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Research Article

### A COMPARISON OF SENSITIVITY AND SPECIFICITY OF TRANSIENT ELASTOGRAPHY I.E. FIBRO SCAN WITH SERUM AMINOTRANSFERASE LEVELS I.E. ALT & AST IN CHRONIC HCV INFECTED PATIENTS, A RETRO PROSPECTIVE CROSS-SECTIONAL STUDY AT LAHORE GENERAL HOSPITAL, LAHORE, PAKISTAN

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**Abstract:**

**Objective:** To assess the validity of Serum Aminotransferase Levels i.e. ALT & AST as fibrosis biomarker, we compared their serum levels with fibro scan for the fibrosis staging and predicting its progression in Pakistani population.

**Methods:** The retrospective 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 1181 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. ALT & AST with fibro scan.

**Results:** An AST had sensitivity of 82.6 and specificity of 79.0 for F4 stage. with AUC=0.883. An ALT for F4 stage, the sensitivity was 57.3, specificity 50.0 with AUC=0.771.

**Conclusion:** An AST and ALT can predict advance stage of fibrosis and cirrhosis in patients with chronic hepatitis C infection. In these patients, a liver biopsy and fibro scan may not be necessary.

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

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**INTRODUCTION:**

Have you heard the term “Serial Killer”? Yes! Right? Then you will be amazed to know that hepatitis C is “Silent Serial Killer”. Death from hep C is due to liver cirrhosis and hepatocellular carcinoma. According to the report of 2015, 167000 deaths occurred from liver cancer while 326000 from cirrhosis in hepatitis C patients. More than 700000 people die from hepatitis C related diseases every year.

HCV can cause both acute and chronic hepatitis. It is spread from blood to blood contact involving intravenous drug users, blood transfusions, needles stick injuries or vertical transmission. Its envelope proteins often vary their antigenic structure and our immune system can't keep up rendering the vaccine obsolete immediately. Hep C causes inflammation of liver which leads to jaundice, right upper quadrant pain and hepatomegaly. 60-80% become chronic. Lymphocytes infiltrate the portal tract and with chronic inflammation and infection, hepatocytes die. Liver cells and parenchyma are irritated and liver quickly needs to replace them. Some come to fibrosis and cirrhosis or alternatively hepatocytes go into frenzy and reproducing cells become malignant leading to hepatocellular carcinoma. Hep C infection leads to development of cryoglobulins or serum proteins containing IgM that precipitate and cool our temperature.

Globally 71 million people are estimated to be chronically infected. A significant number of those will develop cirrhosis or hepatocellular carcinoma. Pakistan has the world's second highest prevalence of the hepatitis C, second only to Egypt. (WHO, n.d.). HCV is “Silent Serial Killer” because the infected person remains symptomless unless a great amount of damage has occurred. According to a research conducted by U.S Department of Health and Human Services(HHS), 51% of persons living with hepatitis C infection do not know they have the virus. Especially in Pakistan, more than 60% of the population lives in rural areas. They do not have access to quality health facilities. Another huge problem is lack of awareness to get themselves screened for such infections periodically. Also, they are not financially that strong to afford tests like

PCR, ELISA and Fibroscan.

As DAAs have made it possible to achieve 95% cure rate. So the major hurdle today in our way to achieve HCV free world is the timely diagnosis of the infection. This research was carried out to assess how effective are AST and ALT in predicting different stages of fibrosis.

**MATERIAL AND METHODS:**

The retrospective 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 1181 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. ALT & AST 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. Receiver Operating Curves (ROC) and AUROC were performed to infer the diagnostic precision of the serum fibrosis indexes along with their cutoff points, sensitivities and specificities.

**RESULTS:****Patients Data:**

In this study we included 1181 patients. There are 690(58.4%) female patients and 491(41.6%) are male as shown in table.1. Among them 1092(92.7%) patients are married while 83(7.2%) are unmarried. Occupation related division shows that 414 patients are the housewives, 727 are the laborers and 40 are the working ladies.

Table 1: Showing gender distribution of 1181 patients.

|              | Frequency | Percent | Valid Percent | Cumulative Percent |
|--------------|-----------|---------|---------------|--------------------|
| Valid Female | 690       | 58.4    | 58.4          | 58.4               |
| Male         | 491       | 41.6    | 41.6          | 100.0              |
| Total        | 1181      | 100.0   | 100.0         |                    |

Table 2: Depicts marital status of patients.

|               | Frequency | Percent | Valid Percent | Cumulative Percent |
|---------------|-----------|---------|---------------|--------------------|
| Valid Married | 1095      | 92.7    | 92.7          | 92.5               |
| Unmarried     | 86        | 7.2     | 7.2           | 99.5               |
| Total         | 1181      | 100.0   | 100.0         |                    |

Table 3: Occupation of the patients.

|                 | Frequency | Percent | Valid Percent | Cumulative Percent |
|-----------------|-----------|---------|---------------|--------------------|
| Valid Housewife | 414       | 35.1    | 35.1          | 35.1               |
| Laborer         | 727       | 61.6    | 61.6          | 96.6               |
| Working Lady    | 40        | 3.4     | 3.4           | 100.0              |
| Total           | 1181      | 100.0   | 100.0         |                    |

Genotype distribution shows that 726(61.5%) patients are 3a, 378(32%) are 1b and 77(6.5%) are 1A.

Table 4: Genotype of the patients.

|          | Frequency | Percent | Valid Percent | Cumulative Percent |
|----------|-----------|---------|---------------|--------------------|
| Valid 3a | 726       | 61.5    | 61.5          | 61.5               |
| 1b       | 378       | 32.0    | 32.0          | 93.5               |
| 1A       | 77        | 6.5     | 6.5           | 100.0              |
| Total    | 1181      | 100.0   | 100.0         |                    |

Fibrosis stage findings among HCV infected patients shows that among 1181 patients, 581(49.2%) patients are in fibrosis stage F0-F1 stage, 71(6%) patients are in F2 stage, 161(13.6%) patients in F3 and 368(31.2%) patients are in F4 leading cirrhosis.

Table 5: Show stage of fibrosis in patients.

|             | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------------|-----------|---------|---------------|--------------------|
| Valid F0-F1 | 581       | 49.2    | 49.2          | 49.2               |
| F2          | 71        | 6.0     | 6.0           | 55.2               |
| F3          | 161       | 13.6    | 13.6          | 68.8               |
| F4          | 368       | 31.2    | 31.2          | 100.0              |
| Total       | 1181      | 100.0   | 100.0         |                    |

#### Fibrosis stage determination using already available variables

The means and standard deviations of age of patients, baseline viral load, fibroscan score, platelet count,

and alkaline phosphatase are  $42.523 \pm 12.9788$ ,  $1453430.51 \pm 7613073.991$ ,  $13.9569 \pm 12.49916$ ,  $198845.2159 \pm 61816.52915$ ,  $296.513 \pm 131.1257$  respectively (table 6).

Table 6: Descriptive Statistics

|                      | N    | Minimum  | Maximum   | Mean        | Std. Deviation |
|----------------------|------|----------|-----------|-------------|----------------|
| Age of Patient       | 1176 | 14.0     | 85.0      | 42.523      | 12.9788        |
| Baseline Viral Load  | 1181 | 135      | 107911144 | 1453430.51  | 7613073.991    |
| Fibroscan score      | 1181 | 2.60     | 75.00     | 13.9569     | 12.49916       |
| Platelet Count       | 1181 | 17900.00 | 281000.00 | 198845.2159 | 61816.52915    |
| Alkaline Phosphatase | 1181 | 51.0     | 1154.0    | 296.513     | 131.1257       |
| Valid N (list wise)  | 1176 |          |           |             |                |

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

Table 7: T test results of F0-F1 and F2

| : T test results of F0-F1 and F2 |                |     |        |                |                 |         |
|----------------------------------|----------------|-----|--------|----------------|-----------------|---------|
|                                  | Fibrosis Stage | N   | Mean   | Std. Deviation | Std. Error Mean | P Value |
| ALT                              | F0-F1          | 581 | 52.382 | 29.2279        | 1.2126          | .000    |
|                                  | F2             | 71  | 74.352 | 46.2228        | 5.4856          |         |
| AST                              | F0-F1          | 581 | 55.240 | 37.6598        | 1.5624          | .001    |
|                                  | F2             | 71  | 76.958 | 49.1913        | 5.8379          |         |

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

Table 8: T test results of F3 &amp; F4

|     | Fibrosis Stage | N   | Mean   | Std. Deviation | Std. Error Mean | P value |
|-----|----------------|-----|--------|----------------|-----------------|---------|
| ALT | F3             | 161 | 80.280 | 35.9945        | 2.8368          | .001    |
|     | F4             | 368 | 96.747 | 81.6962        | 4.2587          |         |
| AST | F3             | 161 | 74.286 | 37.6021        | 2.9635          | .000    |
|     | F4             | 368 | 96.231 | 75.8220        | 3.9525          |         |

**Univariate analysis:** Univariate analysis for ALT and AST score showed a statistically significant relationship with Person's correlation coefficients (R) values. Squared Value = .674 (P value = .000)

### DISCUSSION:

Our study showed that, Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) can predict advance stage of fibrosis and cirrhosis in patients with chronic hepatitis C infection. In these patients, a liver biopsy and fibroscan may not be necessary. Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) are the enzymes present in hepatic cells which are important for the ongoing metabolism. However, any injury to the liver causes the hepatic cells to release these enzymes in blood in a much greater amount than normal which is indicative of liver disease. According to our study, serum aminotransferase levels i.e. AST and ALT have significant relation with advanced stages of fibrosis. The comparison of sensitivity and specificity of aminotransferase levels with fibroscan for F4 stage showed that AST had sensitivity of 82.6 and specificity of 79.0 while for ALT, the sensitivity was 57.3 and specificity was 50.0.

A liver fibroscan or liver biopsy remains the gold standard for characterizing liver histology, but it is expensive and especially liver biopsy carries some morbidity and, very rarely, mortality risk. Thus, it should be performed in those who would benefit the most from the diagnostic and prognostic perspectives. (4. Julius Wilder1, n.d.)

Similar studies also suggested a significant relation between advanced stages of fibrosis and aminotransferases levels.

### CONCLUSION:

AST and ALT can predict advance stage of fibrosis and cirrhosis in patients with chronic hepatitis C infection. In these patients, a liver biopsy and fibro scan may not be necessary.

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