

Original Research Article

Usefulness of fibro scan in assessing liver fibrosis in adult patients with psoriasis

Parimalam Kumar, Suchithra Ganapathi*, Athilakshmi Sivasubramanian

Department of Dermatology, Venereology and Leprosy, Government Kilpauk Medical College, Chennai, Tamil Nadu, India

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***Correspondence:**

Dr. Suchithra Ganapathi,

E-mail: gsuchithra@outlook.com

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ABSTRACT

Background: Patients with psoriasis are at higher risk of developing “systemic” co-morbidities. Non alcoholic fatty liver disease (NAFLD) is found to be more prevalent among psoriasis patients, where it is closely associated with obesity, metabolic syndrome, and psoriatic arthropathy. Elderly participants with psoriasis are 70% more likely to have NAFLD than those without psoriasis independent of common NAFLD risk factors. Methotrexate is a commonly used drug in the management of psoriasis owing to its cost effectiveness and easy administration. In the presence of NAFLD the choice of potentially hepatotoxic drug therapy, such as methotrexate, should be considered with caution. By assessing the liver stiffness measurement (LSM), such drugs can be prescribed with caution in individual with significant liver fibrosis. We have conducted a study to assess the LSM in patients with psoriasis. Aim was to detect the proportion of liver fibrosis (LSM) in adult patients with psoriasis, which will help in choosing the correct treatment.

Methods: Hospital based cross sectional study was conducted in 102 adults with psoriasis who were not treated with methotrexate. Transient elastography (TE) was performed in all and LSM was noted.

Results: There was no statistically significant gender influence on LSM in patients with psoriasis. There was significant increase in liver fibrosis in psoriatic patients as age advances.

Conclusions: Elderly patients with psoriasis are more likely to have liver fibrosis. Hepatotoxic drugs like methotrexate should be prescribed with caution in such patients, preferably after performing LSM.

Keywords: Fibro scan, Liver fibrosis, Methotrexate, Psoriasis

INTRODUCTION

Studies show that patients with psoriasis are 1.5-3 fold more likely to have NAFLD.¹ Miele et al, have shown that 59.2% of patients with psoriasis vulgaris patients were diagnosed to have NAFLD.² It was significantly correlated with metabolic syndrome, obesity, and psoriatic arthritis. The psoriatic patients were more likely to have more severe liver fibrosis when compared to the non- psoriatic group as measured by non-invasive NAFLD fibrosis scores. Elderly participants with

psoriasis were found to be 70% more likely to have NAFLD than those without psoriasis independent of common NAFLD risk factors.¹ Methotrexate is a commonly used in the treatment of psoriasis. Elevated liver enzymes is a predictor of liver fibrosis and indicator to stop methotrexate. However, normal enzyme levels may hide advanced liver fibrosis. According to Sanyal et al 57% of NAFLD patients had normal ALT and 53% of NAFLD subjects had normal GGT. Progression of NAFLD to non-alcoholic steato hepatitis can even lead to hepatocellular carcinoma.³

Aim

The aim of the present study was to detect the proportion of liver fibrosis in adult patients with psoriasis, which will help in choosing the correct drug for treatment.

Objective

- To evaluate proportion of liver fibrosis in adult patients with psoriasis by using TE.
- To correlate the liver stiffness with age, gender of patient, clinical type and duration of disease.

METHODS

We undertook a hospital based cross sectional study at Government Royapettah Hospital, Chennai, over a period of one year from September 2017 to August 2018, including 102 adults with psoriasis. These patients included both genders, having psoriasis, of any duration and all clinical types. Those having normal liver enzyme without systemic hypertension, diabetes, obesity, dyslipidaemia and abnormal BMI were included.

Pregnant women, those with ascites, past liver disease, and patients having active medical device implants like pacemaker were excluded. The study was conducted in a tertiary care hospital. After confirming the diagnosis of psoriasis and obtaining written consent, patients fulfilling the criteria were included in the study.

Liver stiffness was measured using fibroscan machine 402 with power: 100 - 230 volts (+10%/-15%), probe of size- 158 x 52 mm; 7 mm transducer and frequency 3.5 Mhz. A dedicated software and touch screen display which expressed readings in kilopascals (KPa) that ranges from 2 to 75.

Grading of liver fibrosis includes the following five stages namely F0 to F4, viz., F0: 0-1 KPa, F1: 1-7.5 KPa, F2: 7.5-10 KPa, F3: 10-14 KPa, F4: >14 KPa. Those who record a value above 7.5 KPa were taken as having significant liver fibrosis indicating NAFLD. (normal range for a fibro scan: 2 to 7 KPa. With an average normal of 5.3 KPa).

Our observations were compared with previous literature.

Statistical analysis

The collected data were analysed with IBM. SPSS statistics software 23.0 Version. Descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference in the multivariate analysis the Kruskal Walli's test was used. To find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value.05 was considered as significant level.

RESULTS

Out of the total 102 subjects studied majority were in the age group 51-60 years, mean age being 42.12. The age distribution and the fibro scan values are given in Table 1. There were 61 females and 41 males in the study population. Out of the total 102, 19 subjects had LSM value more than 7.5 K Pa. (Figure 1) The prevalence of different stages of Liver fibrosis is given in figure 2. There was no statistically significant gender difference in LSM in our study. The gender distribution with different stages of liver fibrosis is given in Table 2.

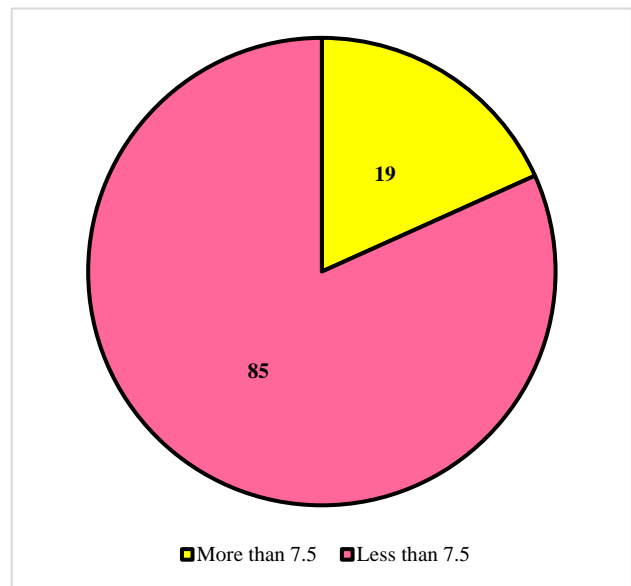


Figure 1: LSM in psoriasis patients (n=102).

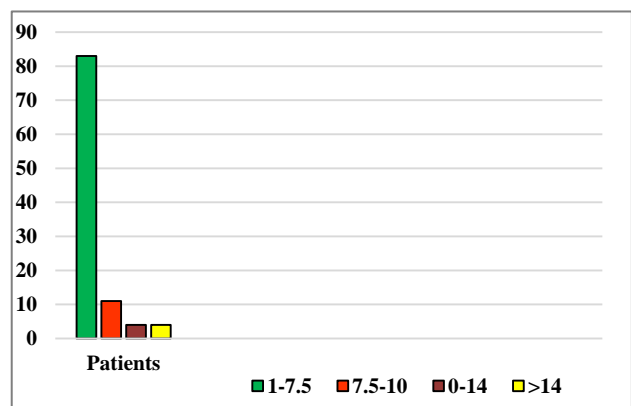


Figure 2: Stages of liver fibrosis in psoriasis patients (n=102).

In our study there was no statistically significant gender influence in relation to fibrosis of liver. However, the comparison of fixed fibroscan value as 5.3 with psoriasis patients, showed statistical significance (p=0.001) with mean±S.D as (6.311±2.8) and mean difference as 1.01. Duration and type of psoriasis did not seem to influence the liver fibrosis. Fibroscan values in different type of psoriasis is given in Table 3.

Table 1: Gender vs fibroscan value (n=102).

			Fibroscan value				Total
			1 - 7.5	7.5 - 10	10 - 14	> 14	
Gender	Female	Count	49	7	4	1	61
		% within Gender	80.3	11.5	6.6	1.6	100.0
	Male	Count	34	4	0	3	41
		% within Gender	82.9	9.8	0.0	7.3	100.0
Total	Count	83	11	4	4	102	
	% within Gender	81.4%	10.8	3.9	3.9	100.0	

Table 2: Age vs liver stiffness measurement (n=102).

			Fibro scan (LSM in KPa)				Total
			1 - 7.5	7.5 - 10	10 - 14	> 14	
Age (in years)	11 - 20	Count	8	1	0	0	9
		%	7.8	1.0	0.0	0.0	8.8
	21 - 30	Count	17	1	0	0	18
		%	16.7	1.0	0.0	0.0	17.6
	31 - 40	Count	19	0	0	0	19
		%	18.6	0.0	0.0	0.0	18.6
	41 - 50	Count	15	3	2	1	21
		%	14.7	2.9	2.0	1.0	20.6
	51 - 60	Count	21	4	2	3	30
		%	20.6	3.9	2.0	2.9	29.4
	Above 60	Count	3	2	0	0	5
		%	2.9	2.0	0.0	0.0	4.9
Total	Count	83	11	4	4	102	
	%	81.4%	10.8	3.9	3.9	100.0	

Table 3: Liver fibrosis in different types of psoriasis (n=102).

			Fibro scan LSM in KPa				Total
			1 - 7.5	7.5 - 10	10 - 14	> 14	
Type	Erythrodermic	Count	3	0	0	0	3
		%	2.9	0.0	0.0	0.0	2.9
	Guttate	Count	1	0	0	0	1
		%	1.0	0.0	0.0	0.0	1.0
	Vulgaris	Count	56	5	3	4	68
		%	54.9	4.9	2.9	3.9	66.7
	Lichenoid	Count	1	0	0	0	1
		%	1.0	0.0	0.0	0.0	1.0
	Arthropathic	Count	1	0	0	0	1
		%	1.0	0.0	0.0	0.0	1.0
	Scalp	Count	2	0	0	0	2
		%	2.0	0.0	0.0	0.0	2.0
	Vulgaris & Palmo Plantar	Count	1	0	0	0	1
		%	1.0	0.0	0.0	0.0	1.0
	Erythrodermic	Count	2	0	0	0	2
		%	2.0	0.0	0.0	0.0	2.0
	Palmo plantar	Count	15	6	1	0	22
		%	14.7	5.9	1.0	0.0	21.6
Palmo plantar & scalp	Count	1	0	0	0	1	
	%	1.0	0.0	0.0	0.0	1.0	
Total	Count	83	11	4	4	102	
	%	81.4	10.8	3.9	3.9	100.0	

DISCUSSION

Psoriasis which was once classified as a skin disease due to increase in keratinocyte turn over time, is now considered as an immune-mediated inflammatory disease (IMID) involving skin, joint and at times other systems as well. Patients with psoriasis are at higher risk of developing “systemic” co-morbidities. IMIDs may impact these co-morbid conditions through shared genetic, environmental factors, or common inflammatory pathways that are co-expressed in skin and target organs.

NAFLD is considered to be the hepatic manifestation of the metabolic syndrome, as it is largely dependent on the underlying insulin resistance state. Considering that metabolic syndrome is associated to psoriasis and NAFLD, it is likely that both entities could coexist in the same patients. The frequency of NAFLD in patients with psoriasis was found to be remarkably greater than in controls.² Even when accounting for other risk factors, the researchers found that elderly people with psoriasis were approximately 70 percent more likely to have NAFLD.¹

NAFLD was directly associated with the severity of psoriasis independently of potential confounders such as age, gender, body mass index, psoriasis duration, and alcohol consumption. Psoriatic patients with NAFLD were much more likely to have psoriatic arthritis. In another study it was found that prevalence of NAFLD was more in patients with psoriasis when compared to the general population. Psoriatic patients with NAFLD are significantly more likely than their non-psoriatic counterparts to develop severe liver disease (steatohepatitis and fibrosis). Since in some, normal liver enzyme levels may hide advanced liver fibrosis treatment with drugs like methotrexate may further worsen liver damage.⁴ In the presence of NAFLD the choice of potentially hepatotoxic drug therapy, as methotrexate, should be considered with caution especially in elderly.

Transient elastography (FibroScan) is a rapid, non-invasive and reproducible method recently developed technique for measuring liver stiffness. Studies have reported the good performance of FibroScan for the diagnosis of fibrosis and cirrhosis in patients with hepatic damage.⁵ This non-invasive procedure will help detect occult liver disease and help in planning for the treatment with particular reference to commonly used drug like methotrexate, follow up of patient during the treatment; pick up high risk individuals and prevent severe steatohepatitis and fibrosis which is a pre-runner for hepato cellular carcinoma.⁶

Metabolic syndrome (MS) which is a risk factor for NAFLD, may coexist with psoriasis. Methotrexate is a cost effective drug frequently used in moderate psoriasis. However, the usage of methotrexate is limited in patients with liver disease in psoriasis. In patients with pre-existing liver fibrosis, the incidence of methotrexate

toxicity will be more which is further worsened with alcohol intake.^{7,8} Apart from methotrexate, factors like MS, long duration, more severe psoriasis and presence of joint involvement play important role in development of liver fibrosis.^{1,9} Using Hepatic ultrasonography scanning procedure Narayanasamy et al found that Non-alcoholic fatty liver disease is highly prevalent among Indian patients with psoriasis, occurring in 45.2% of patients, which was similar to the prevalence noted in Italy, Netherland, and the USA.^{1,10-12} Alsebaey et al have observed that the normal range LSM values using transient elastography in liver transplantation donors with normal liver histology which was not significantly different between men and women which is a similar observation made by us. However, in their study LSM did not correlate with age. However, stiffness values were significantly lower in subjects with a body mass index <26 kg/m² compared to those with an index ≥26 kg/m² indicating that obesity is a risk factor for liver fibrosis.¹³ Whereas, Fung et al have observed that LSM was higher in males compared with females. They also noted that the median LS declined in older age group in contrast to our observation.¹⁴ According to Huang et al LSM was greater in men than in women However, there were no significant differences in the LSM values regarding age or BMI.¹⁵ In study conducted in elderly participants Voor et al observed that older patients with psoriasis are 70% more likely to have NAFLD than those without psoriasis independent of common NAFLD risk factors. They have found that the prevalence of advanced liver fibrosis in elderly was 8.1% in psoriasis patients compared with 3.6% in the reference group (p=0.05).¹ The comparison of fixed LSM value as 5.3 with psoriasis patients in our study showed statistical significance (p=0.001) with mean ±S.D as (6.311±2.8) and mean difference as 1.01. The comparison between the ranges of fibroscan values with age showed statistical significance (p=0.031), revealing that the Fibroscan values are in increasing pattern when the age is increasing

Despite the advantages of TE there are certain limiting factors which can affect the results of LSM. Acute liver injury (as reflected by ALT flares) and extra hepatic cholestasis can influence and are factors of overestimating liver stiffness.¹⁶⁻¹⁹ Performing the test is difficult in obese individuals and those who have narrow intercostal space. In our study we have excluded obese individuals and there was no patient with ascites. Being a reproducible technique, operator experience was not a major concern and factor for variation, as the values were the same with different operators.

Since we have excluded patients with abnormal liver enzymes, it can be said that liver fibrosis can be the result of psoriasis per se more than due to liver disease. In this Indian study the type of psoriasis has not affected the liver fibrosis in a big way. Whereas, duration of disease and age of the patient have. This is similar to other studies adding more evidence to the existing literature.

Factors inducing liver fibrosis in psoriasis still remain to be elucidated clearly. Whether the auto immunity leading to inflammation and scarring of liver is not proved as yet.²⁰ Though there are many studies available to assess the LSM in psoriasis patients, the prevalence of liver fibrosis in patients with psoriasis not having other influencing factors has not been studied in Indian patients. Our study seems to be the first to assess the LSM in patients with psoriasis excluding factors like alcohol intake, MS, past liver disease and treatment with methotrexate, which are important factors inducing liver fibrosis. Age and sex matched case control study in a larger group excluding the above factors will confirm the role of psoriasis as an independent risk factor in inducing liver fibrosis.

CONCLUSION

Our study has shown that there is increasing liver fibrosis with increasing age. This increase was not attributable to MS or therapy. Since elderly patients with psoriasis are more likely to have liver fibrosis, drugs like methotrexate should be prescribed with caution in them. We suggest that for all elderly patients LSM is assessed before starting on methotrexate even if the liver enzymes are normal.

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