Original Research Article

Psoriasis ~~Case~~ and Metabolic syndrome: a gender case-study clinical correlation~~control study about psoriasis: A chronic inflammatory disorder of skin~~

~~Abstract~~ABSTRACT ~~:~~

Background:

~~NAFLD~~Metabolic syndrome and psoriasis are chronic inflammatory conditions resulting from ~~a~~ multifactorial pathogenesis comprising hereditary and environmental factors. The main common factor to link these conditions is intestinal hyperpermeability.

Objective: ~~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 meditators 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~~T ~~t~~o conduct ~~a~~ case-control investigations ~~that report~~reporting an association between psoriasis and ~~NAFLD~~Metabolic Syndrome. ~~[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-α), IL-6 and IL1-β 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~~Metabolic syndrome was diagnosed by ultrasonic evidence of Non-Alcoholic Fatty Liver Disease (~~, N~~NAFLD) in psoriatic patients and asymptomatic controls. ~~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 ±SD of age in cases and control was 48.56±6.69 and 44.23± 7.08 years.~~ In the ~~gender~~ gender-wise distribution of cases and control, 65 (64.85%) ~~-~~males and 61 (35.15%) females were ~~were~~ included in ~~cases~~ the psoriatic group, while~~and~~ 36 (35.15%) males and 40 (39.60%) females were included in the control group. Compared to control the odds of ~~being non-alcoholic fatty liver~~NAFLD was found to be more prevalent in m~~M~~ales as compared to the female ~~patients~~ (-OR = 3.42~~;~~, CI = 1.624 ~~—~~to 7.201, ~~P~~ p-v~~V~~alue < 0.001).

Conclusions:

The rate of NAFLD is significantly increased in psoriatic patients concerning control cases and it was 2 times more likely in male cases as compared to females. ~~It is to be concluded that rate of non-alcoholic fatty liver was 2 times more likely in male population as compare to female.~~

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Introduction.

Metabolic syndrome (MS) and Psoriasis are chronic inflammatory conditions resulting from multifactorial pathogenesis comprising hereditary and environmental factors. The main common factor to link these conditions is Intestinal Hyperpermeability (IHP), also known as the Leaky Gut Syndrome (LGS) [1, 2]. Psoriasis is nowadays considered one of the endotypes of Atopic Dermatitis (AD), a specific presentation of the food hypersensitivities conditions [3]. Psoriasis and AD may be produced by diverse hypersensitivity mechanisms, either IgE-mediated or Non-IgE-mediated [4, 5]. The cytokine profile developed by the absorption of bacterial endotoxins, due to IHP such as the tumour necrosis factor-alpha (TNF-α), IL-6, and IL1-β play a common role in the development of MS and psoriasis [6, 7]. ~~An estimated 125 million patients worldwide suffer psoriasis, a chronic inflammatory disorder of skin, which is 2% of the global population [1]. This disease~~Psoriasis is characterized by cutaneous manifestations as well-demarcated, erythematous plaques with adherent glistening scales [8-9]. Metabolic syndrome characteristics (obesity, hypertension, hyperlipidaemia and insulin resistance) are commonly associated with psoriasis [8]. The relationship between psoriasis and non-alcoholic fatty liver disease (NAFLD) is suggested by non-invasive imaging, which is considered as the hepatic manifestation of metabolic syndrome [10]. ~~[6, 7]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-α), IL-6 and IL1-β play a systematic role in the development of insulin resistance and fatty liver as well as psoriasis.~~

In broader terms, NAFLD is a 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~~11]. NAFLD can be identified with good imaging ultrasonography with a sensitivity of about 85% [~~5~~12]. It has been well documented by studies of the natural history of fatty liver that patients having isolated fatty liver are likely to experience ~~less~~ fewer liver-related mortalities. Despite there ~~has~~ having 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 it is documented by a study done in the Netherlands (46%) [~~6~~13]. The prevalence of NAFLD in psoriasis has also been reported from various studies done in Italy (47%) [~~7~~14] and in India (45%) [~~8~~15]. There is the pertinent finding of~~-~~ the severity of psoriasis since the NAFLD itself lead to more severe psoriatic attacks as is documented by some studies [16~~9~~].

Owing to a 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 out this study was;

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

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Methods

A ~~case~~ case-control study was conducted from February 2018 to August 2018 at the Department of Dermatology, Jinnah Postgraduate Medical Institute, Karachi. Non-Probability Consecutive sampling technique was used to select cases and controls. ~~Sample~~ The sample size was calculated with an expected rate of 47% [~~7~~14] prevalence of NAFLD in Case (P1) and 28% [~~7~~14] prevalence of NAFLD in control (P2) group, power of the test was set at 80% and confidence interval at 95%. The total sample size calculated was 202, with 101 participants in each group. We defined cases as a Diagnosed case of psoriasis as per operational definition with moderate to severe intensity within the age bracket of 18 to 75 years having any gender. Whereas the control ~~were~~ was matched for age and sex and who have any other skin but psoriasis. The exclusion criteria used were:~~as~~ p~~P~~regnan~~t~~cy and~~&~~ lactating mother, ~~H~~history of alcohol, h~~H~~istory of drugs (c~~C~~yclosporin, r~~R~~etinoids, m~~M~~ethotrexate), h~~H~~istory of s~~S~~moking, Hepatitis B and~~&~~ C diagnosed by Elisa Method and o~~O~~besity (BMI > 30) as these were also independent causes of ~~fatty liver~~NAFLD.

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~~NAFLD 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~~NAFLD and gender. Two groups, cases and controls, were compared to assess the association between psoriasis and ~~non-alcoholic fatty liver~~NAFLD and a ~~Chi-~~Chi-square test was applied, where a~~.~~ p~~P~~ ≤ 0.05 was considered ~~as a~~ significant. ODDs ratio was calculated to 95% of confidence level. Effect modifiers like age and gender ~~was~~ were controlled through stratification ~~Post~~ Post-stratification ~~Chi-~~ Chi-square test was applied. In the ~~gender~~ gender-wise distribution of cases and control 65 (64.85%) males and 61 (35.15%) females were included in cases and 75 (65%) males and 36 (35%) females were included in the control group as shown in Table 3.

Result:

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

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Discussion

Psoriasis is one ~~among~~ of the chronic inflammatory diseases of Skin, associated with NAFLD. Moreover, the prevalence of NAFLD is much higher in patients who have psoriasis. There are many explanations of this increased prevalence of NAFLD among psoriatic disease including insulin resistance and metabolic derangement leading to fatty steatosis [411]. The treatment of psoriasis is also associated with factors ~~which~~ that tend to increase the hepatotoxicity as a hepatotoxic agent such as methotrexate are the mainstay of treatment of psoriasis, and psoriatic therapy itself increase the susceptibility of liver damage [17,180,18]. Upon evaluating patients from the United States urban-based tertiary dermatology clinic centre, it was found that a robust system needs to be implemented to check the sensitivity of treatment of psoriasis on NAFLD. We found in our study that the prevalence of NAFLD in the psoriatic patient was higher than in the general population (52.5% vs. 28.7%). Our findings are also contradicted with an Indian hospital-based study which documented the high prevalence of NAFLD in the general population and psoriatic patients (17.4% and 7.9 % in psoriasis patients and age, sex and BMI-matched controls, respectively) [129]. These lower prevalence could be attributed to the use of an 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 to 4.904~~)]~~ and ~~P~~ p-value was found to be highly significant i.e. (P=0.001). Whereas our study findings are consistent with other ~~study~~ studies done in Italy and the Netherlands which also showed a high prevalence of NAFLD in the psoriatic patients [~~7~~14,10~~7~~,11~~8~~].

We found that the male sex is more prone to develop NAFLD in psoriasis. This is a unique finding as the data was also undergone with stratification at the analysis to control for confounders and effect modifiers. In the literature review, it was found that the gender predisposition has never been studied before, however, the prevalence of NAFLD is substantially higher in Psoriasis patients 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 a consecutive sampling method, as our inclusion and exclusion criteria were strict. The bias ~~were~~ was addressed by using objective definitions for predictor and outcome variables in our study. Our main limitations 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~~ L~~L~~iver biopsy is regarded as the gold standard for the staging of liver disease [~~7~~14]. However, using liver biopsy for the determination of fatty liver was beyond our study design as liver biopsy is itself is associated with morbidity and mortality [~~1~~203]. We also want to document the referral bias as we conducted the study at a single tertiary care centre, however, this ~~peculiar~~ particular 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 the rate of ~~non-alcoholic fatty liver~~NAFLD is significantly increased in psoriatic patients concerning control cases and that it was 2 times more likely in male cases as compared to females. Future prospective, there is a need to conduct more observational and comparative studies using a large sample size with multiple study centres in Pakistan are needed to confirm the findings of the present study.

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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 Respondent

Age [Years]		Minimum	Maximum	Mean	±Sd	95% C.I
GROUP	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	36
	64.85%	35.15%
CONTROL	61	40

	60.4%	39.60%

Table 4. Occurrence of NAFLD in Psoriatic cases

GROUP	NONALCOHOLIC FATTY LIVER		p-VALUE	ODD RATIO	95% CONFIDENCE 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	**Group**	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%)			

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