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Original Article

Association of non-alcoholic fatty liver disease and psoriasis: A case-control study at a tertiary care hospital in Pakistan

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Abstract

Objective To compare association of Non-Alcoholic fatty liver disease in psoriatic patients versus age and gender matched healthy controls.

Methods Association of non-alcoholic fatty liver disease in psoriatic patients versus healthy controls was compared. Diagnosis was made on ultrasonography and results were recorded.

Results The prevalence of NAFLD in patients with psoriasis was significantly higher as compared to Controls (52.4% vs. 28.7%). The likelihood of having NAFLD was about 2.5 times greater in patients with PsO than the controls (OR 2.741, 95% CI= 1.53-4.904, p= 0.001). In our study it is more frequently reported in males and those in younger age groups.

Conclusion NAFLD appears to occur more frequently in patients with PsO than in the general population. In our study it is more frequently reported in males and those in younger age groups. Patients of PsO should get screened for NAFLD so that planning of appropriate treatment should be taken into consideration to avoid possible risk related of exacerbation or development of NAFLD.

Key words
Psoriasis, non-alcoholic fatty liver disease, metabolic syndrome, prevalence, case-control study.

Introduction

Psoriasis (PsO) is a chronic inflammatory disease of the skin, affecting an estimated 125 million patients worldwide.[1] which represents almost 2% of the global population.[2] The disease is known for its cutaneous manifestations; described as well-demarcated, erythematous plaques with adherent silvery white scales.[2] However, latest data have linked PsO with several co-morbidities to include metabolic syndrome (obesity, hypertension, hyperlipidemia and insulin resistance).[3] There are numerous studies in past decade, consuming non-invasive imaging, have drawn attention to increased prevalence of non-alcoholic fatty liver disease (NAFLD) in PsO, which ranges from mild steatosis to non-alcoholic steato-hepatitis, which can lead to cirrhosis and end-stage liver disease.[4] In upcoming years, It is expected to become one of the most common indication for liver transplant in United states and Europe due to sedentary and western lifestyle, although the disease is also becoming increasingly prevalent in developing countries.[5] Both NAFLD and PsO can also lead to involvement of many other organ systems, including heart as well.[6] These two are mutually and bi-directionally associated, as both of these conditions share insulin resistance as a common pathophysiological mechanism that is caused by pro-inflammatory

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cytokines (e.g., IL-6, IL-17, TNF-α, hepatocyte cytokine) which form the linkage of pathogenesis between these two conditions.[12] In addition, recent studies also report relationship between the severity of PsO with the severity of NAFLD.[7] To increase awareness about the increased prevalence of NAFLD in psoriatic patient is particular interest of this study, as various drugs used for the treatment of PsO may influence NAFLD development or progression,[8] caution must be taken and also to prevent further complications.

Methods

A case control study was conducted in the department of dermatology, Jinnah Postgraduate Medical Institute, Karachi after taking approval from Ethical Review Board. Subjects ranging from 18 to 75 years in age were included during the study duration of 6 months. 101 diagnosed cases of psO with duration of more than one month were consecutively included in the study. Severity was assessed by the Psoriasis Area Severity index (PASI score) as mild (<10%), moderate (10-20%) and severe (>20%) whereas body surface area (BSA) was determined as mild (<3%), moderate (3-10%) and severe (>10%).[9] Pregnant and lactating mothers, patients with history of alcohol intake, smoking, any other hepatic disease and use of hepatotoxic drugs were excluded from the study. The control group included 101 patients with skin diseases other than psoriasis, fulfilling inclusion and exclusion criteria. Verbal informed consent was provided by all patients prior to participation. Detailed history and examination of the study subjects were collected by a standardized questionnaire. Cases and controls were referred to radiology department for the assessment of NAFLD. A radiological diagnosis of NAFLD was made when there was increased echogenicity relative to the renal parenchyma, increased attenuation of the ultrasound beam with the diaphragm indistinct, or if there was lack of differentiation in peri-portal intensity and the vesicular wall on ultrasonography by trained radiologist as per standard criteria of American Gastroenterological Association after excluding secondary causes of liver disease.[7] Data were entered and analyzed using SPSS v23. Mean and standard deviation were calculated for quantitative variables like age, duration of disease. Frequencies and percentages were calculated for qualitative variables, such as for NAFLD and gender. Chi square test was applied to assess the association between PsO and NAFLD. P-value≤0.05 was considered as significant. Odds ratio was calculated to 95% of confidence level. Effect modifiers like age and gender were controlled through stratification and post stratification chi square test was applied.

Results

A total of 202 patients, with 101 patients in each group. Mean age of cases and controls was 48.56±6.69 years and 44.23±7.08 years respectively. 65 (64.85%) males and 36 (35.15%) females were included in the case group while control group had 61 (60.4%) males and 40 (39.60%) females. Duration of disease, PASI score and BSA for the cases was 130.94±18.28 months, 41.24±6.24 and 0.472±0.052 respectively. The likelihood of having nonalcoholic fatty liver disease was about 2.5 times greater in patients with PsO than the controls (OR 2.741, 95% CI=1.53-4.904, p=0.001). In patients with ages ranging from 18-45 years, there was 3 times greater likelihood of having NAFLD in psoriatic patients as compared to controls (OR 3.712, 95% CI=1.72-7.99, p=0.001). In patients with ages >45 years, the odds of having NAFLD were 1.8 times greater in cases as compared to controls (OR 1.88, 95% CI=0.75-4.71). This is statistically not significant with p value >0.05. The results after gender stratification are shown in **Table 1**.

Table 1 Comparison of cases and controls.

Group	*Nonalcoholic fatty liver*		*P-value*	*Odd ratio*	*95% confidece interval*
	Yes	*No*			
Cases	53 (52.5%)	48 (47.5%)	0.001*	2.741*	1.532–4.904
Controls	29 (28.7%)	72 (71.3%)			

Discussion

PsO is an immune-mediated, chronic inflammatory disease that affects approximately 2–3% of the general adult population worldwide,[10] which involves mainly the skin, although it has systemic pathological effects. Past studies show that metabolic syndrome has been associated with PsO.[3] In parallel, NAFLD is the most frequent liver disease all around the world, which has prevalence of 25% reported in the general population worldwide.[11] PsO and NAFLD are multifactorial diseases with not completely illuminated interactions between genetic, environmental and immunological factors. It is nowadays reflected as the hepatic manifestation of the metabolic syndrome.[6] However the exact etiology of this relationship remains undefined, it has been proposed that inflammatory cytokines play a mechanistic role in the development of insulin resistance and fatty liver as well as PsO.[6] PsO patients are often aspirants to be treated with hepatotoxic agents such as methotrexate, and underlying liver disease could be intensified by these medications.[8] Discernment of factors influencing this population to NAFLD is applicable for the execution of screening and treatment in high-risk PsO patients. In this case-control study, we evaluated the association of NAFLD with or without PsO in patients at Pakistan's urban-based tertiary care hospital.

The prevalence of NAFLD in our patients with PsO was significantly higher than in our reference population (52.5% vs. 28.7%). This prevalence estimate is comparable to the results of a united states (U.S) dermatology clinic-based study in which the occurrence of NAFLD was 21.2 percent and 7.8 percent in PsO patients and age-, sex-, and BMI-matched controls, respectively.[7] The lower NAFLD occurrence in this U.S population could be due to ethnic differences in risk factors. While in the Indian based study, prevalence was 17.4 percent and 7.9 percent in PsO patients and age-, sex-, and BMI-matched controls, respectively.[13] The lower NAFLD occurrence in this Indian population could be explained by the use of a different definition of NAFLD (i.e., evidence of steatosis on liver ultrasound and elevation of liver enzymes and triglycerides) and racial differences in risk factors. In recent study conducted in north Iran, NAFLD prevalence was higher in PsO patients (65.6% vs. 35% in controls) (P <.01, OR = 3.53). Moderately severe NAFLD (grade 2) was more common than mild NAFLD (grade 1) (P <.01) in PsO patients. Hypertension (16.5%), altered liver function (16.4%), and metabolic syndrome (46.6%) rates were also found high in patients with PsO and NAFLD.[17] In Italy and Netherlands, three prior case-control studies were conducted, found higher NAFLD prevalence rates of 46 to 59.2 percent in their patients with PsO.[14,15] Most likely the difference was due to the mean age for participants in the Netherlands study which was 76.2 years, and the prevalence of NAFLD increases with age. On contrary in this study, psoriasis association with NAFLD was less in age group >45years and females. The findings of our study is consistent with a recent meta-analysis of seven case-control studies, where patients with PsO had an increased risk of NAFLD compared to the non-psoriatic populations in six studies (n=267,761; OR:2.15, 95% CI:1.57–2.94) This association

continued noteworthy when only high-quality studies were analyzed (n=3,345; OR: 2.07, 95% CI: 1.62–2.64) but slight conflict to this study is that in our study, PsO was not associated with NAFLD when our patients were matched by age >45 years and female.[16] This could be attributed to the vague ultrasonographic findings in this age group. Our study was done at a single tertiary center making referral bias possible. The findings of our study suggest that assessment of hepatic involvement as a comorbid should be considered in the patients of PsO for early detection of NAFLD and to improve the disease outcome and quality of life of such patients.

Conclusion

The frequency of occurrence of NAFLD in patients with PsO is greater than in the general population and among psoriatic patients, NAFLD is more frequently reported in males and those in younger age groups. So the physicians should consider diagnostic imaging, if and when needed, for early detection and management of PsO associated NAFLD, to improve the quality of their life. There is a need to conduct more observational and comparative studies using large sample sizes, and multiple study centers are needed to confirm the findings of the present study.

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