

# **Original Research Article**

## **Case control study about psoriasis: A chronic inflammatory disorder of skin**

Abstract :

Background:

The liver enzymes tend to rise in Non-alcoholic fatty liver disease (NAFLD) and is among the leading causes for expected liver transplantation by 2020 [1, 2]. NAFLD and psoriasis are chronic inflammatory conditions resulting from a multifactorial pathogenesis comprising hereditary and environmental factors. Same inflammatory mediators are involved in fatty liver, psoriasis, and metabolic syndrome [4]. NAFLD is condition in which macro vesicular fat accumulate more than 5% in hepatocytes in persons who do not consume high level of alcohol (<20 gm/day) [4]. This finding compelled to conduct a case-control investigations that report an association between psoriasis and NAFLD [7, 10–12]. While the exact aetiology of this relationship remains uncertain, it has been postulated that inflammatory cytokines such as tumour necrosis factor alpha (TNF- $\alpha$ ), IL-6 and IL1- $\beta$  play a mechanistic role in the development of insulin resistance and fatty liver as well as psoriasis.

Methods:

All patients who fulfilled the inclusion criteria were included in the study. Informed consent was taken after explaining the procedure, risks and benefits of the study. NAFLD was diagnosed non-alcoholic fatty liver with one of the following findings showing hyper echoic liver parenchyma, impaired visualization of intra hepatic vessels (portal vein and hepatic vein) and increased liver size. All the collected information into predesigned Performa.

Results:

Mean  $\pm$ SD of age in cases and control was  $48.56 \pm 6.69$  and  $44.23 \pm 7.08$  years. In gender wise distribution of cases and control 65 (64.85%) male and 61 (35.15%) female were included in cases and 36 (35.15%) male and 40 (39.60%) female were included in control group. Compared to control the odd of being non-alcoholic fatty liver was found to be more prevalent in Males as compared to female patient ( OR=3.42, CI 1.624---7.201, P Value <0.00).

Conclusions:

It is to be concluded that rate of non-alcoholic fatty liver was 2 times more likely in male population as compare to female.

## **Introduction.**

An estimated 125 million patients worldwide suffer psoriasis, a chronic inflammatory disorder of skin, which is 2% of the global population [1]. This disease characterized by cutaneous manifestations as well-demarcated, erythematous plaques with adherent glistening scales. Certain co-morbidities are listed to include metabolic syndrome (obesity, hypertension, and hyperlipidaemia and insulin resistance) and cardiovascular disease associated with psoriasis [2]. The relationship between psoriasis and non-alcoholic fatty liver disease (NAFLD) is obviously suggested by non-invasive imaging, which is considered as the hepatic manifestation of metabolic syndrome [3]. However definite aetiology of this plausibility remains uncertain, it has been assumed that inflammatory cytokines such as tumor necrosis factor alpha (TNF- $\alpha$ ), IL-6 and IL1- $\beta$  play a systematic role in the development of insulin resistance and fatty liver as well as psoriasis.

In broader terms NAFLD is collection of macro vesicular fat in more than 5% of hepatocytes in those who do not consume alcohol in harmful amounts (<20 gm/day) [4]. NAFLD can be identified with good imaging ultrasonography with sensitivity of about 85% [5]. It has been well documented by studies of natural history of fatty liver that patients having isolated fatty liver are likely to experience less liver-related mortalities. Despite there has been numerous literature available connecting psoriasis with NAFLD, however in this study we will discuss the gender predisposition between NAFLD and psoriasis. It is well evident that NAFLD is more common in psoriasis as is documented by a study done in Netherlands (46%) [6]. The prevalence of NAFLD in psoriasis has also been reported from various studies done in Italy (47%) [7] and in India (45%) [8]. There is pertinent finding of severity of psoriasis since the NAFLD itself lead to more severe psoriatic attacks as is documented by some studies [9].

Owing to high prevalence of NAFLD in psoriasis and vice versa. We wanted to know as if the gender has any impact on the NAFLD and psoriasis. The instinct to carry this study was;

1. There are no local studies available in best of our knowledge to establish impact of gender on development of NAFLD in psoriatic patients.
2. The literature review preclude that strong relationships exist between psoriasis and NAFLD.

## Methods

A case control study was conducted from February 2018 to August 2018 at Department of Dermatology, Jinnah Postgraduate Medical Institute, Karachi. Non-Probability Consecutive sampling technique was used to select cases and controls. Sample size was calculated with expected rate of 47% [7] prevalence of NAFLD in Case (P1) and 28% [7] prevalence of NAFLD in control (P2) group, power of test was set at 80% and confidence interval at 95%. Total sample size calculated was 202, with 101 participants in each group. We defined cases as Diagnosed case of psoriasis as per operational definition with moderate to severe intensity within age bracket of 18 to 75 years having any gender. Whereas the control were matched for age and sex and who have any other skin but psoriasis. The exclusion criteria used was Pregnant & lactating mother, History of alcohol, History of drugs (Cyclosporin, Retinoids, Methotrexate), History of Smoking, Hepatitis B & C diagnosed by Elisa Method and Obesity (BMI > 30) as these were also independent causes of fatty liver.

After approval from CPSP, Psoriasis cases and controls (not having psoriasis) attending dermatology department all were referred to the radiology for the assessment of non-alcoholic fatty liver with one of the following findings showing hyper echoic liver parenchyma, impaired visualization of intra hepatic vessels (portal vein and hepatic vein) and increased liver size, was considered as a fatty liver. This information as age, gender, duration and severity of disease was entered in pro forma.

The data was entered and analysed using SPSS v23.0. Mean± SD of age, duration of disease PASI Score, Body Surface Area, frequency and the percentage of non-alcoholic fatty liver and gender. Two groups, cases and controls, were compared to assess association between psoriasis and non-alcoholic fatty liver and Chi square test was applied.  $P \leq 0.05$  was considered as a significant. ODDs ratio was calculated to 95% of confidence level. Effect modifiers like age and gender was controlled through stratification Post stratification Chi square test was applied. In gender wise distribution of cases and control 65 (64.85%) male and 61 (35.15%) female were included in cases and 75 (65%) male and 36 (35%) female were included in control group as shown in Table 3.

**Result:**

Out of total 201 study participants 65 (64.85%) male and 61 (35.15%) female. All were included in cases and 36 (35.15%) male and 40 (39.60%) female were included in control group. Compared to control the odd of being non-alcoholic fatty liver was  $> 2$  in Psoriasis patients with [OR 2.741, C.I (1.532-----4.904)] and P value was found to be highly significant ( $P=0.001$ ). In age group of 18---45 the odd of being non-alcoholic fatty liver was 3 times more likely in cases as compare to control with [OR 3.712, C.I (1.723----7.998)] and P value was found to be highly significant i.e. ( $P=0.001$ ); similarly in age group of  $> 45$  the odd of being non-alcoholic fatty liver was 1.8 times more likely in cases as compare to control with [OR 1.888, C.I (0.756-----4.717)] and P value was found to be non-significant ( $P=0.171$ ). In stratification of male the odd of being non-alcoholic fatty liver was 3 times more likely in cases as compare to control with [OR 3.42, C.I (1.624----7.201)] and P value was found to be highly significant ( $P=0.001$ ); similarly in stratification of female the odd of being non-alcoholic fatty liver was 1.86 times more likely in cases as compare to control with [OR 1.867, C.I (0.727-----4.794)] and P value was found to be non-significant ( $P=0.192$ ).

**Discussion**

Psoriasis is one among chronic inflammatory diseases of Skin, associated with NAFLD. Moreover the prevalence of NAFLD is much higher in patients who have psoriasis. There are many explanation of this increase prevalence of NAFLD among psoriatic disease including insulin resistance and metabolic derangement leading to fatty steatosis [4]. The treatment of psoriasis is also associated with factors which tend to increase the hepatotoxicity as hepatotoxic agent such as methotrexate are mainstay of treatment of psoriasis, and psoriatic therapy itself increase the susceptibility of liver damage [10,18]. Upon evaluating patients from United States urban-based tertiary dermatology clinic centre, it was found that a robust system need to be implemented to check sensitivity of treatment of psoriasis on NAFLD. We found in our study that prevalence of NAFLD in psoriatic patient was higher than in general population (52.5% vs. 28.7%). Our finding are also contradict with an Indian hospital-based study which documented high prevalence of NAFLD in general population and psoriatic patients (17.4% and 7.9 % in psoriasis patients and age, sex and BMI-matched controls, respectively) [12]. These lower prevalence could be attributed to use of alternative definition of NAFLD (i.e., evidence of steatosis on liver ultrasound and elevation of liver enzymes and triglycerides and ethnic differences in risk factors). However according to our findings the odd of being non-alcoholic fatty liver was  $> 2$  in Psoriasis patients with [OR 2.741, C.I (1.532-----4.904)] and P value was found to be highly significant i.e. ( $P=0.001$ ). Whereas our study finding are consistent with other study done in Italy and Netherlands which also showed high prevalence of NAFLD in psoriatic patient [7,10,11].

We found that male sex is more prone to develop NAFLD in psoriasis. This is unique finding as the data was also undergone with stratification at the analysis to control for confounders and effect modifiers. In literature review it was found that the gender predisposition has never been studied before, however

prevalence of NAFLD is substantially higher in Psoriasis patient at all. However further research is needed to justify this finding by addressing confounders and effect modifier or genetic as well as hormonal factors.

The strength of our study was that we selected consecutive sampling method, as our inclusion and exclusion criteria were strict. The bias were addressed by using objective definitions for predictor and outcome variable in our study. Our main limitation are that ultrasonography and exclusion of secondary causes of chronic liver disease were used to make a clinical diagnosis of NAFLD instead of liver biopsy. So far as Liver biopsy is regarded as gold standard for staging of liver disease [7]. However, using liver biopsy for determination of fatty liver was beyond our study design as liver biopsy is itself is associated with morbidity and mortality [13]. We also want to document the referral bias as we conducted the study at single tertiary care centre, however this peculiar bias is less likely to be interrupting our results as many of the study participants were self-referred and encompassed a diverse geographic distribution.

## Conclusions

It is to be concluded that rate of non-alcoholic fatty liver was 2 times more likely in male cases as compared to female. Future prospective, there is a need to conduct more observational and comparative studies using large sample size with multiple study centres in Pakistan are needed to confirm the findings of the present study.

## References

1. Lalevska V, Andersson S. Global Psoriasis Coalition: Addressing the needs of psoriasis patients in the NCD agenda Vasilka Lalevska. *Eur J Pub Health*. 2017 Nov;27(suppl\_3).
2. Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. *Rook's textbook of dermatology*. John Wiley & Sons; 2016 Feb 29.
3. Roberts KK, Cochet AE, Lamb PB, Brown PJ, Battafarano DF, Brunt EM, et al. The prevalence of NAFLD and NASH among patients with psoriasis in a tertiary care dermatology and rheumatology clinic. *Aliment Pharmacol Therapeut*. 2015 Feb;41(3):293-300.
4. Lonardo A, Ballestri S, Marchesini G, Angulo P, Loria P. Nonalcoholic fatty liver disease: A precursor of the metabolic syndrome. *Dig. Liver Dis*. 2015;47:181–90. doi: 10.1016/j.dld.2014.09.020.
5. AlShaalan R, Aljiffry M, Al-Busafi S, Metrakos P, Hassanain M. Nonalcoholic fatty liver disease: noninvasive methods of diagnosing hepatic steatosis. *Sau J Gastroenterol Offic J Sau Gastroenterol Ass*. 2015 Mar;21(2):64.
6. Mantovani A, Gisondi P, Lonardo A, Targher G. Relationship between non-alcoholic fatty liver disease and psoriasis: a novel hepato-dermal axis?. *Int J Molecu Sci*. 2016 Feb;17(2):17.
7. Van der Voort EA, Koehler EM, Dowlatshahi EA, Hofman A, Stricker BH, Janssen HL, et al. Psoriasis is independently associated with nonalcoholic fatty liver disease in patients 55 years old or older: Results from a population-based study. *J Am Acad Dermatol*. 2014;70:517–24.
8. Narayanasamy K, Sanmarkan AD, Rajendran K, Annasamy C, Ramalingam S. Relationship between psoriasis and non-alcoholic fatty liver disease. *Przeg Gastroenterol*. 2016;11(4):263.

9. Paredes AH, Torres DM, Harrison SA. Nonalcoholic fatty liver disease. Clin Liver Dis. 2012; 16:397–19.
10. Stern RS, Nijsten T, Feldman SR, Margolis DJ, Rolstad T. Psoriasis is common, carries a substantial burden even when not extensive, and is associated with widespread treatment dissatisfaction. J Invest Dermatol Symp Proc. 2004 Mar;9(2):136–139.
11. Seminara NM, Abuabara K, Shin DB, et al. Validity of The Health Improvement Network (THIN) for the study of psoriasis. Br J Dermatol. 2011 Mar;164(3):602–609.
12. Sommer D.M., Jenisch S., Suchan M., Christophers E., Weichenthal M. Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. Arch. Dermatol. Res. 2006;298:321–328.
13. Madanagobalane S., Anandan S. The increased prevalence of non-alcoholic fatty liver disease in psoriatic patients: A study from South India. Australas. J. Dermatol. 2012;53:190–197.

Table 1. Descriptive Statistics of respondent

Variables	N	Minimum	Maximum	Mean	±Sd	95% C. I
Age (Years)	202	18	75	46.395	7.837	45.30----47.48
*Duration of Psoriasis (Months)	101 (Only in cases)	2	300	130.94	18.28	127.33----134.54
*PASI Score (Years)	101 (Only in cases)	29	50	41.24	6.24	40.00----42.47
Body surface Area	101 (Only in cases)	0.28	0.64	0.472	0.052	0.461----0.482

Table 2. Frequency of Ages of Respodent

Age [Years]	Minimum	Maximum	Mean	±Sd	95% C. I
<b>GROUP</b>					
CASES (n=101)	18	75	48.56	6.69	47.23----49.88
CONTROL (n=101)	18	75	44.23	7.08	42.83----45.62

Table 3. Frequency of Gender of Participants

	Male	Female
CASES	65 64.85%	36 35.15%
CONTROL	61 60.4%	40 39.60%

Table 4. Occurrence of NAFLD in Psoriatic cases

GROUP	NONALCOHOLIC FATTY LIVER		P-VALUE	ODD RATIO	95% CONFIDECE INTERVAL
	YES	NO			
CASES	53 (52.5%)	48 (47.5%)			
CONTROLS	29 (28.7%)	72 (71.3%)	0.001*	2.741*	1.532-----4.904

Table 5. Gender wise occurrence of NAFLD in Psoriatic cases

GENDER		NONALCOHOLIC FATTY LIVER		P -VALUE	ODD RATIO	95% CONFIDENCE INTERVAL
		Yes	No			
MALE	Cases	37 (56.9%)	28 (43.1%)	0.001	3.42	1.624-----7.201
	Control	17 (27.9%)	44 (72.1%)			

FEMALE	Group	Cases	16 (44.4%)	20 (55.6%)	0.192	1.867	0.727-----4.794
		Control	12 (30.0%)	28 (70.0%)			

UNDER PEER REVIEW

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