Original paper

Relationship between psoriasis and non-alcoholic fatty liver disease

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Abstract

Introduction: Various components of metabolic syndrome have an important role in the pathogenesis of both non-alcoholic fatty liver disease (NAFLD) and psoriasis, suggesting an association between these diseases. However, at present very few studies have reported on the systematic evaluations of the prevalence of NAFLD in patients with psoriasis disorder.

Aim: To investigate the prevalence of NAFLD in patients with psoriasis vulgaris. The study also evaluated the parallel relationship between both of the diseases.

Material and methods: Patients over18 years old and with a diagnosis of psoriasis vulgaris at the outpatient unit of Department of Dermatology were considered for enrolment and were followed up by the Department of Hepatology, Madras Medical College. Each and every patient completed a questionnaire, underwent a thorough skin evaluation, and had a right upper quadrant ultrasound and fasting blood workup.

Results: Two hundred and fifty patients were enrolled in the study. The participants were predominantly middle aged (mean: 44.74 ±11.989 years), overweight (average body mass index (BMI): 24.772 ±3.611 kg/m^2), and male (68%, n = 170). The overall prevalence of NAFLD among psoriasis was 45.2%.

Conclusions: Non-alcoholic fatty liver disease is highly prevalent among our cohort of patients with psoriasis, occurring in 45.2% of patients. Comorbidity of NAFLD is highly associated with psoriasis, which emphasises that both diseases may develop simultaneously. Health care providers should be mindful of this association since early evaluation and diagnosis of NAFLD in patients with psoriasis may play a vital role in alleviating the progression of liver disease.

Introduction

Psoriasis is a chronic inflammatory disease that affects the skin. Studies have shown that psoriasis is not merely a skin problem; psoriasis is linked with various comorbid conditions, especially obesity and metabolic syndrome [1–5], which are known risk factors for non-alcoholic fatty liver disease (NAFLD). In the past decade, many studies have drawn attention to comorbid conditions in psoriasis, and preliminary epidemiological data suggest that psoriasis could be associated with the development of NAFLD. Non-alcoholic fatty liver disease includes a spectrum of conditions that range from simple fatty liver, which is relatively benign, to non-alcoholic steatohepatitis (NASH), which can give rise to fibrosis, cirrhosis, and end-stage liver disease [6]. Moderate or severe conditions of psoriasis have a high prevalence of chronic liver disease [7]. It is hypothesised that components of metabolic syndrome as the most likely pathogenic basis may play a role in the manifestation of NAFLD and psoriasis.

Aim

In the present work, our aim was to analyse the prevalence of NAFLD among psoriasis and basic aspects of the relationship between psoriasis and NAFLD.

Material and methods

Study population

Patients with an age of above 18 years and with a clinical diagnosis of psoriasis vulgaris, who were outpatients at the Department of Dermatology, Madras Medical College were recruited for the study over a period of 9 months (from July 2014 to March 2015). We excluded patients who were currently on treatment and also those who received methotrexate, cyclosporine, acitretin, psoralens, or systemic steroids 30 days prior to the day of testing. Subjects who had known documented chronic liver disease (alcohol abuse, hepatitis B or C, haemochromatosis, Wilson disease, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis or hepatic malignancy), human immunodeficiency virus (HIV), clinical evidence of malignancy, or other secondary causes of chronic liver disease were also excluded.

Design of study and sample size

This study was designed as a prospective hospital-based observational study in which 250 patients were enrolled. The sample size was determined based on the following assumptions:
1) 17.4% is the previous prevalence reported (our region),
2) 5% absolute precision,
3) 95% confidence interval.

Based on calculation, the samples required were 215 participants.

Anthropometric, clinical, and laboratory variables

Information of the study subjects including age, gender, hypertension, diabetes mellitus, dyslipidaemia, and duration of the psoriasis were collected by a standardized questionnaire. The subject's waist circumference, weight, and height were measured upon enrolment. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres (kg/m^2). Waist circumference was measured according to WHO recommendations [8]. Hypertension or high blood pressure was diagnosed if the participant was on anti-hypertensive medications, if a physician had ever told them that they had high blood pressure, or the average of three blood pressure measurements was 130/85 mm Hg. Diabetes mellitus was diagnosed if participants were taking hypoglycaemic medications or had a fasting glucose concentration 110 mg/dl or had been told by a physician that they had diabetes mellitus. All study participants gave written informed consent, and the study protocol was approved by the Institutional Ethics Committee.

Metabolic syndrome was diagnosed by the National Cholesterol Education Program – Adult Treatment Panel III criteria (NCEP – ATP III) [9]. In accordance with the definition of metabolic syndrome, the patient was classified as having the syndrome if he/she had at least three of the following five risk abnormalities:
1) waist circumference > 102 cm in men or > 88 cm in women,
2) fasting glucose 110 mg/dl or on treatment,
3) triglycerides ≥ 150 mg/dl,
4) HDL men < 40 mg/dl, women < 50 mg/dl or on treatment, and
5) blood pressure 130/85 mm Hg or on treatment.

Venous blood samples were drawn in the morning from each participant after an overnight fast. A panel of blood tests were performed for each participant, which included serum levels of total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum alkaline phosphatase (SAP), serum total protein, albumin, platelet count, viral markers (hepatitis B and C infections), fasting glucose levels, total cholesterol, high density lipoprotein (HDL), and total triglycerides. Low-density lipoprotein (LDL) cholesterol was estimated by the Friedewald's equation (i.e. total cholesterol minus high-density lipoprotein cholesterol minus triglycerides divided by five).

Diagnosis of psoriasis

The diagnosis of psoriasis was made clinically by the dermatologist and disease severity was assessed using the Psoriasis Area and Severity Index (PASI) [10]. The PASI score, ranging from 0 to 72, reflects the erythema, induration, and scaling of the lesions in four body areas (head, trunk, upper limbs, and lower limbs).

Diagnosis of NAFLD

Hepatic ultrasonography scanning procedure was performed in all participants by a qualified radiologist, who was blinded to participant's particulars. The diagnosis of hepatic fatty liver was made on the basis of characteristic sonographic features, i.e. evidence of diffuse hyper-echogenicity of liver relative to kidneys, ultrasound beam attenuation, and poor visualisation of intra-hepatic structures. The fibro scan assesses the fibrosis in liver disease according to the following classification: F0 – no fibrosis, < 6.5; F1 – perisinusoidal fibrosis without septa, 6.6–8.0; F2 – portal and periportal fibrosis with rare septum, 8.1–12.5; F3 – portal and periportal fibrosis with many septa > 12.6; and F4 – cirrhosis.

Statistical analysis

Statistical calculations were performed using of SPSS software (version 20.0). Data were expressed as

mean ± standard deviation for continuous variables and as numbers and percentages for categorical variables. Statistical analyses included the analysis of variance – ANOVA (for continuous variables) and Pearson's χ^2 test (for categorical variables). The association of NAFLD with the psoriasis was assessed by logistic regression analysis. Values at $p < 0.05$ were considered statistically significant.

Results

Baseline characteristics of the psoriasis cohort

To evaluate the prevalence of NAFLD in people with psoriasis, we conducted 9-month hospital-based study. During the enrolment period, 340 adults with psoriasis were eligible for the study and 250 (73.52%) agreed to participate in our study. Their characteristics are summarised in Table I. All participants were diagnosed with psoriasis vulgaris, in which some of the specific types were as follows: 49 had chronic plaque psoriasis, 45 had palmoplantar psoriasis, 38 had scalp psoriasis, 28 patients had psoriasis arthritis, 21 had pustular type, and 7 had nail type.

The participants were largely middle aged (44.74 ±11.989) and the majority were overweight (24.772 ±3.611 kg/m²) and male (68%, $n = 170$). More than two thirds of the participants (70.8%) met the criteria for diagnosis of metabolic syndrome based on NCEP – ATP III. Abdominal obesity was detected in 48% of psoriasis patients. Dyslipidaemia was more commonly observed in 96% of patients (abnormal value at least anyone of lipid profile), and 52.8% of patients were hyperglycaemic. 53.6% of psoriatic patients had hypertension, and 44% of the patients presented with elevated ALT levels.

Prevalence and characteristics of psoriasis-associated NAFLD

The sonographic examination revealed signs of fatty liver (134/250, 53.6%). In 21 of these 134 cases, there was evidence of significant ethanol intake ($n = 14$), chronic hepatitis B infection (HBsAg +ve) ($n = 6$), and chronic hepatitis C (anti-HCV +ve) ($n = 1$). The remaining 113 met the criteria for diagnosis of NAFLD (prevalence: 45.2%).

Psoriasis patients with NAFLD were younger than patients with psoriasis alone, more obese when compared to non-NAFLD patients with psoriasis, more likely to be male and had higher levels of BMI. They also had greater frequency of metabolic syndrome when compared to psoriasis with non-NAFLD and the majority of NAFLD patients had higher serum ALT concentrations. Notably, compared with psoriasis patients with NAFLD had a more severe form of psoriasis than with non-NAFLD

Table I. Characteristics of psoriasis subjects ($n = 250$)

Characteristics	Value
Age	44.74 ±11.989
Gender (male)	170 (68%)
Weight	62.54 ±9.608
Height	158.84 ±7.833
BMI	24.772 ±3.611
Waist circumference	91.53 ±13.910
Systolic	120.26 ±15.222
Diastolic	81.43 ±11.335
FBS	114.23 ±25.328
TGL	202.87 ±109.762
Cholesterol	214.04 ±40.969
HDL	44.28 ±8.572
Obese	46 (18.4%)
Metabolic syndrome	177 (70.8%)
Fatty liver	134 (53.6%)
NAFLD	113 (45.2%)
Alcoholic	22 (8.8%)
Abdominal obesity	120 (48%)
Hypercholesterolaemia	160 (64%)
Hypertriglyceridaemia	166 (66.4%)
Low HDL	117 (46.8%)
Hyperglycaemia	132 (52.8%)
Hypertension	134 (53.6%)
Diabetes	133 (53.2%)
Elevated ALT	110 (44%)
HBsAg +ve	9 (3.6%)
Anti-HCV +ve	1 (0.4%)
AST	28.15 ±12.009
ALT	29.75 ±13.005
AST/ALT	1.044 ±0.419
Duration	4.14 ±2.696
Fibro Scan	5.974 ±1.7435
PASI	27.80 ±13.494
S. Bilirubin – total	0.664 ±0.5997
S. Bilirubin – direct	0.304 ±0.1360
SAP	68.49 ±24.514
Serum protein	7.530 ±1.003
Albumin	4.239 ±0.4704
Platelet	2.7158 ±0.85809

according to PASI score (mean ± SD: 32.88 ±13.542 vs. 23.19 ±12.052; $p < 0.0001$) (Table II).

Fibrosis scores of NAFLD patients with psoriasis were higher than non-NAFLD patients with psoriasis. Among the NAFLD patients with psoriasis, 36.2% showed portal and periportal fibrosis with septum (F2–F3). Most of the NAFLD patients with psoriasis (63.8%) showed fibrosis in F1 stage. Cirrhosis of the liver did not occur in any of the NAFLD patients with psoriasis.

Correlation between psoriasis with NAFLD and psoriasis without NAFLD

Univariate logistic regression analysis was performed to explore the mechanisms underlying the cor-

Table II. Correlation between psoriasis with non-NAFLD and NAFLD

Characteristics	Psoriasis with NAFLD (*n* = 113)	Psoriasis with non-NAFLD (*n* = 105)	*P*-value
Age	42.23 ±11. 004	46.02 ±12.622	0.019
Gender (male)	84 (74.3%)	64 (61%)	0.042
Weight	63.74 ±9.456	61.11 ±9.923	0.046
Height	158.85 ±7.480	157.52 ±8.156	0.212
BMI	25.217 ±3.462	24.655 ±3.956	0.265
Systolic	122.01 ±13.218	118.93 ±17.791	0.147
Diastolic	81.56 ±11.721	82.39 ±11.442	0.596
FBS	120.69 ±24.570	110.70 ±27.273	0.005
TGL	238.18 ±129.895	172.23 ±83.368	0.0001
Cholesterol	217.03 ±43.198	210.28 ±40.723	0.237
HDL	44.54 ±8.206	43.43 ±9.038	0.342
LDL	124.23 ±37.242	132.07 ±34.716	0.110
Obese	16 (14.2%)	13 (12.4%)	0.842
Metabolic syndrome	94 (83.2%)	69 (65.7%)	0.005
Waist circumference	94.07 ±11.401	88.00 ±15.038	0.001
Abdominal obesity	63 (55.8%)	39 (37.1%)	0.007
Hypercholesterolaemia	69 (61.1%)	66 (62.9%)	0.889
Hypertriglyceridaemia	89 (78.8%)	54 (51.4%)	0.0001
Low HDL	51 (45.1%)	56 (53.3%)	0.278
Hyperglycaemia	76 (67.3%)	43 (41%)	0.0001
Hypertension	65 (57.5%)	59 (56.2%)	0.891
Diabetes	77 (68.1%)	45 (42.9%)	0.0001
Elevated ALT	66 (58.4%)	35 (33.3%)	0.0001
ALT	34.21 ±13.666	26.23 ±11.532	0.0001
AST	32.04 ±13.320	29.30 ±9.617	0.084
AST/ALT	0.989 ±0.386	1.258 ±0.500	0.0001
Duration	4.61 ±2.932	3.69 ±2.339	0.011
Fibro Scan	6.596 ±1.852	5.422 ±1.431	0.0001
PASI	32.88 ±13.542	23.19 ±12.052	0.0001
S. Bilirubin – total	0.748 ±0.841	0.672 ±0.335	0.392
S. Bilirubin – direct	0.341 ±0.152	0.332 ±0.170	0.703
SAP	64.69 ±25.771	69.87 ±23.355	0.123
Serum protein	7.635 ±0.849	7.430 ±1.176	0.140
Albumin	4.179 ±0.395	4.262 ±0.476	0.160
Platelet	2.647 ±0.540	2.813 ±1.173	0.178

relation between psoriasis and NAFLD in the 218 patients. The significant were observed between NAFLD and non-NAFLD subjects in age, sex, weight, waist circumference, fasting blood sugar, PASI, metabolic syndrome, ALT, duration of psoriasis, fibroscan, direct serum bilirbin, serum protein and statistical significant was not observed in other variables in univariate analysis (Table III).

Table III. Univariate analysis

Characteristics	*P*-value	OR (95% CI)
Age	0.020	1.028 (1.004–1.052)
Gender (male)	0.035	1.856 (1.043–3.301)
Weight	0.048	0.972 (0.945–1.0)
Height	0.212	0.978 (0.945–1.013)
BMI	0.264	0.960 (0.893–1.032)
Systolic	0.149	0.987 (0.970–1.005)
Diastolic	0.595	1.006 (0.983–1.030)
FBS	0.006	0.984 (0.973–0.996)
TGL	0.0001	0.993 (0.990–0.997)
Cholesterol	0.237	0.996 (0.990–1.003)
HDL	0.341	0.985 (0.955–1.016)
LDL	0.111	1.006 (0.999–1.014)
Obese	0.699	1.167 (0.532–2.560)
Metabolic syndrome	0.004	2.581 (1.366–4.879)
Waist circumference	0.001	0.966 (0.947–0.987)
Abdominal obesity	0.006	2.132 (1.239–3.669)
Hypercholesterolaemia	0.785	0.927 (0.536–1.602)
Hypertriglyceridaemia	0.0001	3.510 (1.939–6.327)
Low HDL	0.227	0.720 (0.422–1.227)
Hyperglycaemia	0.0001	2.962 (1.704–5.148)
Hypertension	0.843	1.056 (0.617–1.805)
Diabetes	0.0001	2.852 (1.640–4.959)
Elevated ALT	0.0001	2.809 (1.617–4.877)
ALT	0.0001	0.951 (0.929–0.973)
AST	0.087	0.980 (0.957–1.003)
AST/ALT	0.0001	4.889 (2.202–10.852)
Duration	0.013	0.877 (0.792–0.972)
Fibro Scan	0.0001	0.642 (0.533–0.774)
PASI	0.0001	0.941 (0.918–0.965)
S. Bilirubin – total	0.425	0.805 (0.472–1.373)
S. Bilirubin – direct	0.702	0.723 (0.137–3.805)
SAP	0.124	1.009 (0.998–1.020)
Serum protein	0.147	0.816 (0.620–1.074)
Albumin	0.168	1.576 (0.825–3.012)
Platelet	0.198	1.248 (0.891–1.749)

Another important finding of our study is multivariate analysis, which has not been carried out in previous reports. The variables that were independently associated with NAFLD among patients with psoriasis were hypertriglyceridaemia (OR = 3.174, 95% CI: 1.565–6.438, *p* < 0.001), hyperglycaemia (OR = 2.495, 95% CI: 1.191–5.227, *p* < 0.015), fibro scan (OR = 0.692, 95% CI: 0.553–0.867, *p* < 0.001), PASI (OR = 0.950, 95% CI: 0.922–0.979, *p* < 0.001), and duration (OR = 0.865, 95% CI: 0.756–0.990, *p* < 0.035) and gender (OR = 2.681, 95% CI: 1.244–5.778, *p* < 0.012) (Table IV).

Discussion

The hallmark of NAFLD refers to the accumulation of fat in the liver. Non-alcoholic fatty liver disease is regarded as the hepatic manifestation of metabolic syndrome and the most common form of chronic liver disease throughout world [11–13]. The previously well-described risk factors for NAFLD include metabolic syndrome and lifestyle habits, such as fructose consumption and physical activity level, which impact disease severity [14]. Recent reports have shown that people with psoriasis may be at greater risk for developing of NAFLD [15, 16].

Non-alcoholic fatty liver disease prevalence has been estimated to be in the 20–30% range in the general population in various countries and is rapidly increasing. The prevalence of NAFLD has become a major public health concern in developed and developing countries [17, 18]. Non-alcoholic fatty liver disease is one such disease that now has potentially enormous public health consequences due to its progression to more severe forms of the disease ranging from steatosis to steatohepatitis (NASH), which, in turn, can progress into cirrhosis and end stage liver disease and finally the need for liver transplantation. The increasing incidence of NAFLD throughout world has contributed to rising numbers of HCC incidents [19]. There is also

Table IV. Multivariate analysis

Characteristics	*P*-value	AOR (95% CI)
Age	0.136	1.022 (0.993–1.052)
Gender (male)	0.012	2.681 (1.244–5.778)
Weight	0.069	0.967 (0.933–1.003)
Abdominal obesity	0.474	1.291 (0.642–2.593)
Hypertriglyceridemia	0.001	3.174 (1.565–6.438)
Hyperglycaemia	0.015	2.495 (1.191–5.227)
Elevated ALT	0.224	1.563 (0.761–3.209)
Duration	0.035	0.865 (0.756–0.990)
Fibro Scan	0.001	0.692 (0.553–0.867)
PASI	0.001	0.950 (0.922–0.979)

evidence suggesting that NAFLD individuals are at risk of developing cardiovascular events independently of conventional risk factors and metabolic syndrome components [20].

Psoriasis is a chronic, inflammatory, immune-mediated skin disease. Both innate and adaptive immunity are crucial in the initiation and maintenance of psoriatic plaques. Non-alcoholic fatty liver disease began to be considered a part of the metabolic syndrome spectrum, and the relationship between NAFLD and psoriasis became grounded in their association with metabolic syndrome and secretion of proinflammatory cytokines. The first report of patients with psoriasis and concomitant hepatic steatosis was unexpectedly found during a survey conducted in 2002, which aimed to evaluate patients with NAFLD. These patients presented with liver abnormalities seen on ultrasonography and underwent a liver biopsy, which revealed hepatic fibrosis. Since then, different population-based surveys have shown a higher prevalence of NAFLD in patients with psoriasis compared with the general population. It was also observed that the PASI was higher in patients with both psoriasis and NAFLD than in those with psoriasis only.

We have conducted a study to determine the prevalence of NAFLD among patients with psoriasis in our region. The present study reports a notable increase in the prevalence of NAFLD when compared with a previous study in 2012 carried out in our region, in which 17% prevalence was reported [21]. Our study is the first to confirm that patients with psoriasis are at increased risk for NAFLD, as suggested by previous studies that used the same evaluating measures for fatty liver; however, our study showed that the prevalence of NAFLD was 45.2%, i.e. the prevalence rate of NAFLD is more than 2.5-fold higher. It should be noted that we do not feel the results of our study discredit the possibility of NAFLD prevalence among psoriasis as determined in other studies conducted in Italy, Netherland, and the USA, which demonstrated that the prevalence was 46%, 47%, and 47%, respectively [22–24].

Many studies showed that elderly patients are at increased risk of NAFLD with psoriasis even if the skin disease is mild or moderate and not requiring systemic therapy [24, 25]. But an important finding of our study showed that a high prevalence is observed even in middle-aged psoriatic populations; the mean age of patients was 44.02 years.

We observed a significant relationship between NAFLD and gender. NAFLD was more prevalent in male gender than in female gender. High BMI levels were frequent in our NAFLD patients with psoriasis, and this finding confirmed the previous findings [21].

It is reported that metabolic syndrome is more common in psoriasis patients [26]. We found higher rates of metabolic syndrome among NAFLD than non-NAFLD patients with psoriasis. However, our major finding in this study was that psoriasis with NAFLD was positively correlated with three components of metabolic syndrome: hyperglycaemia, hypertriglyceridemia, and abdominal obesity, but significant correlation was not observed with hypertension and low level of HDL in univariate logistic regression analysis, although the levels of HDL and blood pressure were reported to be higher in psoriasis patients with NAFLD than in those with non-NAFLD.

Although obesity is reported to be highly prevalent among psoriasis patients, we did not find significant correlation between BMI and NAFLD in psoriasis patients. However, we observed a higher number of obese among psoriasis with NAFLD patients than non-NAFLD psoriasis patients. This may be explained by which concluded that the predominant of our psoriasis patients were overweight.

In our study we observed that ALT was increased in psoriasis patients with NAFLD and highly associated with psoriasis. We did not detect any significant association of NAFLD in other liver function tests in our psoriasis patients. Our study found that DM was common in psoriasis patients. We also found that hypercholesterolaemia was not associated with NAFLD patients with psoriasis even though TGL was highly significantly associated with NAFLD patients with psoriasis.

In multivariate analysis, NAFLD was associated with both the severity and duration of psoriasis. We also observed that psoriasis is associated with hyperglycaemia and hypertriglyceridemia. Therefore, it was concluded that NAFLD is related to the duration of the disease, components of metabolic syndrome such hyperglycaemia and hypertriglyceridemia, and closely associated with the development of psoriasis and NAFLD.

Conclusions

Our findings suggest that NAFLD is frequent in patients with psoriasis and is also associated with the duration and severity of the disease. Physicians must be careful of this association and evaluation of NAFLD in patients with psoriasis, but future investigation is required to determine the most appropriate diagnostic and treatment strategies for these patients.

Conflict of interest

The authors declare no conflict of interest.

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