons for the low sensitivity and accuracy of ultrasound may be due to many factors. The pattern of fibrosis affects the extent of nodularity and echogenicity, and may account for the differences in the diagnostic performance seen between hepatitis B- and hepatitis C-related cirrhosis on ultrasound. However, the complex pattern of changes in chronic liver disease that is reflected in histopathology includes mixed features of steatosis, necrosis, and inflammation. These may affect the morphological appearance of the liver on ultrasound, rather than the presence of fibrous tissue alone.

Bonekamp et al. [38] demonstrated that wide range of ultrasound parameters and variable recommended algorithms reflect the limitations

of ultrasound, including operator dependency and limited accuracy in the staging of fibrosis. Currently, transient elastography (Fibroscan) and magnetic resonance elastography (MRE) provide the most reliable results in predicting fibrosis. However there is a need for larger longitudinal studies to define standardized diagnostic criteria for staging fibrosis with reproducible results before a noninvasive imaging technique can replace liver biopsy.

In this study statistical comparison between studied groups from aspect of degree of fibrosis and PCR level (HCV RNA) revealed no significant difference. This is in disagreement with Ahmad et al. [14] who showed that viral load was significant among fibrosis stages. It gradually increased in advanced fibrosis, and then suddenly dropped in cirrhosis.

In this study Statistical comparison between studied groups from aspect of degree of fibrosis and MPV showed significant difference (p-value <0.05) and positive correlation and cut off point at 9.22 fl, sensitivity (75.7%), specificity (62%) NPV (93.4%), PPV(40.3%) and AR (61.8%). This is in agreement with Karaman et al. [12] who found that MPV was significantly higher in patients with CHC when compared to control subjects. In contrast, PC was significantly lower in CHC patients. Portal hypertension and hyper-splenism in some of the subjects with advanced fibrosis may be the cause of this significant difference. And also suggest that high MPV levels (especially those over 8.4 fL) may help to predict advanced fibrosis in patients with CHC. However, it should not be forgotten that MPV is not a specific marker for fibrosis and a high NPR (Negative Predictive Rate) seems to be more important in helping to exclude a high fibrosis ratio in patients with CHC.

## CONCLUSION

- Statistical analysis between HCV patients (group I) with different degrees of fibrosis (F0/F1-F2-F3-F4) regarding age, sex and PCR level of HCV RNA showed no significant differences between them, but showed significant differences with MPV- Platelets counts- Schistosomiasis -Ultra sounds findings- ALT-AST- Prothrombin time.
- Uni-variate Logistic regression analysis showed association between different degrees of the fibrosis (F0/F1-F2-F3) with (MPV- Platelets counts-Schistosomiasis-Ultra sounds findings-

ALT- AST- Prothrombin time). Multi-variate Logistic regression analysis shows only 5 variables remained as independent risk factors: (MPV, Schistosomiasis, ALT, AST and Prothrombin time).

- The results of this study suggest that high MPV level especially  $\geq 9.22$  fl as a cutoff point, may help to predict advanced fibrosis in patients with CHC. However, it should not be forgotten that MPV is not a specific marker for fibrosis where sensitivity (75.7%) and specificity (62%), PPV (40.3%) and AR (61.8%) and also high NPV (93.4%) seems to be more important in helping to exclude a high and fibrosis degree in patients with CHC.

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