https://doi.org/10.48047/AFJBS.6.14.2024.6145-6160

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

A prospective study on comparing biochemical parameters and fibroscores - Aspartate transaminase to Platelet Ratio Index, FIB 4 in liver disease patients in a tertiary care hospital in South Indian population

Dr.M.V.Tejaswi Nagesh[1], Dr.Ch.Mounika[2], Dr.V.M.Jyotsnaa Grace[3], Prof.Dr.V.R.Mohan Rao[4]

[1]Final Year Post Graduate, Department of General Medicine, Chettinad Hospital & Research Institute, Chennai, India.

[2]Assistant Professor, Department of General Medicine, Chettinad Hospital & Research Institute, Chennai, India.

[3]Fellow, Department of Immuno-Hematology & Transfusion Medicine, Dr. Rela Institute and Medical Center, Chennai, India.

[4]Professor & HOD, Department of General Medicine, Chettinad Hospital & Research Institute, Chennai, India.

Email : [1]mnagesh95@gamil.com , [2]mouni.chevuri@gmail.com, [3]jyos6995@gmail.com , [4]vrmohan_rao@yahoo.co.in ;

Orchid ID : [1]0009-0007-6727-4160 , [2]0009-0000-2323-6823 , [3]0009-0007-4761-9547, [4]0009-0004-4973-0431

Corresponding Author : Dr.M.V.Tejaswi Nagesh[1]

Volume 6, Issue 14, Aug 2024

Received: 15 June 2024

Accepted: 25 July 2024

Published: 15 Aug 2024

doi: 10.48047/AFJBS.6.14.2024.6145-6160

ABSTRACT:

Background : Liver disorders account for about 1/3rd of the cases leading to mortality across the globe. Amongst all liver disorders, decompensated chronic liver disease, alcohol liver disease, alcohol dependence syndrome, infectious etiology and diseases secondary to other causes contribute to most of the liver disease patients. To stage a liver disease, we need to measure the fibrosis undergoing in patient. For measuring liver fibrosis, previously, there were liver biopsy, but in today's practice, we have non invasive tests like APRI, FIB 4 scores which denotes fibrosis with near accurate values. Here, we would like to study correlation between these important fibroscores and GGT, coagulation profile.

Materials and methods: Our study is done in a tertiary care hospital with 50 subjects to find out the fibrosis using fibroscores and correlating them with GGT, coagulation profile values. This is an observational study, done with participants' consent and participants included were all explained about the study being done. SPSS software was used for calculating descriptive analysis and correlation studies for interpretation of fibroscores with GGT & coagulation profile values.

Results: Among 50 samples studied, we found that DCLD and ADS were found to have significant fibrosis and their values with APRI and FIB 4 were higher when compared to all 5 entities included. APRI showed positive correlation with AST, APTT levels, whereas FIB 4 showed positive correlation with AST, GGT, platelet values respectively.

Conclusion: We conclude the study by implying that though APRI and FIB 4 are the important fibroscores, assessment of liver fibrosis would be incomplete when GGT and coagulation profile aren't taken into consideration. Hence, whenever we study a liver disease patient, always knowing GGT value and coagulation status is important apart from Fibroscores measurement, to tell us the risk of morbidity and mortality in them.

KEYWORDS : Decompensated Chronic Liver Disease (DCLD), Alcohol Dependence Syndrome(ADS) , Aspartate transaminase Platelet Ratio Index(APRI), Fibrosis 4 index (FIB 4)

INTRODUCTION:

Liver disease, which includes cirrhosis, hepatocellular carcinoma, and viral hepatitis, is a global health concern that results in over two million deaths every year. A million people die from liver disease due to complications from cirrhosis, and another million die from hepatocellular carcinoma and viral hepatitis.[1] Risk factors for liver disease include obesity, elderly age, alcohol consumption, smoking , aflatoxins, microcystins contamination, hepatitis B and hepatitis C virus infection. Hepatotoxic and cholestatic liver injuries are the two types of chronic liver injury that lead to liver fibrosis. Hepatitis B and C (HBV and HCV), alcoholic and non-alcoholic steatohepatitis and …….. are among the external causes that can cause hepatotoxic harm to cells. Primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), and biliary atresia are among the primary (and secondary) diseases that induce cholestatic damage, which is defined by decreased or obstructed bile flow in the liver. Extracellular matrix (ECM) proteins, primarily collagens Type I and Type III, accumulate as a result of liver fibrosis. This leads to the creation of fibrous scars, which can eventually impair normal liver function. The common molecular pathways of liver fibrosis, regardless of the etiology, include hepatocyte mortality, chronic inflammation with cytokine release, HSC activation, and disruption of the epithelial or endothelial barrier. Therefore, cellular and extracellular signals are necessary for the complex process of hepatic fibrogenesis.[2,3,4]

There has been a 46% increase in cirrhosis mortality in the world from 1980 to 2013. In India too, cirrhosis of liver is a major health problem. According to the latest WHO data published in 2017, liver disease deaths in India reached 259,749 or 2.95% of total deaths, accounting for one-fifth (18.3%) of all cirrhosis deaths globally.[5,6] Alcohol is the most common etiology of cirrhosis in adults in India. The proportions of alcohol and NAFLD-related cirrhosis are increasing, and those of viral hepatitis-related cirrhosis are reducing.[7]

APRI is a straightforward, non-invasive biochemical indicator of cirrhosis and liver fibrosis that is especially useful for patients with chronic hepatitis C. APRI may be able to reduce the quantity of liver biopsies performed. According to published research, patients with hepatocellular carcinoma, hepatitis B, and hepatitis C had advanced fibrosis diagnosed through APRI rather than liver biopsy.[8] As of right now, the majority of guidelines advise using FIB-4 or NFS (NAFLD Fibrosis score) as a test to identify patients with advanced liver fibrosis. In the average-risk group, we assessed FIB-4 and NFS's diagnostic performance. When it came to screening for hepatic fibrosis in the average-risk group, FIB-4 outperformed NFS in terms of diagnostic performance, but in the metabolically healthy group, it was on par with NFS. In a medical check-up context, FIB-4 can be a highly alluring first screening tool because subsequent sequential testing can support the low positive-predictive value. Thus, FIB-4 can become the most economical first-line screening test in average-risk groups if we can raise its sensitivity by modifying the low cut-off settings.[9]

Scores in Liver diseases :

King's college criteria, Clichy criteria are two important scoring systems for Acute liver failure. Both of these scores include age as their common criterion. Child T Pugh score, MELD score, UKELD score are commonly used scores for Chronic Liver disease patients. Among these scores, albumin, International normalised Ratio (INR) are some of their criteria. Hence, we can know that age, coagulation profile will interpret us the severity of liver disorders. Would severity necessarily means fibrosis or just functional liver failure, studies were lapse. Here is a study which would tell us the correlation between Coagulation profile, fibroscores APRI, FIB 4; a study which measures fibrosis and looks for its correlation with age, GGT, coagulation profile parameters.

There are many studies stating the use of fibroscores like APRI, FIB 4 in Hepatitis, Chronic Liver disease and Hepatocellular carcinoma. But literature doesn't have a comparison between Gamma glutamyl transferase and Fibroscores; also studies on coagulation profile with fibroscores correlation is scarce. This respective study tells us about correlation among Gamma glutamyl transferase, Coagulation profile and 2 fibroscores APRI, FIB 4 in various liver disorders.

MATERIALS AND METHODS :

Study details :

Our study is a prospective study including all liver disorder patients with a sample size of 50 in a tertiary care hospital. Participants included in the study were all explained about the details of the study and their verbal consent for the study was taken. All patients underwent basic blood investigations which include complete blood count, liver function test, coagulation profile with their consent using sterile blood collection techniques. Inclusion criteria is as follows:-

- patients aged more than 18 years
- patients who present with any abdominal symptoms.
- both diabetics and non-diabetics
- previously diagnosed liver disease patients are also included.

Exclusion criteria was only patients aged less than 18 years. Using fibroscores APRI and FIB 4 formulas, fibroscores' values were calculated for all subjects. Then comparison between fibroscores, coagulation profile and other demographic parameters were interpretated. Compilation of data, descriptive analysis and correlations were studied using SPSS software.

Inclusion & exclusion criteria

Informed consent was taken

Blood collection and tests details

Compiling data, correlation using SPSS

RESULTS :

Fifty patients (46 males, 4 females) were included in this study after applying inclusion and exclusion criteria. The average age was 44.8±14 years of age. Among them, 17 were decompensated liver disease patients, 8 were alcohol liver disease patients, 12 were alcohol dependence syndrome patients, 3 were infectious hepatitis patients and rest 10 were of other etiology. The primary objective of this study was to see the correlation between GGT, Coagulation profile and fibroscores APRI, FIB 4.

In descriptive analysis, APRI interpretation revealed DCLD patient group were having both severe and significant fibrosis compared to other 4 etiology groups; whereas ADS patient group was having lowest, which meant the severity of fibrosis was lower and unable to determine in this group. FIB 4 descriptive analysis interpretation revealed similar results, DCLD patient group were having both high risk and intermediate risk to hepatic fibrosis compared to other 4 etiology groups; whereas ADS patient group were having lowest risk to fibrosis.

Correlation studies revealed APRI showed positive correlation with AST, APTT values ; whereas FIB 4 showed positive correlation with AST, GGT, Platelet count values. APRI values didn't show any correlation with platelet count, PT and INR values. FIB 4 values were insignificant with PT, APTT, INR and ALT.

Hence, with this study statistics, we can tell that though age, AST, Platelet count are only included in formulas for calculating APRI, FIB 4 fibroscores ; APRI still holds good and correlates with APTT values. FIB 4, now being the important non invasive biomarker for hepatic fibrosis showed correlation with GGT values and platelet count values.

DISCUSSION :

Introduction :

Globally, liver diseases are one of the most common diseases which can be fatal if not intervened on time. Amongst all the liver diseases, decompensated chronic liver disease accounts highest number of patients leading to death. Liver is a major vital organ in human body which normally functions on carbohydrate, fat and lipid metabolism; toxin removal; drug metabolism; coagulation factors production; glucose & insulin action; amino-acid production and many more physiological functions.

This important organ in body has a maximum level of compensation when it is damaged or injured by various toxins, infectious agents, alcohol, smoking etc. Hepatic fibrosis starts only after maximum compensation by liver fails to attribute to normal functioning of the body.

Decompensated chronic liver disease is defined as structural and functional damage of the liver by various risk factors like alcoholism, drugs like NSAIDs, poisons exposure, smoking, infections like Hepatitis virus B,C,D more commonly. To study grading of fibrosis, previously fibroscan was done for every liver disease. Recently, non invasive methods of assessing hepatic fibrosis are being used like APRI, FIB 4 etc. These fibroscores, though non invasive approximately gives us the level of fibrosis near to grades of fibrosis studied by invasive fibroscan method.

PT,APTT,INR :

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) are standard initial tests used to evaluate patients with suspected bleeding disorders. PT assesses the extrinsic and common pathways, while aPTT measures the intrinsic and common pathways. The international normalized ratio (INR) is a calculation that standardizes and allows comparison of PT clotting times across different laboratories.

PT and aPTT assays determine the time required for fibrin clot formation, with results reported in seconds. The INR is derived from PT clotting time values, providing a standardized method to monitor warfarin anticoagulant therapy.

PT (INR) :

In simple terms, the PT (Prothrombin Time) measures the integrity of the extrinsic and final common pathways in the blood coagulation cascade. PT is the time, measured in seconds, for a patient's plasma to clot after adding calcium and an activator for the extrinsic pathway (thromboplastin). If there are deficiencies or inhibitors of clotting factors within these pathways, the PT will be prolonged.[29]

PT is commonly used to monitor warfarin anticoagulation. However, PT results can vary between laboratories, complicating warfarin monitoring, especially for patients whose samples are tested in multiple labs. This variability arises due to the different sensitivities of thromboplastin reagents from various manufacturers to coagulation factor deficiencies. To address this, the international normalized ratio (INR) was developed. The INR is a standardized calculation of a patient's PT, adjusting for the thromboplastin sensitivity used in a specific laboratory by incorporating the international sensitivity index (ISI) provided by the manufacturer. The formula for INR is:

$$INR = (\text{patient PT}/\text{MNPT})^{ISI}$$

where MNPT is the geometric mean of the PT from at least 20 healthy individuals tested at the performing laboratory. The introduction of INR has reduced interlaboratory variations in PT results.

PT reagents vary in sensitivity to different clotting factors. Generally, PT reagents are more sensitive to deficiencies in factor VII within the extrinsic pathway and less sensitive to deficiencies in the final common pathway factors (factors V, X, II, and fibrinogen).

APTT:

The APTT (Activated Partial Thromboplastin Time) measures the integrity of the intrinsic and common final pathways of the coagulation cascade. It is the time, measured in seconds, for patient plasma to clot after the addition of phospholipid (an intrinsic pathway activator) and calcium. The APTT reagent, called partial thromboplastin, does not contain tissue factor, unlike the PT reagent, which includes tissue factor along with the phospholipid. Therefore, deficiencies or inhibitors of clotting factors in the intrinsic and final common pathways result in an extended APTT.[29]

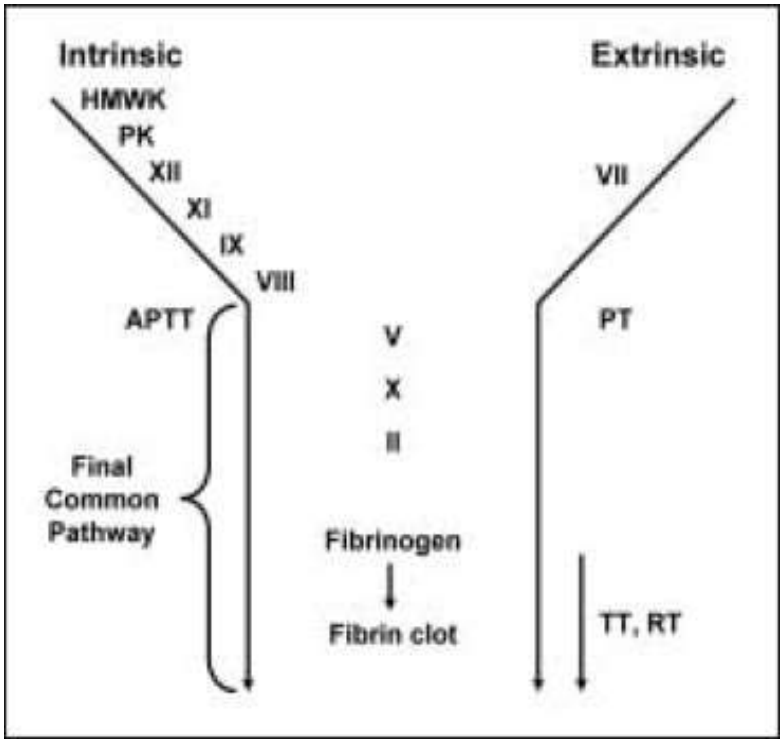

Figure 1 : Coagulation Cascade

Everything about GGT :

GGT is produced by epithelium of small bile ductules and hepatocytes. The primary use of serum GGT levels is to identify the source of isolated elevation of serum ALP level; GGT is not elevated in bone disease. This is one of the most sensitive tests for presence of hepatobiliary disease and similarly absence of raised GGT correlates well with absence of hepatic metastasis. GGT levels are higher in biliary tract disease and cholestasis than in hepatocellular disease. An elevated GGT is used to confirm that a raised ALP is of hepatobiliary origin. Hence it is a more sensitive marker compared to ALP.

The following drugs may elevate GGT giving rise to false positive diagnosis of hepatobiliary disease – anticonvulsants, NNRTI and Protease inhibitors, TCAs, anticoagulant like warfarin, lipid lowering agents and analgesics.

An isolated raise in GGT is an early indicator of alcohol consumption in otherwise healthy individuals. During recovery in acute hepatitis, serum GGT is the last enzyme to return to normal following acute hepatitis and its normalization is indicative of a favourable outcome.

Hepatic and Non-Hepatic causes for abnormal Coagulation Profile :

Clotting time prolonged	Key differential diagnoses
Prothrombin time (PT)	• Factor deficiency or inhibitor (VII, X, V, II) • Warfarin • Vitamin K deficiency • Liver disease • Direct Xa inhibitor
Activated partial thromboplastin time (aPTT)	• Factor deficiency or inhibitor (VIII, IX, XI, contact factors) • Rarely, von Willebrand disease (if VIII is low enough to prolong aPTT) • Heparin • Direct thrombin inhibitor • Lupus anticoagulant
PT and aPTT	• Common pathway factor deficiency or inhibitor (X, V, II) • Warfarin (high doses) or superwarfarin • Vitamin K deficiency • Disseminated intravascular coagulation • Liver disease • Direct thrombin inhibitors • Direct Xa inhibitors • Lupus anticoagulant (rarely) • Heparin (very high doses)

Figure 2 : Medical disorders with abnormal coagulation profile

Standard Current Guidelines :

AGA study says the pooled effect estimates of test characteristics for the diagnosis of cirrhosis in patients with chronic hepatitis C were obtained from 36 studies evaluating VCTE, 24 studies evaluating

APRI, and 2 studies evaluating FIB-4. The test characteristics for these noninvasive fibrosis assessment tools were as follows: VCTE: sensitivity, 0.89; 95% confidence interval [CI], 0.840.92; specificity, 0.91; 95% CI, 0.890.92; APRI: sensitivity, 0.77; 95% CI, 0.730.81; specificity, 0.78; 95% CI, 0.740.81; and FIB-4: sensitivity, 0.87; 95% CI, 0.740.94; specificity, 0.91; 95% CI, 0.890.92.[21]

Although FIB-4 is increasingly used in clinical practice, historical studies have often used APRI as a comparator, likely due to availability and accepted validation in viral hepatitis. Data on comparing markers in cholestatic disease is lacking. Due to the absence of an adequate number and quality of studies, we were unable to address if a combination of markers was superior to a single marker.[22]

In summary, we found that blood-based biomarkers were associated with small-to-moderate improvement in pre-test probability for the diagnosis of F2-4, F3-4, and F4 in viral hepatitis, HIV-HCV co-infection, and NAFLD. There were a limited number of studies in other CLD. Diagnostic performance was comparable between nonproprietary and proprietary direct and indirect tests but we were not able to determine whether the diagnostic performance of two biomarkers was better compared to a single test.[22]

FIB-4 and NFS showed sensitivities ranging from 60% to 75% and the lowest negative LR at proposed cutoff values across etiologies. [22] Regarding imaging-based testing, a recent study including >16,000 individuals revealed normal TE-LSM to be below 5 kPa, with the consideration that obesity, steatosis, and diabetes mellitus can increase LSM.[24,25,26] As such, significant/advanced fibrosis can be confidently ruled out with a TE/SWE-LSM.[23]

As per British guidelines Journal of hepatology, in a similar vein, post-SVR LSM decrease has been documented with various tools, including MRE. and pSWE (Virtual Touch). In similar vein, non-invasive blood biomarkers such as APRI, FIB-4, or ELFTM have been shown to cause post-SVR reductions. In spite of divergent findings, these investigations also demonstrated good diagnostic accuracy for advanced fibrosis following SVR utilizing liver biopsy as a reference for LSM by pSWE (AUROC from 0.88 and 0.91) and for APRI, FIB-4, and ELFTM.

The primary factor influencing prognosis in NAFLD patients is liver fibrosis; extensive fibrosis stands alone as a risk factor for liver-related and overall mortality, as well as extrahepatic and hepatic events. Thus, in investigations on NITs in individuals with NAFLD, progressive liver fibrosis has been employed as the primary outcome. NAFLD fibrosis score (NFS), FIB-4, BARD score, AST to platelet ratio (APRI), AST to ALT ratio (AAR), eLIFT, HEPAMET score, pro-C3, FibroMeterTM, FibroTest®, and ELFTM are some of the suggested blood indicators and scores for the evaluation of fibrosis severity. The non-patented tests NFS and FIB-4 have been validated the most. While FIB-4 is based solely on the combination of age, BMI, AST/ALT ratio, platelet count, hyperglycemia, and albumin, NFS is based on six variables. These scores employ two thresholds to exclude or include advanced fibrosis: a high specificity threshold (0.676 for NFS and 1.3 for FIB-4) and a high sensitivity threshold (1.3 for FIB-4).

In 292 patients with paired liver biopsies and non-alcoholic fatty liver disease (NAFLD), a new retrospective longitudinal study assessed the utility of non-invasive measures in identifying the progression of fibrosis over a median of 2.6 years. The development of fibrosis, which is defined as one fibrosis stage, was substantially correlated with changes over time in APRI, FIB-4, and NFS (cross-validated C-statistic for detecting progression to advanced fibrosis of 0.82 for APRI, 0.81 for FIB-4, and 0.80 for NFS). While NPVs for FIB-4 and NFS were excellent (about 90%), PPVs for predicting the progression to advanced fibrosis were subpar.

The accuracy of blood biomarkers for liver fibrosis, such as hyaluronic acid, procollagen III aminoterminal propeptide, collagen IV, and FibroTest®, is insufficient to distinguish between early and advanced fibrosis in patients with prostate cancer. In a similar vein, non-invasive scores such as APRI, FIB-4, AAR, neutrophil to lymphocyte ratio, red blood cell distribution width to platelet ratio, and red blood cell distribution width to lymphocyte ratio show a subpar diagnostic performance (AUROC

<0.80) in predicting PBC's histological stage. The ability of the platelet count to spleen diameter ratio to predict advanced fibrosis stage was demonstrated in one study.

It has recently been demonstrated that an APRI score more than 0.54 following a year of UDCA medication and biochemical non-response, as measured by the GLOBE score, are independently linked to the likelihood of cirrhosis decompensation. These two factors when used together enhance risk stratification in these patients.

Particularly in the early stages of liver fibrosis, non-invasive ratings like APRI, FIB-4, and AAR show low diagnostic accuracy in predicting hepatic fibrosis. In fact, with advanced fibrosis (F>−3), the summary AUROCs of FIB-4, APRI, and AAR were 0.76, 0.74, and 0.73, respectively. In a similar vein, the APRI and FIB-4 summary AUROCs for cirrhosis were 0.75 and 0.66, respectively.

Non Invasive fibroscores in today's clinical practice :

Non invasive testing for assessing liver fibrosis has been slowly taken over the need for invasive method of liver biopsy. APRI and FIB 4 fibroscores are most commonly used scores to assess hepatic fibrosis in recent times. A study concluded APRI has shown accuracy to hepatic fibrosis in chronic hepatitis C and non alcoholic fatty liver disease patients, but not with chronic hepatitis B patient group.[10]

The main factor influencing the course of developing chronic liver disease, including cirrhosis, is hepatic fibrosis, a reparative reaction to several forms of liver injury.[11,12,13,14] Noninvasive, straightforward, reproducible, and trustworthy biomarkers that can detect patients with liver fibrosis are desperately needed in light of the sharp rise in the prevalence of NAFLD.[14] By reducing the requirement for liver biopsy, the availability of such biomarkers has the enormous potential to drastically change diagnostic and monitoring procedures.[12] Because the APRI is based on standard laboratory test findings, it can be easily accessed in clinical settings. Numerous studies have revealed that this index can predict the existence of cirrhosis and severe fibrosis.[10]

Our Study & Results :

Descriptive analysis interpretation have shown similar results between APRI and FIB 4 groups. DCLD and ADS patient groups are highest and lowest among 5 etiology groups; implying DCLD patient group had severe and significant fibrosis, high risk for hepatic fibrosis & ADS patient group had unable to determine , low risk for hepatic fibrosis in APRI and FIB 4 respectively.

Besides primary outcome, there is also positive correlation observed in APRI and AST, APTT values; FIB 4 and AST, GGT & Platelet count values respectively.

Our study was done with 50 liver disease patients admitted in tertiary care hospital and among them pattern of fibrosis and its correlation with GGT, coagulation profile and Platelet count was studied. APRI and FIB 4, being most known fibroscores in the field of Hepatology, are being used in clinical practice as non invasive markers to find out severity of fibrosis. Hence, our study also aimed to see how well they could correlate with severity of liver disease.

Analysis :

Chi-square

	APRI-Interpretation			Total
	Unable to Determine	Significant Fibrosis	Severe Fibrosis	

Diagnosis	Alcohol dependence syndrome	6	2	4	12
	Alcoholic Liver disease	3	1	4	8
	DCLD	5	6	6	17
	Infectious hepatitis	1	0	2	3
	Others	4	2	4	10
Total		19	11	20	50
χ^2=4.301;P>0.05					

Table 1 : Descriptive analysis of APRI interpretation in various liver diseases

APRI has been divided into 3 subgroups, unable to determine, significant fibrosis and severe fibrosis groups. Among 50 patients, we had majority of patients showing significant and severe fibrosis in Decompensated liver disease patients, which were 6 and 6 respectively. Furthermore, fibrosis was more evidently seen in Alcohol dependence syndrome group and Alcoholic liver disease group, although duration of alcohol abuse plays an important role for severity of fibrosis.[1]

Infectious hepatitis and other etiology group were showing minimal amount of fibrosis as expected, their pathophysiology mainly remain acute and reverses once we treat the underlying cause like infection etc.

		FIB-4-Interpretation			Total
		Low Risk	Intermediate Risk	High Risk	
Diagnosis	Alcohol dependence syndrome	5	2	5	12
	Alcoholic Liver disease	3	2	3	8
	DCLD	2	5	10	17
	Infectious hepatitis	1	0	2	3
	Others	3	4	3	10
Total		14	13	23	50
χ^2=6.336;P>0.05					

Table 2 : Descriptive analysis of FIB-4 interpretation in various liver diseases

Amongst APRI and FIB 4, FIB 4 is more accurate to know fibrosis in a liver disease patient.[1] In our study, FIB 4 was again shown higher in Decompensated Liver disease entity. FIB 4 is divided into low risk, intermediate risk and high risk for fibrosis groups. DCLD group showed 5 and 10 patients towards intermediate and high risk to fibrosis, which is expected. Similar to APRI results, again Alcohol dependence syndrome was having high risk to fibrosis after DCLD group.

APRI	Unable to Determine	Significant Fibrosis	Severe Fibrosis	P value
Age	43.84±11.805	49.27±11.808	43.25±17.183	NS
AST	35.42±28.599	71.73±72.944	364.3±393.446	.000 Ɏ$
ALT	53.47±113.863	30±12.311	309.95±482.702	.023 Ɏ$
GGT	92.95±97.286	195.64±207.371	422.35±702.14	.086 Ɏ
PLT Count	4423.55±19270.31	28000.91±33282.78	15101.25±27727.09	.068 ɸ
PT	18.217±18.3927	15.225±3.0236	14.474±3.7036	Ns
INR	1.7742±2.20281	1.3762±0.27882	1.3168±0.39095	Ns
APTT	32.55±5.482	31.91±3.835	35.05±11.712	Ns
HCT	37.02±8.46	36.15±9.63	35.97±7.96	Ns
Albumin	3.44±.759	3.19±.651	3.10±.774	Ns

ɸ-Unable to Determine with Significant Fibrosis

Ɏ- Unable to Determine with Severe Fibrosis

$ -Significant Fibrosis with Severe Fibrosis

Table 3 : Table showing APRI Correlation with AST, APTT

Correlation studies revealed APRI showed positive correlation with AST, APTT values ; whereas FIB 4 showed positive correlation with AST, GGT, Platelet count values. APRI values didn't show any correlation with platelet count, PT and INR values. FIB 4 values were insignificant with PT, APTT, INR and ALT.

FIB-4	Low Risk	Intermediate Risk	High Risk	ANOVA
Age	43.93±12.767	40±8.456	48.04±16.881	Ns
AST	29.43±27.928	112.85±210.13	298.65±367.714	.014 Ɏ
ALT	64.14±132.161	117.69±304.743	231.23±430.452	Ns
GGT	83.93±87.488	224±234.648	359.91±661.598	Ns
PLT Count	6002.7±22449.1	4617.1±16640.4	23913.9±31706.6	.052 Ɏ$
PT	13.038±1.4491	19.26±20.1676	15.167±3.6996	Ns
INR	1.15±0.1368	1.913±2.41021	1.3805±0.38306	Ns
APTT	31.33±6.86	32.05±4.211	35.21±10.873	Ns

HCT	38.61±7.57	35.14±10.85	35.78±7.35	Ns
Albumin	3.64±.641	3.22±.779	3.03±.718	Ns

ϕ-Low Risk with Intermediate Risk

Ɏ- Low Risk with High Risk

$ -Intermediate Risk with High Risk

Table 4 : Above table shows FIB 4 Correlation with AST, GGT and PLATELET values

Pearson Correlation	Mean ± SD	APRI	FIB-4
Age	44.8±14.141	-0.307*	NS
AST	174.96±293.23	.521**	.439**
ALT	153.37±338.31	NS	NS
GGT	247.3±475.14	NS	.300*
PLT Count	13881.6±27214.5	NS	.371**
PT	15.77±10.43	NS	NS
Aptt	33.71±9.008	.363*	NS
INR	1.4697±1.23861	NS	NS
HCT	36.41±8.37	NS	NS
Albumin	3.25 ± .745	NS	NS
Valid N (listwise)			

* <0.05

**<0,01

Table 5 : Pearson correlation table of APRI & FIB 4

SCATTER PLOT :

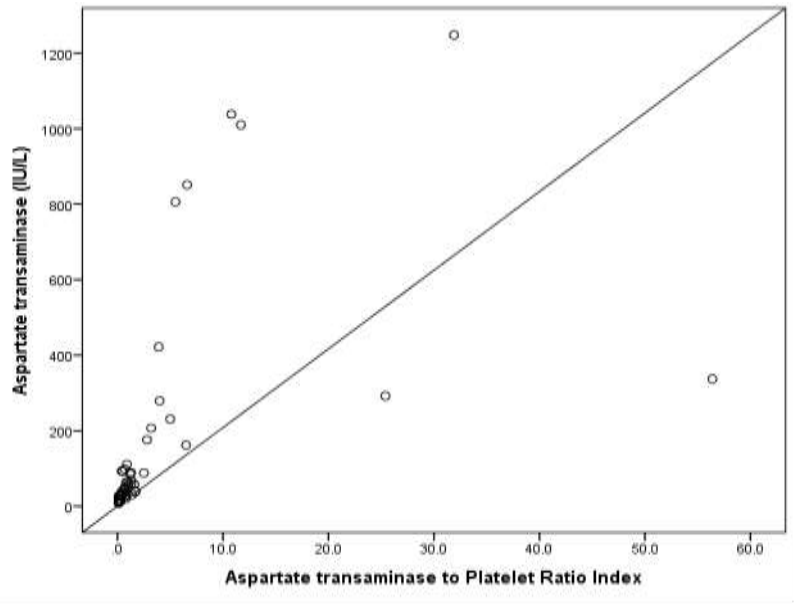

Figure 3 : Scatter plot between APRI and AST

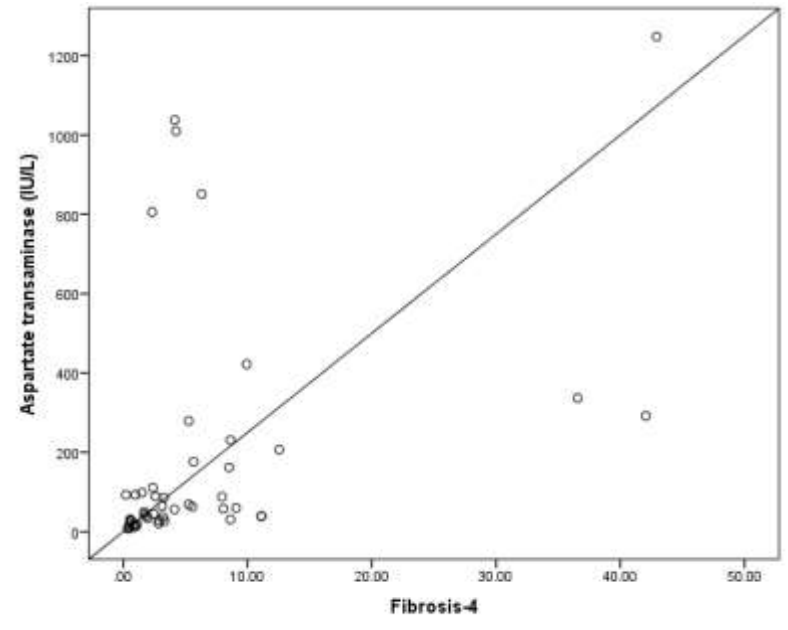

Figure 4 : Scatter plot between FIB 4 and AST

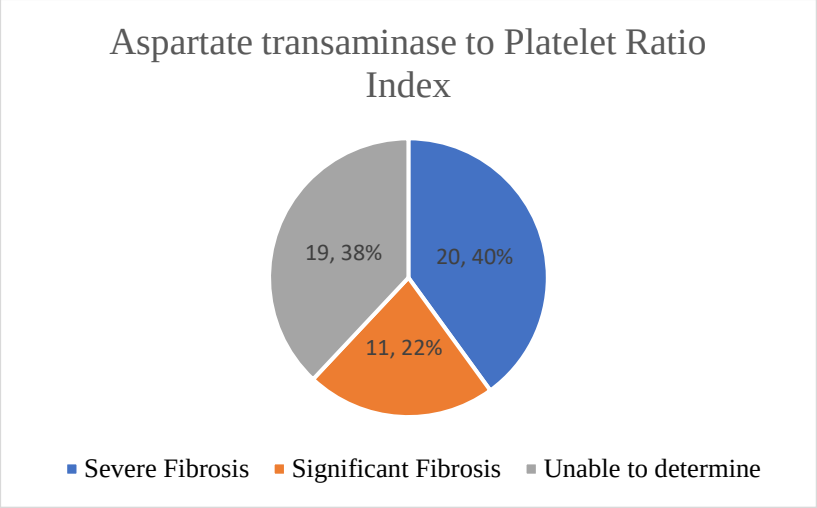

Figure 5 : Pie diagram showing APRI grading

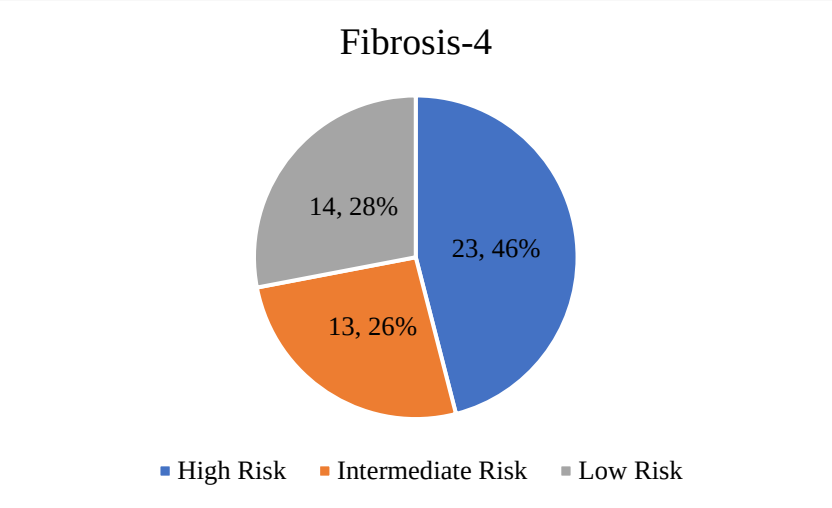

Figure 6 : Pie diagram showing FIB 4 grading

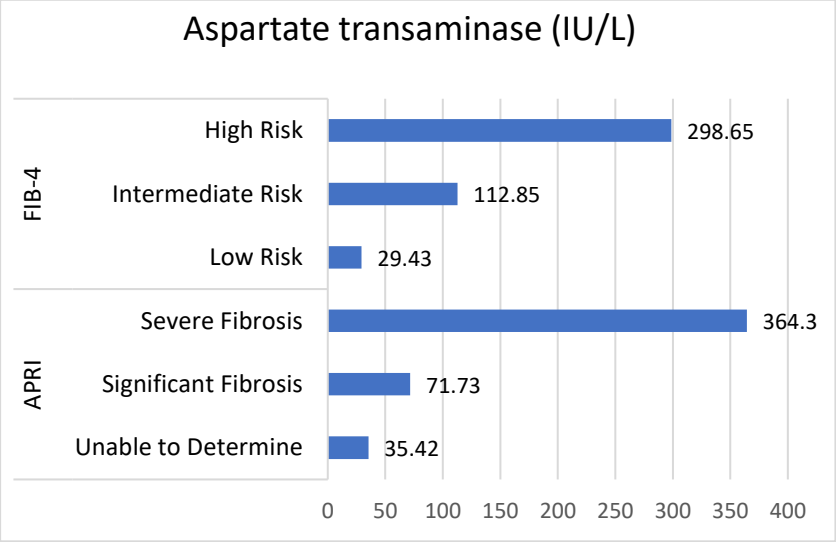

Figure 7 : Bar diagram showing correlation of AST levels with APRI & FIB 4

CONCLUSION :

In the world of advanced era in medical field, to measure stage of liver disease, we would like to move towards non invasive tests over invasive as preferred by renowned hepatologists. This respective study demonstrates us that fibroscores like APRI, FIB 4 not only have correlation with AST levels, but also have correlation with GGT values; less likely correlates with coagulation profile values. Amongst these fibroscores, our study showed FIB 4 had good correlation with GGT and didn't correlate with APTT levels in studied population. Our study also focuses on other important parameters in liver function tests like GGT, which tells us acute disease in liver disorders and secondly, we must also look into coagulation parameters whenever fibroscores are measured in liver disease patients.

Ethical approval : All the participants involved in this study have been explained clearly and informed consent has been taken. Institutional ethics approval has been taken for performing the study.

Declaration of patients : Participants studied were informed about the study in detail and after their informed consent, study data was collected and further analysis was measured.

Financial support and sponsorship: No funding or sponsorship was taken or obtained from the institution or any other educational body for performing the above study.

Conflicts of interest : No conflicts of interest were seen for the study.

Acknowledgement : I would like to thank Prof. Dr.Mohan Rao sir, Dr.Mounika madam and Dr.Jyostnaa Grace madam for their extreme support & guidance. Special thanks to hospital staff for helping me in conducting the study.

REFERENCES:

1.Melaram, R. (2021). Environmental risk factors implicated in liver disease: a mini-review. *Frontiers in Public Health*, *9*, 683719.

2. Berumen, J., Baglieri, J., Kisseleva, T., & Mekeel, K. (2021). Liver fibrosis: Pathophysiology and clinical implications. *WIREs mechanisms of disease*, *13*(1), e1499.

3.Bataller R, & Brenner DA (2005). Liver fibrosis. *J Clin Invest*, 115(2), 209–218. doi: 10.1172/JCI24282

4.Dhar D, Baglieri J, Kisseleva T, & Brenner DA (2020). Mechanisms of liver fibrosis and its role in liver cancer. *Exp Biol Med (Maywood)*, 245(2), 96–108. doi: 10.1177/1535370219898141

7. Swaroop, S., Vaishnav, M., Arora, U., Biswas, S., Aggarwal, A., Sarkar, S., ... & Goel, A. (2024). Etiological Spectrum of Cirrhosis in India: A Systematic Review and Meta-analysis. *Journal of Clinical and Experimental Hepatology*, *14*(2), 101291.

5. Mokdad AA, Lopez AD, Shahraz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med.* 2014;;12((1):):145.. doi: 10.1186/s12916-014-0145-y. DOI:

6. World Life Expectancy. India: Liver Disease. *World Health Rankings. World Life Expectancy.* 2018..

8. Lin, C. S., Chang, C. S., Yang, S. S., Yeh, H. Z., & Lin, C. W. (2008). Retrospective evaluation of serum markers APRI and AST/ALT for assessing liver fibrosis and cirrhosis in

chronic hepatitis B and C patients with hepatocellular carcinoma. *Internal Medicine*, *47*(7), 569-575.

9. Park, H., Yoon, E. L., Kim, M., Lee, J., Cho, S., Jun, D. W., & Nah, E. H. (2022). Reappraisal of fibrosis-4 index and non-alcoholic fatty liver disease fibrosis score for advanced fibrosis in average-risk population. *Frontiers in Medicine*, *9*, 1024836.

10. Yilmaz, Y., Yonal, O., Kurt, R., Bayrak, M., Aktas, B., & Ozdogan, O. (2011). Noninvasive assessment of liver fibrosis with the aspartate transaminase to platelet ratio index (APRI): Usefulness in patients with chronic liver disease: APRI in chronic liver disease. *Hepatitis monthly*, *11*(2), 103.

11.Iredale, J. (2008). Defining therapeutic targets for liver fibrosis: exploiting the biology of inflammation and repair. *Pharmacological research*, *58*(2), 129-136.

12.Denzer, U. W., & Lüth, S. (2009). Non-invasive diagnosis and monitoring of liver fibrosis and cirrhosis. *Best practice & research Clinical gastroenterology*, *23*(3), 453-460.

13.Castera, L. (2008). Assessing liver fibrosis. *Expert Review of Gastroenterology & Hepatology*, *2*(4), 541-552.

14.Afdhal, N. H., & Nunes, D. (2004). Evaluation of liver fibrosis: a concise review. *Official journal of the American College of Gastroenterology| ACG*, *99*(6), 1160-1174.

15.Wai, C. T., Greenson, J. K., Fontana, R. J., Kalbfleisch, J. D., Marrero, J. A., Conjeevaram, H. S., & Lok, A. S. F. (2003). A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology*, *38*(2), 518-526.

16.Viana, M. S. V. B., Takei, K., Yamaguti, D. C. C., Guz, B., & Strauss, E. (2009). Use of AST platelet ratio index (APRI Score) as an alternative to liver biopsy for treatment indication in chronic hepatitis C. *Annals of hepatology*, *8*(1), 26-31.

17.Loaeza-del-Castillo, A., Paz-Pineda, F., Oviedo-Cárdenas, E., Sánchez-Avila, F., & Vargas-Voráckova, F. (2008). AST to platelet ratio index (APRI) for the noninvasive evaluation of liver fibrosis. *Annals of hepatology*, *7*(4), 350-357.

18.Khan, D. A., Fatima-Tuz-Zuhra, K. F., & Mubarak, A. (2008). Evaluation of diagnostic accuracy of APRI for prediction of fibrosis in hepatitis C patients. *J Ayub Med Coll Abbottabad*, *20*(4), 122-6.

19.Cheung, R. C., Currie, S., Shen, H., Bini, E. J., Ho, S. B., Anand, B. S., ... & VA HCV-001 Study Group. (2008). Can we predict the degree of fibrosis in chronic hepatitis C patients using routine blood tests in our daily practice?. *Journal of clinical gastroenterology*, *42*(7), 827-834.

20.Shaheen, A. A. M., & Myers, R. P. (2008). Systematic review and meta–analysis of the diagnostic accuracy of fibrosis marker panels in patients with HIV/hepatitis C coinfection. *HIV clinical trials*, *9*(1), 43-51.

21. Lim, J. K., Flamm, S. L., Singh, S., Falck-Ytter, Y. T., Gerson, L., Hirano, I., ... & Yang, Y. X. (2017). American Gastroenterological Association Institute guideline on the role of elastography in the evaluation of liver fibrosis. *Gastroenterology*, *152*(6), 1536-1543.

22. Patel, K., Asrani, S. K., Fiel, M. I., Levine, D., Leung, D. H., Duarte-Rojo, A., ... & Sterling, R. K. (2023). Accuracy of blood-based biomarkers for staging liver fibrosis in chronic liver disease: A systematic review supporting the AASLD Practice Guideline. *Hepatology*, 10-1097.

23. Sterling, R. K., Duarte-Rojo, A., Patel, K., Asrani, S. K., Alsawas, M., Dranoff, J., ... & Rockey, D. C. (2024). AASLD Practice Guideline on imaging-based non-invasive liver disease assessments of hepatic fibrosis and steatosis. *Hepatology*, 10-1097.

24. Bazerbachi, F., Haffar, S., Wang, Z., Cabezas, J., Arias-Loste, M. T., Crespo, J., ... & Watt, K. D. (2019). Range of normal liver stiffness and factors associated with increased stiffness measurements in apparently healthy individuals. *Clinical Gastroenterology and Hepatology*, *17*(1), 54-64.

25. Unalp-Arida, A., & Ruhl, C. E. (2022). Transient Elastography–Assessed Hepatic Steatosis and Fibrosis Are Associated With Body Composition in the United States. *Clinical Gastroenterology and Hepatology*, *20*(4), e808-e830.

26. Selvaraj, E. A., Mózes, F. E., Jayaswal, A. N. A., Zafarmand, M. H., Vali, Y., Lee, J. A., ... & Doward, L. (2021). Diagnostic accuracy of elastography and magnetic resonance imaging in patients with NAFLD: a systematic review and meta-analysis. *Journal of hepatology*, *75*(4), 770-785.

27. Panel, C. P. G., Berzigotti, A., Tsochatzis, E., Boursier, J., Castera, L., Cazzagon, N., ... & European Association for the Study of the Liver. (2021). EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis–2021 update. *Journal of hepatology*, *75*(3), 659-689.

28 Tachi, Y., Hirai, T., Kojima, Y., Miyata, A., Ohara, K., Ishizu, Y., ... & Goto, H. (2016). Liver stiffness measurement using acoustic radiation force impulse elastography in hepatitis C virus-infected patients with a sustained virological response. *Alimentary pharmacology & therapeutics*, *44*(4), 346-355.

29. Kamal, A. H., Tefferi, A., & Pruthi, R. K. (2007, July). How to interpret and pursue an abnormal prothrombin time, activated partial thromboplastin time, and bleeding time in adults. In *Mayo Clinic Proceedings* (Vol. 82, No. 7, pp. 864-873). Elsevier.