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Original Research Article

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

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Abstract: 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. The objective is 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). 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. 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). 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.

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]. 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 [4,5] and sampling errors which generate around 24% false negative response for cirrhosis [6,7]. Therefore, non-invasive test has been introduced to appraise liver fibrosis i.e. AST-to-platelet ratio index (APRI) [8], Forns test [9] and FibroTest which coalesce numerous biochemical parameters [10-16]. In recent times, an innovative morphological technique i.e. transient elastography (FibroScan, Echosens, and Paris, France) has been introduced that measures liver stiffness [17]. All the former mentioned non invasive tools are the fine predictors in identifying nil, minimum and extended fibrosis [18, 19]. In spite of being a probable substitute to liver biopsy, standard use of these tools is restricted by its cost and errors [17-20]. 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 [21]. 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 [22] (<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

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. 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.

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.

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

Table 2: FIB-04 SCORE

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%)

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)	.000

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)

DISCUSSION

Non-invasive markers of fibrosis i.e. FIB-04 score is exceedingly becoming proficient tool in accessing liver fibrosis [9]. Despite of this, it is simple to use and does not entail any intricate calculations [10]. Furthermore, it is expeditious and prompt and does not stipulate any sort of standardization [17]. 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 [20]. In spite of this, patients with FIB-04 score <1.45 and >3.25 are indicative of moderate and significant fibrosis respectively [21]. 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 N.Tamaki, there was an obvious decrease in FIB-O4 score by the end of treatment, justifying our findings [22]. Likewise, previous longitudinal studies have shown no change in FIB-04 score [19]. Similarly, in another study, improvement in fibrosis was noted in Hep C patients treated with pegylated interferon and ribavirin [23]. 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 [17].

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 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.

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