IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 8 Ver. III (Aug. 2017), PP 66-70
www.iosrjournals.org

Fib-04 Score At the End of Treatment in Chronic Hepatitis C Patients Treated with Pegylated Interferon And Ribavirin: An Observational Study

[*1]Dr. Muhammad Imran, [2]Prof Dr. Karim Kammeruddin, [3]Dr. Nida Sajid, [4]Dr. Amjad Iqbal, [5]Dr. Syeda Zufiesha zehra, [6]Mahboob Ali

[1]*Department of Medicine, Baqai Medical University*
[2]*Professor of Department of medicine, Baqai Medical University*
[3]*Assistant professor Department of Medicine, Baqai Medical University*
[4]*Department of Medicine, Baqai Medical University*
[5]*House officer, DIKIOHS, DUHS Karachi*
[6]*Dow University of Health Sciences, Institute of Nursing (MSN)*
Corresponding Author : [*] Dr. Muhammad Imran

Abstract
Background: *FIB-4 Score is a simple formula to predict liver fibrosis based on the standard biochemical / hematological values i.e. AST, ALT, Platelet count and age. The Score lower than 1.45 has a Negative Predictive Value (NPV) of 95% for significant fibrosis i.e. F3-F4 while, a Score of greater than 3.25 has a PPV of 80% for advance fibrosis i.e. F3-F4. So an improvement of FIB-4 Score is a possible indicator of change in liver fibrosis.*
Objective*: To observe the disparity in paired FIB-04 Score in hepatitis C patients treated with pegylated interferon and ribavirin at the beginning of the treatment and at the end of treatment evaluation (ETR).*
Method*: An observational study was carried out in patients with mono-infected, compensated CHC patients ,treated with Pegylated Interferon & Ribavirin for 24weeks to 48 weeks (according to genotype)in a tertiary care hospital (i.e. Baqai Medical University Hospital Nazimabad) from Jan 2010 to March 2015 in a paired manner i.e. before (at beginning) and at the End of treatment evaluation (ETR). Responses were analyzed by using 'Wilcoxon signed rank test. SPSS 23.00 version was used to analyze data.*
Results: *Fifty eight patients diagnosed with hepatitis C took part in the study out of which 24 were males (41.4%) with mean age 38.8 (22y-60y) and 34 were females (58.6%) with mean age 43.6 (31y-60y). Out of 58 participants, 8 patients were type 1 genotype, 48 patients were type 3 genotype and 1 was type 4. Genotype of 1 participant was not recorded. According to result evaluated, there is a statically significant decrease in FIB04 score from beginning of treatment (M=2.52, SD=1.35) to ETR (M=1.74, SD=1.37) justifying that there is a definite positive change in FIB-04 score (i.e. improvement in fibrosis)*
Conclusion: *Distinct positive change in FIB-4 Score was observed in Chronic Hepatitis C patients treated with pegylated interferon/ribavirin at the end of treatment.*
Keywords: *FIB-04 Score, hepatitis C, ribavirin, pegylated interferon*

I. Introduction

In chronic hepatitis C, it is essential to do clear-cut assessment of liver fibrosis to access therapeutic indication and complication [1]. These complications are primarily coupled with advance stage of the disease [2]. Liver biopsy is deemed to be gold standard in ruling out hepatic fibrosis [3, 4]. However, liver biopsy is constrained by its invasive character; deprived acceptance, esp. when constant measures are essential; expenditure and availability, predominantly in non-western countries; intra- and inter-observer variability [5, 6] and sampling errors which generate around 24% false negative response for cirrhosis [7, 8]. Therefore, non-invasive test has been introduced to appraise liver fibrosis i.e. AST-to-platelet ratio index (APRI) [9], Forns test [10] and FibroTest, which coalesce numerous biochemical parameters [11, 12, 13, 14, 15]. In recent times, an innovative morphological technique i.e. transient elastography (FibroScan, Echosens, and Paris, France) has been introduced that measures liver stiffness [16]. All the former mentioned non-invasive tools are the fine predictors in identifying nil, minimum and extended fibrosis [17, 18]. In spite of being a probable substitute to liver biopsy, standard use of these tools is restricted by its cost and errors [19, 20, 21, 22]. Recently Pegasys Ribavirin International Co infection Trial (Apricot study) executed a pivotal study that projected simple non-invasive test for liver fibrosis named FIB-04 [23]. It is an apricot database derived test that distinguish mild to

moderate fibrosis from advanced fibrosis in HCV-mono-infected patients by mean of following formula (age (years) _ AST [U/L]/(platelets [109/L] _ (ALT [U/L]). If FIB-04 score is less 1.45, it has a Negative Predictive Value (NPV) of 95% for significant fibrosis i.e. F3-F4 while, if FIB-04 score is greater than 3.25 than it has a PPV of 80% for advance fibrosis i.e. F3-F4 (Tamaki et al., 2013) (<1.45=mild fibrosis, 1.45-3.25= inconclusive, >3.25= advance fibrosis).

Aims And Objective

- To study the disparity in paired FIB-04 Score in hepatitis C patients treated with pegylated interferon and ribavirin at the beginning of the treatment and at the end of treatment evaluation (ETR).

Hypothesis

- **H1:** By the end of treatment, there is a distinct positive change in FIB-04 score (i.e. FIB-04 score decreases) in hepatitis C patients treated with pegylated interferon and ribavirin

II. Literature Review

Noninvasive markers of fibrosis i.e. Fibrosis 4 score may substitute LB in the majority of the cases in the diagnosis of fibrosis [24, 25]. These noninvasive tools enclose a relatively good positive predictive value for the identification of moderate or significant fibrosis. Besides this, they are also straightforward, economical, and simply reproducible [26, 27, 28, 29, 30]. None of the existing biomarkers rally these criterions. The tool for elastometry is pricey (_70,000 euros); Fibrosis 4 score presumes to be a standardization of the biochemical assays to be pertinent, and there is a threat (as in LB) of overestimation or underestimation of fibrosis [31]. The FIB-4 index may be of worth in numerous respects. Firstly, it is simple to use; the calculations are straightforward, prompt and do not necessitate standardization. Secondly, outcomes are accessible instantly during the patient's appointment. Thirdly, it is low-cost; there is no necessitate to spend in a pricey apparatus, and there are no added costs, since the constitutive FIB-4 parameters are incorporated in the standard investigation of any liver disease (age, AST, ALT, platelet count)—a reality that may be of meticulous significance in emerging countries, making the FIB-4 index a superior test than the most evaluated noninvasive markers on the market [32, 33, 34, 35]. In terms of concordance with the outcome of LB and positive predictive value, it generate results similar to those attained with other noninvasive markers of fibrosis, since 3/ 4 of patients were classified properly— a figure that correlates well with the presentation of Fibrosis 4 score [36, 37].

III. Methodology

An observational study was carried out in mono-infected, compensated chronic hepatitis C patients via Non-probability sampling technique. A figure of 58 patients contributed in the study and was treated with pegylated interferon and ribavirin for 24 weeks-48 weeks depending upon the type of genotype. The study was carried out in a tertiary care hospital i.e. Baqai Medical University Hospital, Nazimabad, Karachi from Jan 2010 to Mar 2015. In addition, FIB-04 index (age (years) _ AST [U/L]/ (platelets [109/L] _ (ALT [U/L]) was used to analyze the responses in paired manner i.e. at the beginning of treatment and at the end of treatment (ETR=end of treatment evaluation) via 'Wilcoxon signed rank test'. Moreover, consent was signed by willing participants. Furthermore, we adopted 'triangulation approach' followed by social science researches to increase credibility, validity, and reliability [38, 39, 40]. Additionally, confidentiality was guaranteed to the participants. SPSS 23.00 version was used to analyze the data. A 'p' value of less than 0.05 was deemed to be statistically significant.

IV. Results

Table 1

Tests of Normality						
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	Df	Sig.
At the beginning	.129	58	.017	.931	58	.003
ETR	.250	58	.000	.776	58	.000
a. Lilliefors Significance Correction						

Fifty-eight patients diagnosed with hepatitis C took part in the study out of which 24 were males (41.4%) with mean age 38.8 (22y-60y) and 34 were females (58.6%) with mean age 43.6 (31y-60y). Out of 58 participants, 8 patients were type 1 genotype, 48 patients were type 3 genotype and 1 was type 4. Genotype of 1 participant was not recorded. To confirm whether data was normally distributed or not we executed NORMALITY TEST. As specified in abovementioned table 1, Shapiro-Wilk was calculated to be 0.03 at the beginning of the treatment and 0.00 at ETR which shows that our data is not normally distributed.

Table 2

FIB-04 SCORE	At the beginning of treatment	ETR
< 1.45	30 (51.7%)	36 (62.1%)
1.45-3.25	16 (27.6%)	12 (20.7%)
>3.25	12 (20.7%)	10 (17.2%)

FIB-04 score at the beginning of the treatment and at the end of treatment evaluation (ETR) is illustrated in above table 2.

Table 3

Descriptive Statistics								
	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
At the beginning	58	2.5246	1.35306	.45	6.06	1.4750	2.1250	3.4425
ETR	58	1.7400	1.37115	.24	5.90	.8325	1.2800	2.0600

Table 4

Test Statistics[a]	
	At the beginning- ETR
Z	-6.210[b]
Asymp. Sig. (2-tailed)	.0001
a. Wilcoxon Signed Ranks Test	
b. Based on positive ranks.	

The FIB-04 score at the beginning of the treatment at and the end of treatment evaluation (ETR) was analyzed by using Wilcoxon signed rank test. Since, the probability value (p) is less than the alpha value as indicated in table 4 (p=0.00, alpha <0.05, N=58) it concludes that the data is statically significant i.e. rejecting null hypothesis. Moreover, as illustrated by table 3 that mean FIB-04 score at the beginning of treatment is 2.52 and mean ETR is 1.74, which indicates that FIB-04 score decreases by the end of treatment. Hence, there is a statically significant decrease in FIB04 score from beginning of treatment (M=2.52, SD=1.35) to ETR (M=1.74, SD=1.37) justifying that there is a definite positive change in FIB-04 score (i.e. improvement in fibrosis).

V. Discussion

Non-invasive markers of fibrosis i.e. FIB-04 score is exceedingly becoming proficient tool in accessing liver fibrosis [41]. Despite of this, it is simple to use and does not entail any intricate calculations [42]. Furthermore, it is expeditious and prompt and does not stipulate any sort of standardization [43]. Besides, it is a cost efficient tool in minimizing the burden of patients. The embraced parameters in FIB-04 score are age, AST, ALT and platelet count, making it the finest and premium tool [44]. In spite of this, patients with FIB-04 score <1.45 and >3.25 are indicative of moderate and significant fibrosis respectively [45]. The aim of the study was to evaluate the disparity in FIB-04 score in hepatitis C patients treated with pegylated interferon and ribavirin in paired manner i.e. at the beginning of the treatment and at the end of treatment evaluation (ETR). According to the results evaluated, there is distinct positive change in FIB-04 score by the end of the treatment, which means that there is an apparent decline in liver fibrosis. According to a study conducted by Tamaki, there was an obvious decrease in FIB-O4 score by the end of treatment, justifying our findings [46]. Likewise, previous longitudinal studies have shown no change in FIB-04 score [47]. Similarly, in another study, improvement in fibrosis was noted in Hep C patients treated with pegylated interferon and ribavirin [48]. Similarly, our results are in accordance to cohort study in which, before treatment 50 patients presented FIB-04 score >3.25 which after treatment with pegylated interferon and ribavirin was reduced to 3.25-1.45 in 43 patients and <1.45 in 7 patients [49].

VI. Conclusion

The FIB-4 index is a latest and novel noninvasive test for the appraisal of liver fibrosis. The index is readily available, economical, and merely reproducible. Moreover, it might swiftly replace costly and invasive techniques to evaluate liver fibrosis, especially in developing countries. A score of less than 1.45 and greater than 3.25 permits the precise identification of patients with moderate to significant fibrosis, respectively and may possibly shun liver biopsy examination. According to our study, there was a definite positive change in FIB-04 score in patients treated with pegylated interferon and ribavirin. Other studies are currently vital to

authenticate this new score in combination with other noninvasive tests to augment its diagnostic performance, especially for intermediate values.

References

[1]. Cadranel, J.F., Rufat, P., & Degos, F. (2000). Practices of liver biopsy in France: results of a prospective nationwide survey. For the Group of Epidemiology of the French Association for the Study of the Liver (AFEF). HEPATOLOGY; 32:477-481.

[2]. Castera, L., Negre, I., Samii, K., & Buffet, C. (1999). Pain experienced during percutaneous liver biopsy. HEPATOLOGY, 30:1529-1530.

[3]. Bravo, A. A., Sheth, S. G., & Chopra, S. (2001). Liver biopsy. New England Journal of Medicine, 344:495-500.

[4]. Myers, R. P., De Torres, M., Imbert-Bismut, F., Ratziu, V., Charlotte, F., & Poynard, T. (2003). Biochemical markers of fibrosis in patients with chronic hepatitis C: a comparison with prothrombin time, platelet count, and age-platelet index. Digestive Diseases and Sciences, 48:146-153.

[5]. Berho, M., & Suster, M. (1994), Mucinous meningioma. Report of an unusual variant of meningioma that may mimic metastatic mucin-producing carcinoma. The American Journal of Surgical Pathology, 18; 100-106.

[6]. Regev, A., Berho, M., Jeffers, L. J., Milikowski, C., Molina, E. G., Pyrsopoulos, N. T., et al. (2002). Sampling error and intraobserver variation in liver biopsy in patientswith chronic HCV infection. American Journal of Gastroenterology, 97:2614-2618.

[7]. Bedossa, P., Dargere, D., & Paradis, V. (2003). Sampling variability of liver fibrosis in chronic hepatitis C. HEPATOLOGY, 38:1449-1457.

[8]. Colloredo, G., Guido, M., Sonzogni, A., & Leandro, G. (2003). Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: the smaller the sample, the milder the disease. Journal of Hepatology, 39:239-244.

[9]. Wai, C. T., Greenson, J. K., Fontana, R. J., Kalbfleisch, J. D., Marrero, J. A., Conjeevaram, H. S., et al. (2003). A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. HEPATOLOGY, 38:518-526.

[10]. Forns, X., Ampurdanes, S., Llovet, J. M., Aponte, J., Quinto, L., & Martinez-Bauer, E., et al. (2002), Identification of chronic hepatitis C patients without hepatic fibrosis by a simple predictive model. HEPATOLOGY, 36:986-992.

[11]. Imbert-Bismut, F., Ratziu, V., Pieroni, L., Charlotte, F., Benhamou, Y., & Poynard, T. (2001). Biochemical markers of liver fibrosis in patients with hepatitis C virus infection: a prospective study. Lancet, 357:1069-1075.

[12]. Myers, R. P., Ratziu, V., Imbert-Bismut, F., Charlotte, F., & Poynard, T. (2002). Biochemical markers of liver fibrosis: a comparison with historical features in patients with chronic hepatitis C. American Journal of Gastroenterology, 97:2419-2425.

[13]. Poynard, T., Imbert-Bismut, F., Ratziu, V., Chevret, S., Jardel, C., & Moussalli, J., et al. (2002). Biochemical markers of liver fibrosis in patients infected by hepatitis C virus: longitudinal validation in a randomized trial. Journal of Viral Hepatology, 9: 128-133.

[14]. Rossi, E., Adams, L., Prins, A., Bulsara, M., de Boer, B., & Garas, G., et al. (2003). Validation of FibroTest biochemical markers score in assessing liver fibrosis in hepatitis C patients. Clinical Chemistry, 49:450-454.

[15]. Thabut, D., Simon, M., Myers, R. P., Messous, D., Thibault, V., & Imbert-Bismut, F., et al. (2003). Noninvasive prediction of fibrosis in patients with chronic hepatitis C. HEPATOLOGY 37:1220-1221.

[16]. Castera, L., Vergniol, J., Foucher, J., Le Bail, B., Chanteloup, E., & Haaser, M., et al. (2005). Prospective comparison of transient elastography, FibroTest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology, 128:343-350.

[17]. Adams, L. A., Bulsara, M., Rossi, E., DeBoer, B., Speers, D., & George, J., et al. (2005). Hepascore: an accurate validated predictor of liver fibrosis in chronic hepatitis C infection. Clinical Chemistry, 51:1867-1873.

[18]. Cales, P., Oberti, F., Michalak, S., Hubert-Fouchard, I., Rousselet, M. C., & Konate, A., et al. (2005). A novel panel of blood markers to assess the degree of liver fibrosis. HEPATOLOGY, 42:1373-1381.

[19]. Adams, L. A., Bulsara, M., Rossi, E., DeBoer, B., Speers, D., & George, J., et al. (2005). Hepascore: an accurate validated predictor of liver fibrosis in chronic hepatitis C infection. Clinical Chemistry, 51:1867-1873.

[20]. Cales, P., Oberti, F., Michalak, S., Hubert-Fouchard, I., Rousselet, M. C., & Konate, A., et al. (2005). A novel panel of blood markers to assess the degree of liver fibrosis. HEPATOLOGY, 42:1373-1381.

[21]. Elpek, G. O. (2015). Angiogenesis and liver fibrosis, World Journal of Hepatology, 7(3), 377-391.

[22]. Poynard, T., Imbert-Bismut, F., Munteanu, M., & Ratziu, V. (2005). FibroTest-Fibro- SURE: towards a universal biomarker of liver fibrosis? Expert Review of Molecular Diagnostics, 5:15-21.

[23]. Torriani, F. J., Rodriguez-Torres, M., Rockstroh, J. K., Lissen, E., Gonzalez-Garcia, J., & Lazzarin, A., et al. (2004). Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. New England Journal of Medicine, 351:438-450.

[24]. Adams, L. A., Bulsara, M., Rossi, E., DeBoer, B., Speers, D., & George, J., et al. (2005). Hepascore: an accurate validated predictor of liver fibrosis in chronic hepatitis C infection. Clinical Chemistry, 51:1867-1873.

[25]. Cales, P., Oberti, F., Michalak, S., Hubert-Fouchard, I., Rousselet, M. C., & Konate, A., et al. (2005). A novel panel of blood markers to assess the degree of liver fibrosis. HEPATOLOGY, 42:1373-1381.

[26]. Imbert-Bismut, F., Ratziu, V., Pieroni, L., Charlotte, F., Benhamou, Y., & Poynard, T. (2001). Biochemical markers of liver fibrosis in patients with hepatitis C virus infection: a prospective study. Lancet, 357:1069-1075.

[27]. Myers, R. P., Ratziu, V., Imbert-Bismut, F., Charlotte, F., & Poynard, T. (2002). Biochemical markers of liver fibrosis: a comparison with historical features in patients with chronic hepatitis C. American Journal of Gastroenterology, 97:2419-2425.

[28]. Poynard, T., Imbert-Bismut, F., Ratziu, V., Chevret, S., Jardel, C., & Moussalli, J., et al. (2002). Biochemical markers of liver fibrosis in patients infected by hepatitis C virus: longitudinal validation in a randomized trial. Journal of Viral Hepatology, 9: 128-133.

[29]. Rossi, E., Adams, L., Prins, A., Bulsara, M., de Boer, B., & Garas, G., et al. (2003). Validation of FibroTest biochemical markers score in assessing liver fibrosis in hepatitis C patients. Clinical Chemistry, 49:450-454.

[30]. Thabut, D., Simon, M., Myers, R. P., Messous, D., Thibault, V., & Imbert-Bismut, F., et al. (2003). Noninvasive prediction of fibrosis in patients with chronic hepatitis C. HEPATOLOGY 37:1220-1221.

[31]. Forns, X., Ampurdanes, S., Llovet, J. M., Aponte, J., Quinto, L., & Martinez-Bauer, E., et al. (2002), Identification of chronic hepatitis C patients without hepatic fibrosis by a simple predictive model. HEPATOLOGY, 36:986-992.

[32]. Adams, L. A., Bulsara, M., Rossi, E., DeBoer, B., Speers, D., & George, J., et al. (2005). Hepascore: an accurate validated predictor of liver fibrosis in chronic hepatitis C infection. Clinical Chemistry, 51:1867-1873.

[33]. Cales, P., Oberti, F., Michalak, S., Hubert-Fouchard, I., Rousselet, M. C., & Konate, A., et al. (2005). A novel panel of blood markers to assess the degree of liver fibrosis. HEPATOLOGY, 42:1373-1381.

[34]. Myers, R. P., Ratziu, V., Imbert-Bismut, F., Charlotte, F., & Poynard, T. (2002). Biochemical markers of liver fibrosis: a comparison with historical features in patients with chronic hepatitis C. American Journal of Gastroenterology, 97:2419-2425.
[35]. Poynard, T., Imbert-Bismut, F., Ratziu, V., Chevret, S., Jardel, C., & Moussalli, J., et al. (2002). Biochemical markers of liver fibrosis in patients infected by hepatitis C virus: longitudinal validation in a randomized trial. Journal of Viral Hepatology, 9: 128-133.
[36]. Berho, M., & Suster, M. (1994), Mucinous meningioma. Report of an unusual variant of meningioma that may mimic metastatic mucin-producing carcinoma. The American Journal of Surgical Pathology, 18; 100-106.
[37]. Regev, A., Berho, M., Jeffers, L. J., Milikowski, C., Molina, E. G., Pyrsopoulos, N. T., et al. (2002). Sampling error and intraobserver variation in liver biopsy in patientswith chronic HCV infection. American Journal of Gastroenterology, 97:2614-2618.
[38]. Haque, A. U., & Aston, J. (2016). A Relationship between Occupational Stress and Organizational Commitment of I.T Sector's Employees in Contrasting Economies, Polish Journal of Management Studies, 14(1), 95-105.
[39]. Haque, A. U., Aston, J., & Kozlovski, E. (2016). Do causes and consequences of stress affect genders differently at operational level? Comparison of the IT sectors in the UK and Pakistan, International Journal of Applied Business, 1(1), 1-7.
[40]. Haque, A. U., Faizan, R., & Cockrill, A. (2017). The Relationship between Female Representation at Strategic Level and Firm's Competitiveness: Evidences from Cargo Logistic Firms of Pakistan and Canada, Polish Journal of Management Studies, 15(2), 69-81.
[41]. Forns, X., Ampurdanes, S., Llovet, J. M., Aponte, J., Quinto, L., & Martinez-Bauer, E., et al. (2002), Identification of chronic hepatitis C patients without hepatic fibrosis by a simple predictive model. HEPATOLOGY, 36:986-992.
[42]. Imbert-Bismut, F., Ratziu, V., Pieroni, L., Charlotte, F., Benhamou, Y., & Poynard, T. (2001). Biochemical markers of liver fibrosis in patients with hepatitis C virus infection: a prospective study. Lancet, 357:1069-1075.
[43]. Castera, L., Vergniol, J., Foucher, J., Le Bail, B., Chanteloup, E., & Haaser, M., et al. (2005). Prospective comparison of transient elastography, FibroTest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology, 128:343-350.
[44]. Poynard, T., Imbert-Bismut, F., Ratziu, V., Chevret, S., Jardel, C., & Moussalli, J., et al. (2002). Biochemical markers of liver fibrosis in patients infected by hepatitis C virus: longitudinal validation in a randomized trial. Journal of Viral Hepatology, 9: 128-133.
[45]. Torriani, F. J., Rodriguez-Torres, M., Rockstroh, J. K., Lissen, E., Gonzalez-Garcia, J., & Lazzarin, A., et al. (2004). Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. New England Journal of Medicine, 351:438-450.
[46]. Tamaki, N., Korsaki, M., Tanaka, K., Suzuki, Y., Kato, T., Yasvi, Y., Hosokawa, T., Veda, K., Tsuchiya, K., Nakawishi, H., Itakara, J., Asahina, Y., & Izumi, N. (2013). Non-Invasive estimation of fibrosis progression over time using FIB-04 index in CHC. Journal of Viral Hepatology, 20(1):72-76.
[47]. Adams, L. A., Bulsara, M., Rossi, E., DeBoer, B., Speers, D., & George, J., et al. (2005). Hepascore: an accurate validated predictor of liver fibrosis in chronic hepatitis C infection. Clinical Chemistry, 51:1867-1873.
[48]. Anais, V. P., Mallet, V., Nalpas, B., Verkarre, V., Nalpas, A., Dhalluin-Venier, V., Fontaine, H., & Pol, S. (2013). FIB-4: an Inexpensive and Accurate Marker of Fibrosisin HCV Infection. Comparison with Liver Biopsy and FibroTest
[49]. Castera, L., Vergniol, J., Foucher, J., Le Bail, B., Chanteloup, E., & Haaser, M., et al. (2005). Prospective comparison of transient elastography, FibroTest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology, 128:343-350.

*Dr. Muhammad Imran. "Fib-04 Score At the End of Treatment in Chronic Hepatitis C Patients Treated with Pegylated Interferon And Ribavirin: An Observational Study." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.8 (2017): 66-70.