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Nonalcoholic Fatty Liver Disease in Patients with Psoriasis

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Abstract

Psoriasis is a chronic inflammatory skin disease associated with an increased risk for non-alcoholic fatty liver disease (NAFLD) compared with general population. Chronic low-grade inflammation in psoriasis plays role in the development of NAFLD. However, there is scarcity of studies reporting on the systematic evaluations of the prevalence of NAFLD in patients with psoriasis disorder. This cross-sectional, comparative study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Bangladesh, from September 2019 to August 2020, to observe association between NAFLD and psoriasis. A total of 50 patients with psoriasis were selected as case group and another 50, age and sex matched participants were selected as control group according to selection criteria. Informed written consent was taken from each patient. Detail history was taken; thorough physical examination and relevant investigations were done. All information's were recorded in a separate case record form. Most of psoriasis patients were in 36-50 years (36%) group with a mean age of 40.74±11.61 years. Male dominance was found in psoriatic patient (74%). Prevalence of NAFLD was significantly higher in psoriatic patient than in control (70% vs 26%; p<.05). Among the patients with NAFLD 18% had Grade I, 20% had Grade II, 10% had Grade III. Among psoriasis patient 14% had mild, 56% had moderate and 30% had severe psoriasis according to psoriasis area and severity index (PASI). While increasing PASI score, the stage of fibro scan of liver also increased. The association of PASI and steatosis grade of fatty liver stage was found significant (p<0.001). The study revealed that NAFLD was very frequent among patients having psoriasis (70%) and a statistically significant association was observed between the severity of NAFLD and psoriasis. However, further studies with lager samples are recommended.

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Introduction

Psoriasis is a complex chronic inflammatory immune mediated skin disorder which mostly affect skin but it also have several extra cutaneous systemic manifestations. It is associated with several comorbid conditions including psoriatic arthritis, nonalcoholic fatty liver disease (NAFLD), obesity, cardiovascular disease and metabolic syndrome.[1] NAFLD is a liver disease which develop due to excessive accumulation of triglyceride in liver. It encompasses a wide spectrum of liver disease ranging from benign steatosis to nonalcoholic steatohepatitis, pericellular fibrosis (cirrhosis) and hepatocellular carcinoma.[2] Psoriasis has been associated with a high prevalence of liver function test abnormalities and liver disease.[2,3] Previous studies have reported an increased prevalence of liver disease, in particular fatty liver disease in patients with psoriasis.[4-10] The incidence of liver disease among patients with psoriasis compared with the general population is unknown. Relatively little is known about how the liver responds to chronic inflammation and how this may differ by the type or severity of inflammation. Furthermore, little is known about how skin disease severity, obesity, diabetes, and medication use play a role in the development of liver disease in patients with these diseases.[11] Paralleling the increasing prevalence of obesity, diabetes mellitus and nonalcoholic fatty liver disease (NAFLD) has become the most common

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cause of chronic liver disease worldwide. One in 3 adult Americans and one in 4 or 5 Italians suffer from NAFLD. NAFLD also reached epidemic proportions among population typically considered at low risk, with a prevalence of 15% in China and 14% in Japan. The clinical implications of this alarming prevalence of NAFLD are derived from the fact that NAFLD may progress to cirrhosis, liver failure and hepatocellular carcinoma. Liver injury in psoriasis has been postulated to result from cytokine release from skin-derived cells. This so-called hepato-dermal axis postulates that psoriatic skin-derived lymphocytes and keratinocytes produced inflammatory cytokines such as IL-6, IL-17, and tumor necrosis factor-α that circulate systemically to the liver and induce an array of metabolic derangements that promote insulin resistance, a hallmark feature of nonalcoholic fatty liver disease pathogenesis.[12] The converse may also be true in that the ensuing hepatic inflammation promotes keratinocyte proliferation and cutaneous inflammation.[12] If such an axis exists, it is conceivable that patients with either longer duration of inflammation or increased psoriasis severity would have an increased risk of developing liver disease and propensity for developing cirrhosis, the most advanced form of liver disease. Hence, this study aimed to evaluate the association of NAFLD in patients with psoriasis.

Methods

This cross-sectional, comparative study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Bangladesh, from September 2019 to August 2020. The psoriasis patients and the age and gender matched patients without psoriasis attended to outdoor of Dermatology and Venereology Department, Dhaka Medical College and Hospital within the study period was considered as study population. We adopted a purposive sampling technique.

Inclusion criteria:

1) Both male and female aged between 18 and 60 years;
2) Clinical and/or histopathologically diagnosed psoriasis (lasting at least 6 months); and
3) Patients who agreed to give informed consent to take part in this study.

Exclusion criteria:

1) Aged below 18 years;
2) Pregnancy;
3) Patients or attendants refused to give informed consent to take part in the study;
4) Patients who have others co-morbidities such as DM, CKD, CLD or COPD, cancer etc.;
5) Patients having autoimmune disease (e.g. Autoimmune bullous disease, SLE etc.);
6) Patients having history of taking steroid, tamoxifen etc.; and
7) Patients having history of HBsAg positive, Anti-HCV positive, Anti-HIV positive.

After scrutiny, a total of 50 patients with psoriasis were selected as case group based on inclusion and exclusion criteria. Another 50 age and sex matched participants were chosen as control group according to inclusion and exclusion criteria. Informed written consent was taken from each patient. Demographic and clinical history was taken from each patient. Everyone underwent a thorough physical examination. All patients underwent relevant investigations serum albumin, AST, ALT, Fasting glucose level, serum lipid profile and USG of hepatobiliary system. All information were collected in separate case record form. Collected data were checked for errors and analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0 for Windows. Continuous parameters were expressed as

mean±SD and categorical parameters as frequency and percentage. Comparisons between groups for continuous parameters was done by using Student's t-test. Categorical parameters were compared by Chi-Square test. The significance of the results as determined in 95% confidence interval and value of p<0.05 was considered to be statistically significant.

This research was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh.

Results

Figure 1 demonstrates distribution of study participants by age-group. Most of psoriasis patients were in 36-50 years (36%) group. Mean age of psoriasis patients was 40.74±11.61 years and control group was 38.4±11.84 years. The mean age difference between patients of psoriasis and non-psoriasis group was not statistically significant (p>0.05). Figure 2 demonstrates gender of the participants; male predominance was observed in both psoriasis and non-psoriasis group (74% and 62% respectively). No difference was observed in gender distribution between two groups (p>0.05). We observed statistically significant differences in AST, ALT, AST/ALT, total cholesterol, LDL cholesterol, HDL cholesterol and serum albumin between psoriasis and non-psoriasis group (p<0.001). However, there was no difference in fasting glucose level between two groups (p>0.05). Moreover, a higher body mass index (BMI) was observed in patients with psoriasis compared to the non-psoriasis (control) group (p<0.001) (Table-I). In psoriasis group, 70% had non-alcoholic fatty liver disease(NAFLD) and in non-psoriasis group, only26% had NAFLD (p<0.001) (Table-II). Regarding fatty liver findings by ultrasonography, 30% had no fatty liver disease (Grade 0), 10% had grade I, 40% had Grade II, and 20% had Grade III fatty liver in patients of psoriasis, while in non-psoriasis group, 74% had no fatty liver disease (Grade 0) and only 26% had grade I. The difference between two groups was statistically significant (p<0.001) (Table-III). Histopathological findings of skin biopsy in psoriasis patients revealed that the majority of the had dilated tortuous vessels in the papillary dermi (46%), followed by loss of granular layer (18%), thinning in supra papillary dermis (6%), others (10%), parakeratosis (6%), spongiosis (4%) and regular acanthosis (4%) (Table-IV).

Figure 3 shows that among the patients with psoriasis, 14% had mild psoriasis, 56% had moderate psoriasis (11-20) and 30% had severe psoriasis (>20), as measured by psoriasis area and severity index (PASI). Relating to psoriasis area and severity index (PASI) and staging through of fibroscan in patients of psoriasis with NAFLD, a significant association of psoriasis area and severity index (PASI) and stage of fibroscan was found (p<0.001), i.e., with increasing PASI score, the stage of fibroscan of liver also increased (Table-V). Moreover, the association of psoriasis area and severity index (PASI) score and mean fibroscan score of liver was also found significant (p<0.001), i.e., increased severity of psoriasis was associated with advanced fibrosis (Table-VI). A significant association was observed between psoriasis area and severity index (PASI) and steatosis grade of fatty liver (p<0.01), which indicates that an increased PASI score was related to increased steatosis grade of fatty liver (Table-VII). Similarly, a significant association was found between psoriasis area and severity index(PASI) score and CAP score of fatty liver (p<0.001), which indicates that increased severity of psoriasis was associated with elevated CAP score (Table-VIII).

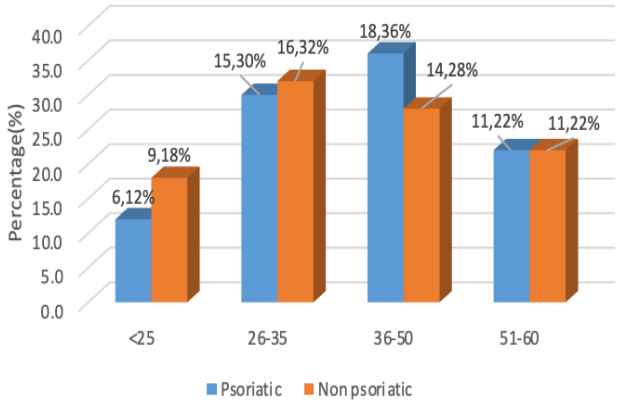

Fig. 1: Distribution of participants by age group (N=100)

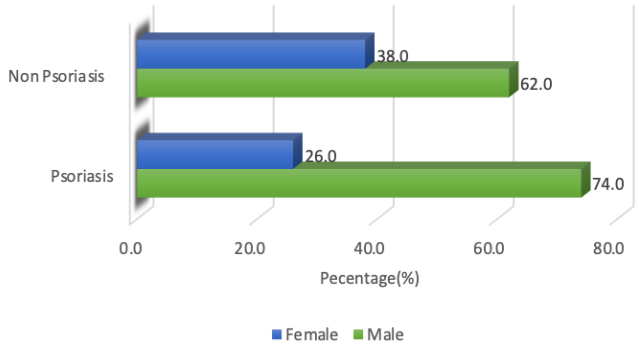

Fig. 2: Distribution of respondents by gender (N=100)

Table-I: Results of laboratory investigations (N=100)

Variables	Psoriasis Mean±SD	Non-Psoriasis Mean±SD	p-value
Aspartate aminotransferase (AST) U/L	31.38±5.07	24.4±2.59	<0.001
Alanine aminotransferase (ALT) U/L	42.21±5.12	23.64±0.98	<0.001
AST: ALT	0.696±0.99	1.23±0.749	<0.001
Serum albumin (g/dL)	3.1±6.5	4.7±0.52	<0.001
Fasting glucose (mmol/l)	5.35±0.64	5.21±7.1	>0.05
Total cholesterol(mg/dl)	286.8±66.7	167.7±34.5	<0.001
LDL cholesterol (mg/dl)	150.7±30.8	81.4±70.3	<0.001
HDL cholesterol (mg/dl)	34.6±12.24	62.2±10.25	<0.001
Body Mass Index (BMI)	28.46±3.69	22.38±2.13	<0.001

p-value was determined by unpaired Student's t-test.

Table-II: Prevalence of non-alcoholic fatty liver disease (NAFLD) in psoriasis and non-psoriasis group (N=100)

Prevalence of NAFLD	Psoriasis		Non-Psoriasis		p-value
	Frequency	Percentage	Frequency	Percentage	
Present	35	70	13	26	<0.001
Absent	15	30	37	74	
Total	50	100	50	100	

p-value was determined by Chi-square test.

Table-III: Grade of fatty liver findings by ultrasonography in patients of psoriasis and non-psoriasis group (N=100)

Grade of fatty liver	Psoriasis		Non-Psoriasis		Total	p-value
	Frequency	Percentage	Frequency	Percentage		
Grade 0	15	30	37	74	52	<0.001
Grade I	05	10	13	26	18	
Grade II	20	40	00	00	20	
Grade III	10	20	00	00	10	
Total	50	100	50	100	100	

p-value was determined by Chi-square test.

Table-IV: Histopathological findings of skin biopsy in psoriasis patients (n=50)

Histopathological findings	Frequency	Percentage
Dilated tortuous vessels in the papillary dermis	23	46
Loss of granular layer	09	18
Regular acanthosis	02	04
Thinning in supra papillary dermis	06	12
Spongiosis	02	04
Parakeratosis	03	06
Others	05	10
Total	50	100

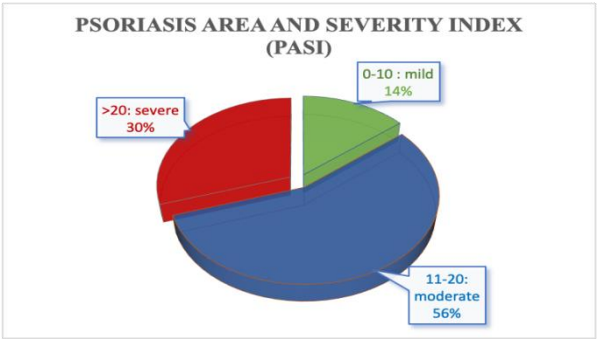

Fig. 3: Psoriasis area and severity index (PASI) in psoriasis patients (n=50)

Table V: Psoriasis area and severity index (PASI) and stage of fibroscan of liver in patients having psoriasis with NAFLD (n=35)

Psoriasis area and severity index (PASI)	Stage of fibroscan of liver					p-value
	F0: No fibrosis n (%)	F1: Mild fibrosis n (%)	F2: Moderate fibrosis n (%)	F3: Severe fibrosis n (%)	F4: Cirrhosis n (%)	
0-10: mild	1(2.9)	1(2.9)	0	0	0	<0.001
11-20: moderate	0(0)	2(8.6)	10(28.6)	05(14.2)	1(2.9)	
>20: severe	0(0)	0(0)	0(0)	10(28.6)	5(14.2)	
Total	1(2.9)	3(8.6)	10(28.6)	15(42.9)	6(17.1)	

p-value was determined by Chi-square test.

Table VI: Relation of Psoriasis area and severity index (PASI) score and fibroscan score of liver in patients having psoriasis with NAFLD (n=35)

Psoriasis area and severity index (PASI)	Fibroscan score of liver (mean±SD)	p-value
0-10: mild	9.1±0.28 (8.9–9.3)	<0.001
11-20: moderate	10.08±1.05(8.2–12.4)	
>20: severe	12.63±1.41(11.2–15.5)	

p-value was determined by unpaired Student's t-test.

Table VII: Relation of Psoriasis area and severity index (PASI) and steatosis grade of fatty liver in patients having psoriasis with NAFLD (n=35)

Psoriasis area and severity index (PASI)	Steatosis grade of fatty liver			P value
	S1 n (%)	S2 n (%)	S3 n (%)	
0-10: mild	1(2.8)	1(2.8)	0(0)	<0.01
11-20: moderate	0(0)	15(42.8)	3(8.5)	
>20: severe	0(0)	4(11.4)	11(31.4)	
Total	01(2.8)	20(57.2)	14(40)	

p-value was determined by Chi-square test.

Table-VIII: Relation of Psoriasis area and severity index (PASI) score and CAP score of fatty liver among the patients of psoriasis with NAFLD (n=35)

Psoriasis area and severity index (PASI)	CAP score of liver (mean±SD)	p-value
0-10: mild	270.1±7.1(270-285)	<0.001
11-20: moderate	289.45±14.56(260-320)	
>20: severe	340.33±30.21(300-390)	

p-value was determined unpaired Student's t-test.

Discussion

In the present study, mean age difference between patients of psoriasis and non-psoriasis group was found statistically not significant (p>0.05). Most of psoriasis patients were in 36–50 years (36%) group. Mean age of psoriasis patients was 40.74±11.61 years and control group was 38.4±11.84 years. Liluashvili *et al*. found that the mean age of patients was 45.96±15.64 years which was nearly similar to our study result.[12] In our study, in patients of psoriasis, 74% were male and in control group male were 62%. Michalek *et al.* also found psoriasis was more common in male patients which corresponds with our study.[13] Similarly, Hagg *et al.* reported that men had more severe psoriasis than women based on Psoriasis Area and Severity Index (PASI).[14] Maybury *et al.* found most of patients of psoriasis were found overweight (body mass index, 25to<30), which corresponds with the results of our study.[2] Evidence also showed that psoriasis patients with NAFLD were more obese and overweight, more likely to be male and had higher levels of BMI.[12]

In the present study, there were significant associations found in serum AST, ALT, AST/ALT, total cholesterol, LDL cholesterol, HDL cholesterol and serum albumin with psoriais (p<0.001). Narayanasamy *et al.* found that the majority of NAFLD patients had higher serum ALT, AST concentrations and decreased AST: ALT level and serum albumin level.[15] In another study done by Das *et al*. reported altered liver functions with elevated AST, ALT, lipid profile in nonalcoholic fatty liver disease (NAFLD) patients.[16]

According to the present study, the majority of the patients had dilated tortuous vessels in the papillary dermis (46%) followed in decreasing order by loss of granular layer (18%), thinning in supra papillary dermis (6%), others (10%), parakeratosis (6%), spongiosis (4%) and regular acanthosis (4%) on histopathological findings of skin biopsy in psoriasis patients. Ozkanli *et al.* found dilated tortuous vessels in the papillary dermi, loss of the granular layer, parakeratosis, regular acanthosis and loss of the granular layer were found commonly on skin biopsy which corresponds with the results.[17]

Among our study patients of psoriasis, 70% had NAFLD and in non-psoriasis group 26% had NAFLD (p<0.001). Gisondi *et al.* also found that the frequency of ultrasound-diagnosed NAFLD was remarkably greater in psoriasis patients than in matched control subjects which corresponds with our study findings.6 We observed that 10% had grade I, 40% had grade II, and 20% had grade III fatty liver in patients of psoriasis, while in non-psoriasis group, 74% had no fatty liver disease (Grade 0) and only 26% had grade I. Ganzetti *et al.* found that in psoriasis patients, non-alcoholic fatty liver disease (NAFLD) more common than control group which corresponds with our results. They also found patients with psoriasis showed a greater prevalence of NAFLD and metabolic syndrome than the general population. Moreover, patients with NAFLD and psoriasis are at higher risk of severe liver fibrosis than those with NAFLD and without psoriasis.[18]

In this study, the association of psoriasis area and severity index (PASI) score and fibro scan score was found significant, i.e., increased severity of psoriasis was associated with advanced stages of fibrosis. Narayanasamy *et al.* also found that the score of fibroscan of liver increased with the increased psoriasis area and severity index (PASI), which corresponds with our results.[15] Moreover, in non-alcoholic fatty liver disease may have 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; those results are similar to our findings.[15] The incidence of NAFLD and its advanced consequences are also rising among psoriasis patients in US population.[19] Moreover, the association of psoriasis area and severity index (PASI) score and CAP score of fatty liver was found significant ($p<0.001$). Newsome et al. reported that CAP score, as measured by fibroscan of liver, increased in psoriasis.[20] Pongpit et al. found that psoriatic patients had high liver stiffness, significant liver fibrosis and high steatosis grade of fatty liver.[21] Those findings are similar to our results.

However, our study was hospital based; therefore, those who did not visit the hospital were outside the study. Our small sample size might fail to be representative of the whole population and thus, be unable to generalize the findings. Further studies with larger scale and multi-centre involvement are recommended.

Conclusion

NAFLD was quite frequent among our patients with psoriasis. Significant association was found between the severity of NAFLD and psoriasis. NAFLD was highly associated with psoriasis, which emphasizes that both diseases may develop simultaneously. The majority of the patients with psoriasis had grade II fatty liver. The stage of fibroscan of liver also increased with increasing PASI; similaly, the grade of steatosis of liver also increased with increasing PASI. Healthcare providers should be mindful of such association for early evaluation and diagnosis of NAFLD in patient with psoriasis. Based on facilities, patients with psoriasis should be screened and followed up regularly to prevent progression to such liver disease.

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