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THE ASSOCIATION OF PLATELET COUNTS AND ALKALINE PHOSPHATASE LEVELS WITH FIBRO SCAN SCORE OF PATIENTS WITH HEPATITIS C

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Abstract:

Background: *Hepatitis C has become a challenge for developing countries like Pakistan. Up until now, liver biopsy and fibro scan have been the most reliable methods to gauge the intensity of this disease. However, as patients with liver disease need frequent check-ups, carrying out such invasive or expensive techniques regularly seems highly infeasible. Therefore, the need for devising a noninvasive and inexpensive method is greatly on the rise.*

Objectives*: Our aim was to examine the relation of platelet counts and alkaline phosphatase levels with fibro scan scores of patients with hepatitis C.*

Patients and Methods:

Methods: *The retrospective cross sectional study was carried out in medicine unit 1 & 2 and hepatitis clinic of Lahore General Hospital, Lahore, starting from February 15, 2018 to January 11, 2019. We studied 1898 HCV infected patients which were got CBC, LFTs, ELISA, PCR and fibro scan done to perfectly diagnose ongoing hepatitis C infection. In order to differentiate HCV fibrosis progression, we compared the serum platelet and alkaline phosphatase levels with fibro scan.*

Results: *Patients with moderate and severe liver disease had lower platelet counts and increased alkaline phosphatase levels. No threshold value of platelet count could, however, accurately predict the grade of fibrosis of liver. Thus, no noticeable relationship of platelet counts with fibro scan score was found although alkaline phosphatase levels did show a statistically significant relationship with fibro scan score.*

Conclusions: *Platelet count and alkaline phosphatase levels in hepatitis C can help determine the severity of the disease, but they cannot be exclusively relied upon in monitoring its progress.*

Keywords: *Hepatitis C, Blood Platelets, Fibro scan score.*

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INTRODUCTION:

Hepatitis C virus (HCV), a blood borne pathogen, is a single stranded enveloped RNA virus [1][2]. Infection from Hepatitis C virus is known to be a major risk factor in the generation of liver cirrhosis and hepatocellular carcinoma accounting for up to 0.5 million deaths every year. [3][4][5]. In 2015, 71 million people were estimated to be affected globally with chronic HCV infection [6]. Highly endemic in Pakistan, HCV prevalence was estimated to be 4.8% by a national survey conducted in 2007 which accounts to roughly one tenth of the global burden [7]. Major transmission routes include intravenous drug use, blood transfusion, hemodialysis, organ transplantation and sexual intercourse [8].

Immune mediated and metabolic factors, both, play a role in the pathogenesis of HCV marked by viral replication inside liver cells and eventually cellular necrosis [9]. In a vast majority of infected individuals, the virus is able to escape innate and adaptive immunity leading to chronicity. Cytotoxic lymphocytes are then implicated in hepatocellular damage in an attempt to clear the infection. The inflammation and necrosis eventually cause fibrosis of the liver, which, over a span of time, leads to cirrhosis [10].

Determination of the stage of fibrosis and presence of cirrhosis is usually necessary for consideration of treatment options. Liver biopsy has long been used for this purpose albeit being expensive and with a risk of potential life-threatening complications [11]. Transient Elastography (*FibroScan*®) is another rapid, non-invasive technique which measures liver stiffness [12]. These measurements have been shown to reliably predict fibrosis stages in chronically infected HCV patients [13].

Our retrospective cross sectional study analyses the relationship of "alkaline phosphatase" and "platelet count" with *FibroScan*® score of HCV infected patients. Furthermore, we also consider the usefulness of these blood tests in predicting the stage of fibrosis in HCV infected patients as an alternate to *FibroScan*®.

MATERIAL AND METHODS:

The retroprospective cross sectional study was conducted in medicine unit 1&2 and hepatitis clinic of Lahore General Hospital, Lahore starting from February 15, 2018 to January 11, 2019. We studied 1898 HCV infected patients which were got CBC, LFTs, ELISA, PCR and fibro scan done to perfectly diagnose ongoing hepatitis C infection . In order to differentiate HCV fibrosis progression, we compared the effectiveness of readily available serum aminotransferase Levels i.e. PLT and ALP with fibro scan

Statistical analysis:

SPSS windows version 22 was used to analyze the data. p value of less than 0.05 was considered statically significant. To signify the marked association between stages of liver fibrosis and continuous variables, Spearman's rank correlation was used. We used student t-test to relate arithmetic means and parameters. Various univariate analysis was performed for multiple biomarkers.

RESULTS:

Patient's data:

1181 patients were included in our study. Among them 858(72.7%) patients are female and 323 (27.3%) are male shown in table.1. According to data of marital status 1102(93.3%) patients are married while 74(6.3%) are unmarried. 891(75.4%) patients had genotype 3a, 285(24.1%) had 1b and 5(4%) had 1A genotype.

Table 1: Showing gender distribution of 1898 patients.

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	858	72.7	72.7	72.7
	Male	323	27.3	27.3	100.0
	Total	1181	100.0	100.0	

Table 2: Showing marital status distribution of 1898 patients.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Married	1102	93.3	93.3	93.3
	Unmarried	79	6.6	6.6	99.6
	Total	1181	100.0	100.0	

Table 3: Showing distribution of occupation of 1898 patients.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Housewife	529	44.8	44.8	44.8
	Laborer	541	45.8	45.8	90.6
	Working Lady	111	9.4	9.4	100.0
	Total	1181	100.0	100.0	

Table 4: Showing distribution of genotype of 1898 patients.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3a	891	75.4	75.4	75.4
	1b	285	24.1	24.1	99.6
	1A	5	.4	.4	100.0
	Total	1181	100.0	100.0	

The determination of fibrosis stage among HCV infected patients depicts that among 1181 patients 758(64.2%) patients are in fibrosis stage F0-F1 stage, 82(6.9%) patients are in F2 stage, 141(11.9%) patients in F3 and 200(16.9%) patients are in F4 leading cirrhosis.

Table 5: Showing distribution of fibrosis stages in 1898 patients.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F0-F1	758	64.2	64.2	64.2
	F2	82	6.9	6.9	71.1
	F3	141	11.9	11.9	83.1
	F4	200	16.9	16.9	100.0
	Total	1181	100.0	100.0	

Determination of fibrosis stage using already available variables.

The means and standard deviations of age of patients ,Baseline Viral Load, Albumin , ALT , AST , Bilirubin , Fibroscan score, AAR, Platelet count, Alkaline Phosphatase, were 39.748±12.76, 606581.84± 2222871.620, 3.4560±1.37807, 84.411±214.0812., 76.912 ±71.0574, 1.2592±1.41396, 11.3780±12.17512, 708836.7070 ± 2895341.78023, 302.025+138.4340 respectively (Table of Descriptive Statistics).

Table 6: Showing descriptive statistics of 1898 patients.

	N	Minimum	Maximum	Mean	Std. Deviation
Age of Patient	1176	14.0	100.0	39.748	12.7610
Baseline Viral Load	1181	119	29403943	606581.84	2222871.620
Albumin	1181	.70	6.00	3.4560	1.37807
ALT	1181	10.0	7000.0	84.411	214.0812
AST	1181	15.0	1085.0	76.912	71.0574
Bilirubin	1181	.50	24.00	1.2592	1.41396
Fibroscan score	1181	2.70	76.00	11.3780	12.17512
Platelet Count	1181	234000.00	26800000.00	708836.7070	2895341.78023
Alkaline Phosphatase	1181	51.0	1154.0	302.025	138.4340
Valid N (list wise)	1176				

The Independent sample T- test results for stage F0-F1 & F2 for different variables i.e. Platelet Count and Alkaline Phosphatase is given in the table below showing statistically significant relationship of all these variables with fibrosis stages of F0-F1 and F2 determined fibro scan score with $p<0.05$.

Table 7: Showing T test results for F0-F2 of 1898 patients.

Group Statistics						
	Fibrosis Stage	N	Mean	Std. Deviation	Std. Error Mean	p value
Platelet Count	F0-F1	758	918653.4644	3597298.02809	130659.74817	0.000
	F2	82	294000.0000	54394.76191	6006.89657	
Alkaline Phosphatase	F0-F1	758	299.422	137.7645	5.0038	0.213
	F2	82	279.598	126.1940	13.9358	

The Independent sample T- test results for stage F3 & F4 for different variables i.e. Platelet Count and Alkaline Phosphatase is given in the table below showing statistically significant relationship of all these variables with fibrosis stages determined fibro scan score with $p<0.05$.

Table8: Showing T test results for F3 &F4 of 1898 patients.

Group Statistics						
	Fibrosis Stage	N	Mean	Std. Deviation	Std. Error Mean	P value
Platelet Count	F3	141	322403.0142	60250.31294	5073.99168	0.000
	F4	200	356150.0000	94685.23628	6695.25727	
Alkaline Phosphatase	F3	141	325.901	129.0367	10.8669	0.166
	F4	200	304.251	150.3362	10.6304	

Univariate analysis:

Univariate analysis of Platelet Count and Alkaline Phosphatase showed a statistically significant relationship with Pearson's correlation coefficients (R) values given below.

. R Squared (platelet count) = .103 (p value =)
. R Squared (alkaline phosphatases) = .245 (p value =)

Linear curve estimation analysis with Analysis of variances (ANOVA):
Linear curve estimation analysis with Analysis of variances (ANOVA) for Platelet Count and Alkaline Phosphatase showed a statistically significant relationship with Spearman's correlation coefficients (R) values of 0.087(p<0.05) , 0.492(p< .05) , 0.091(p<.05), 0.334(p<.05), 0.568(p<.05) , 0.234(p<.05) and 0.066(p<.05) respectively.

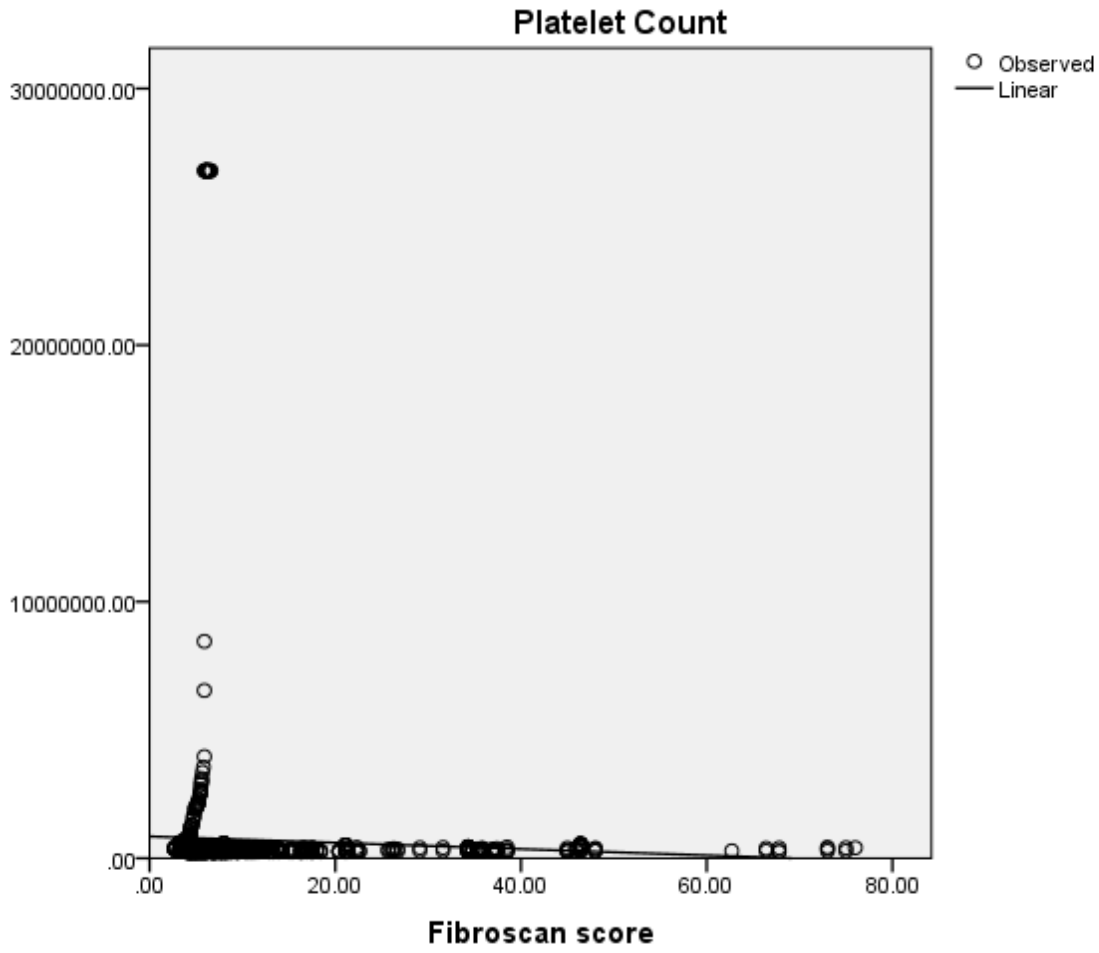

Fig. 1: Linear curve estimation analysis for platelet count vs fibroscan score

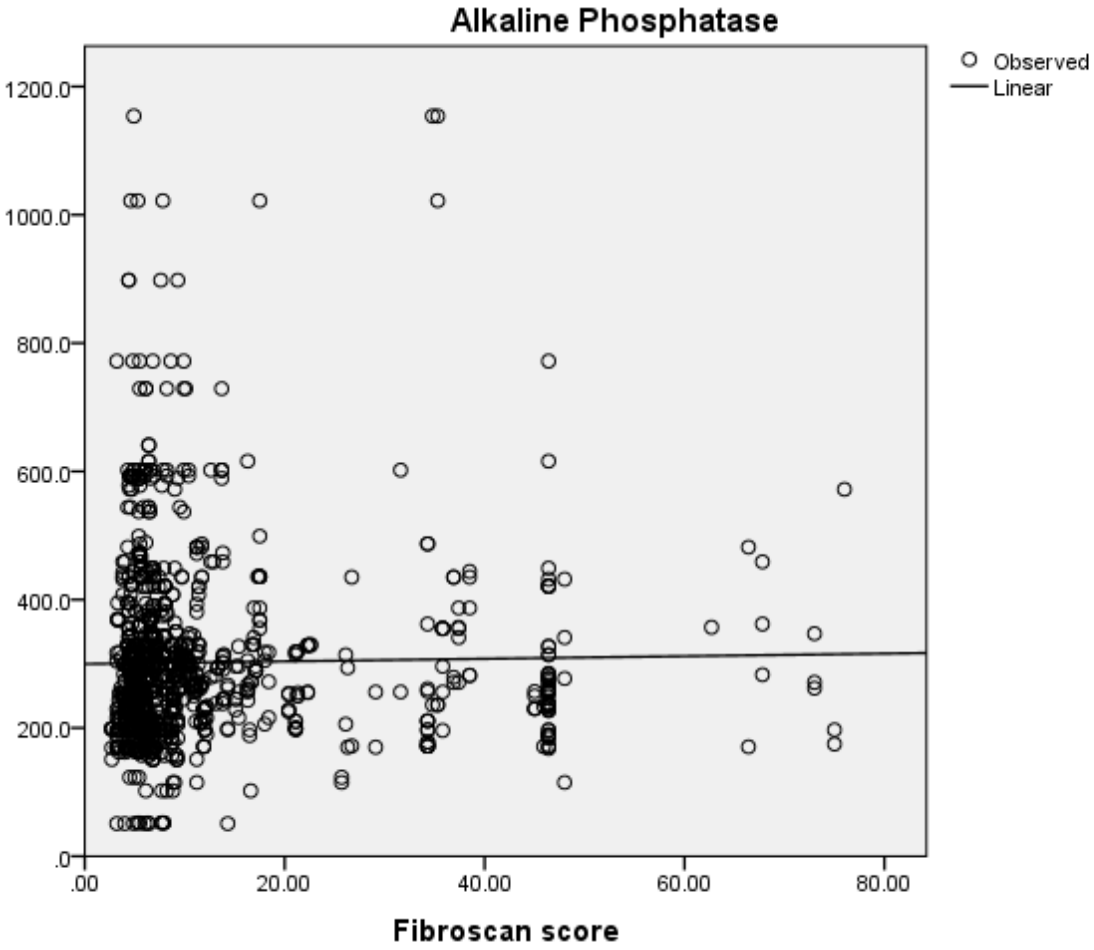

Fig. 2: Linear curve estimation analysis for alkaline phosphatase vs fibroscan score

DISCUSSION:

Hepatitis C infection, one of the leading cause of liver cirrhosis and hepatocellular carcinoma, is highly prevalent in Pakistan. Liver biopsy has long been used to determine the stage of fibrosis and cirrhosis in HCV infected patients but with the risk of complications. Transient Elastography (*FibroScan*®) is another procedure used to ascertain the degree of liver damage in chronically infected HCV patients. The aim of this study was to analyze the relationship between "alkaline phosphatase" and "platelet count" with *FibroScan*® score of HCV infected patients and the usefulness of these blood tests in predicting the stage of as an alternate to *FibroScan*®.

Our study included a total of 1181 patients. 72.7% of the presenting patients were female and 27.3% of the total count were male. Females appear more prone to infection possibly due to the fact that they are more exposed to risk factors such as getting blood transfusion during pregnancy.

In our study, 75% patients had genotype 3a which is more prevalent in Pakistan [11]. Among 1181 patients 93.3 % were married which alludes to the fact that sexual activity could be a contributing factor in the causation of disease [12].

The mean and standard deviation of baseline Viral load, ALT, AST, Fibroscan score, Platelet count, and Alkaline phosphatase were 606581.84± 2222871.620, 84.41171.0574±214.0812, 76.912 ±71.05,

708836.7070±2895341.78, 11.3780±12.17512, 302.025+138.4340 respectively.

The Independent sample T- test results for stage F0-F1 & F2 for the variable, Platelet Count, showed a significant relationship for platelet count with fibrosis. A possible explanation takes into consideration the fact that liver synthesizes much of the proteins required for platelet formation [13]. Liver fibrosis impairs this process resulting in a decrease in platelet formation and thrombocytopenia .

The relationship found was linear which suggests that with an increase in fibroscan score, there is a decrease in the platelet count. F3 and F4 stages can, to a certain extent, be predicted without using fibroscan which is an expensive method to use.

CONCLUSIONS:

Platelet count and alkaline phosphatase levels in hepatitis C can help determine the severity of the disease, but they cannot be exclusively relied upon in monitoring its progress.

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