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Original Article

Bridging the diagnostic gap: liver function tests and IL-6 as potential early predictors of non-alcoholic fatty liver disease in psoriasis

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Abstract

Background: Psoriasis goes beyond skin, intertwining with body systems, notably connecting to nonalcoholic fatty liver disease (NAFLD). This study aims to explore the predictive potential: liver function tests and IL-6 as early markers for non-alcoholic fatty liver disease in psoriasis patients.

Methods: From March to November 2023, a case-control study was performed at the dermatological outpatient clinic of Baquba Teaching Hospital, Iraq. Individuals with confirmed psoriasis and those without underwent comprehensive clinical history and overall health examinations. The diagnosis of non-alcoholic fatty liver disease (NAFLD) was established using the Fatty Liver Index (FLI).

Results: Among the 290 participants in this study, 103 with confirmed psoriasis displayed a Fatty Liver Index (FLI) score >60, indicative of non-alcoholic fatty liver disease (NAFLD). The control group, comprising 101 individuals without psoriasis or NAFLD, provided a baseline for comparison. The mean ages were 32.5 ± 16.2 and 31.5 ± 14.3 years for the case and control groups, respectively. Notably, the case group exhibited significantly higher mean ± SD levels of ALT and AST (61 ± 29 vs. 33 ± 17 U/L, $p < 0.0001$) and (55 ± 27 vs. 25 ± 15 U/L, $p < 0.0001$), respectively. Moreover, FLI criteria were markedly elevated in the case group ($p = 0.0007$, $p = 0.0005$, $p < 0.0001$, and $p < 0.0001$, respectively), and IL-6 levels were significantly higher ($p = 0.0003$).

Conclusion: The results proposed that liver function tests and IL-6 could act as early predictors for the detection of non-alcoholic fatty liver disease among individuals grappling with psoriasis.

Keywords: Psoriasis, Liver Function Tests, Fatty Live Index, IL-6, Non-Alcoholic Fatty Liver Disease, Iraq

Background

Psoriasis, characterized by persistent inflammation and distinctive skin lesions, is not limited to its dermatologic manifestations. Beyond its impact on the skin, psoriasis has been associated with various comorbidities, including cardiovascular disease, metabolic syndrome, and nonalcoholic fatty liver disease (NAFLD) [1]. NAFLD, a condition marked by an abnormal accumulation of triglycerides within liver cells, is closely linked to factors such as male gender, age, obesity, insulin resistance, and metabolic syndrome [2]. The connection between psoriasis and NAFLD stems from shared pathogenic mechanisms and systemic inflammation. Psoriasis induces chronic inflammation, triggering a cascade of events that can affect different organs, including the liver. The chronic inflammatory state in psoriasis may contribute to insulin resistance, a key factor in NAFLD development. Moreover, the prevalence of metabolic syndrome, often seen in individuals with psoriasis, further accentuates the risk of NAFLD [3]. Several studies have explored the relationship between psoriasis and NAFLD [2-6]. The chronic inflammation associated with psoriasis may exacerbate liver damage, promoting the progression of NAFLD [4]. Additionally, common risk factors such as obesity, which plays a central role in both psoriasis and NAFLD, contribute to the intricate interplay between these conditions [6]. Lifestyle modifications, including weight management and interventions to address insulin resistance, become pivotal strategies in mitigating the risk and managing the progression of NAFLD in individuals with psoriasis [4,7]. The intricate relationship between psoriasis and nonalcoholic fatty liver disease (NAFLD) is increasingly recognized, though the precise etiopathogenic mechanisms remain elusive [8]. Both conditions are now acknowledged as

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systemic disorders, suggesting a broader impact beyond their primary manifestations [2-8]. One key player in this complex interplay is interleukin-6 (IL-6), a multifaceted cytokine with diverse effects on various cell types [9]. IL-6 plays a dual role in the context of psoriasis and NAFLD. While it promotes keratinocyte proliferation and differentiation in the skin, it also exerts systemic effects, contributing to insulin resistance and fostering the release of pro-inflammatory cytokines [5]. The widespread influence of IL-6 on cellular functions underscores its significance in the pathogenesis of both psoriasis and NAFLD [6]. A notable aspect of IL-6's impact is its role in rendering effector T cells (Teff) resistant to suppression [7, 8]. This resistance to regulatory control contributes to the chronic inflammatory state observed in psoriasis and may extend its influence on the development and progression of NAFLD. The intricate connections between IL-6 and psoriasis-related pathways provide a plausible link between these systemic conditions [9]. This study aimed to explore the role of liver function tests and IL-6 as early predictors in the diagnosis of non-alcoholic fatty liver disease among psoriasis patients.

Methods

Study design and participants

Case-control study recruited psoriasis patients and healthy controls attending the dermatological outpatient clinic at the Baquba Teachings Hospital from 1st March 2023 to 30th November 2023.

Inclusion and exclusion criteria

In the case group, we included the willing participating adults, aged eighteen years and above, of both genders, diagnosed with psoriasis, and the "Fatty Liver Index (FLI)" scored sixty or above. While the control group are volunteers in the same age range, in good general health, and willing to participate. The excluded criteria included those with other skin diseases, or other liver diseases and unwilling to participate.

Samples Size

We anticipated a 50.0% reduction in the control group at a significance level of 6.0% and a power of 95%. The initial sample size was set at 264 participants. Additional 10% (26) for non-response. The total estimated sample size is 290. Due to exclusion criteria, 174 patients confirmed psoriasis, and 116 were non-psoriasis patients. Out of 174 psoriatic patients, 103 had FLI scores of > 60 and were included in the final analysis. Among the non-psoriatic patients, 15 were excluded for many reasons (Figure 1) and the remaining 101 individuals agreed to be the control group. Throughout the data collection process, rigorous supervision was maintained at every stage to ensure data quality.

Procedure

From March to November 2023, the eligible individuals underwent extensive evaluations, encompassing in-depth analysis of their clinical history, and overall health examinations. Information on the age of participants, gender, family medical history, existing health conditions, prescribed medications, and autoimmune disorders was meticulously documented. An expert dermatologist conducted a full dermatological assessment including a thorough examination of the skin and a detailed evaluation of psoriasis lesions.

The Body Mass Index (BMI) was determined by dividing weight (in kilograms) by the square of stature (in meters). To assess waist circumference, encircle your midsection with a tape measure midway between the ribs and hips (just above the navel). Ensure a snug fit without pressing into the skin. Breathe naturally and record the measurement. Repeat for accuracy. For men, a waist below 94cm is 'low risk,' 94–102cm is 'high risk,' and over 102cm is 'very high.' For women, below 80cm is low risk, 80–88cm is high risk, and over 88cm is very high. Five milliliters of venous blood were collected from confirmed eligible psoriatic participants and the control group and subsequently placed in a gel tube. Following coagulation at room temperature, the serum was separated through centrifugation at 4000 xg for 15 minutes. The separated serum was then distributed into four Eppendorf tubes. Two of these tubes were promptly utilized for liver function testing (alanine transaminase, aspartate transaminase, gamma-glutamyl-transferase (GGT), glucose, insulin, triglycerides, and cholesterol. While the remaining two were stored at -80°C for subsequent analysis of serum interleukin 6 (Human IL-6). The analysis was performed using a sandwich enzyme-linked immunosorbent assay (ELISA) with the 2 Elisa kit provided by Sinogeneclon Biotech Co., Ltd., China.

Fatty Liver Index (FLI)

The initial evaluation excluded liver ultrasound, relying exclusively on the Fatty Liver Index (FLI) to diagnose Non-Alcoholic Fatty Liver Disease (NAFLD). The FLI calculation incorporated four criteria (BMI, waist circumference, triglycerides, and GGT) based on the algorithm established by Bedogni et al. [10] in 2006. The FLI formula is expressed as follows:

$$FLI=1+e(0.953\times\ln(TG)+0.139\times BMI+0.718\times\ln(GGT)+0.053\times WC-15.745/e(0.953\times\ln(TG)+0.139\times BMI+0.718\times\ln(GGT)+0.053\times WC-15.745)\times100$$

Where TG represents triglycerides (mg/dL), GGT is γ-glutamyl transferase (U/L), and WC is waist circumference (cm). Bedogni et al. [10] established the FLI range from 0 to 100, with a score of less than 30 indicating the absence of fatty liver disease and a score of FLI ≥60 confirming its presence.

Statistics analysis

Data analysis was conducted using SPSS software version 21 for Windows (SPSS, Inc., Chicago, IL). Numerical data are presented as mean ± SD. The Chi-square (X2) test compared percentages for categorical variables. Independent-sample Student's t-test and Mann–Whitney U-test assessed differences in parametric and non-parametric variables between the study groups. A P value of 0.05 or below was considered statistically significant.

Results

Baseline characteristics

Table 1 presents a summary of the baseline characteristics for the case-control groups. Among the 290 participants in this study, 103 were confirmed to have psoriasis and diagnosed with NAFLD in the case group, comprising 58 (56.3%) males and 45 (43.7%) females, with a mean age of 32.5 ± 16.2 years. The mean IL-6 level was 3.56 ± 2.3 pg/ml. Serum ALT, AST, and GGT levels were 61 ± 29, 55 ± 27, and 63 ± 25 U/L, respectively, and FLI criteria values were 28.3 ± 4.7 kg/m², 97 ± 14.5 cm, 225 ±

112 mg/dL, and 63 ± 25 U/L. The control group, consisting of 101 individuals without psoriasis or NAFLD, included 51 (50.5%) males and 50 (49.5%) females, with a mean age of 31.5 ± 14.3 years. The mean IL-6 level was 1.82 ± 1.7 pg/ml. Serum ALT and AST levels were 33 ± 17 and 25 ± 15, respectively, and FLI criteria values were 24.5 ± 3.6 kg/m², 85 ± 12.8 cm, 119 ± 79 mg/dL, and 31 ± 19 U/L.

Bivariate analysis

There were no significant differences in age and sex between the two groups (p = 0.720, p = 0.061, and 0.235, respectively). In the case group, the mean ± SD of ALT and AST was significantly higher compared to the control group (61 ± 29 vs. 33 ± 17 U/L, p < 0.0001) and (55 ± 27 vs. 25 ± 15 U/L, p < 0.0001), respectively. Additionally, the mean ± SD of FLI criteria was significantly elevated in the case group compared to the control (p = 0.0007, p = 0.0005, p < 0.0001, and p < 0.0001, respectively). Interleukin 6 (IL-6) levels were significantly higher in the case group than in the control (p = 0.0003). Moreover, the mean ± SD serum total cholesterol and fasting blood sugar levels were significantly higher in the case group than in the control group (p < 0.0001 and p = 0.0002, respectively).

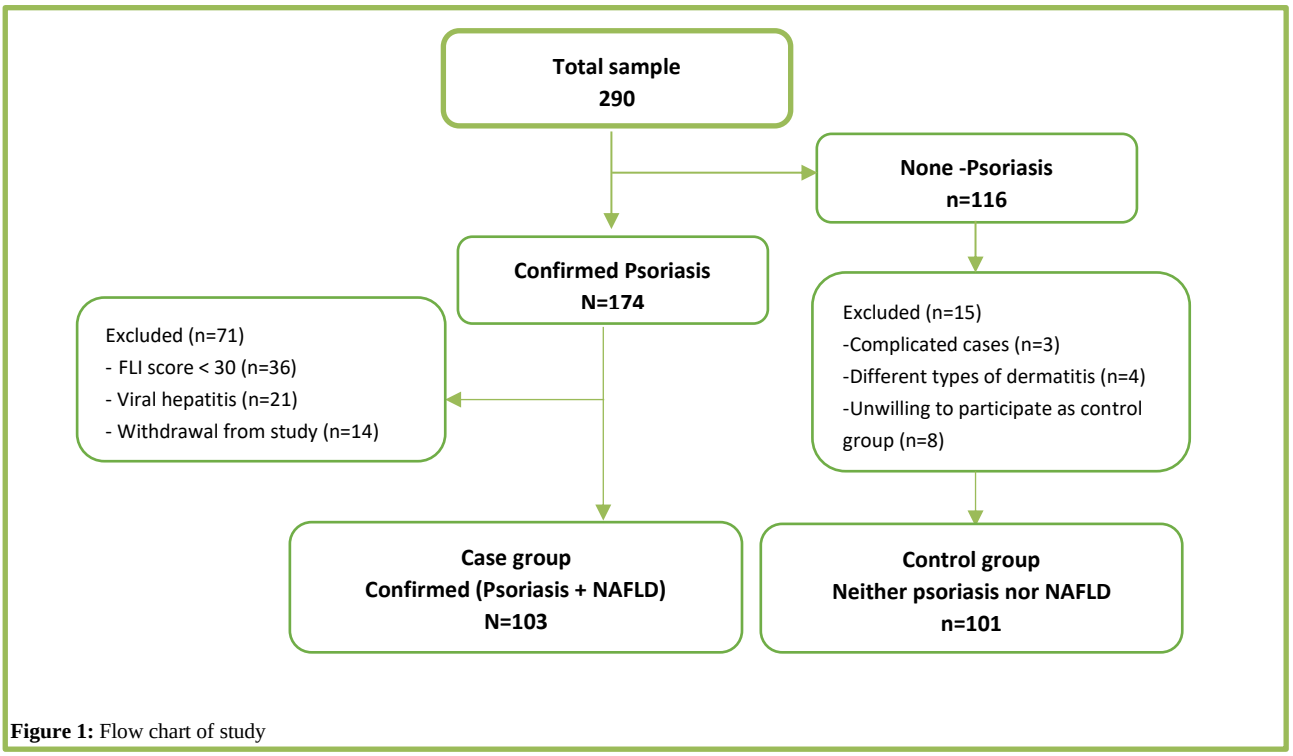

Figure 1: Flow chart of study

Table 1: Basic characteristic of case-control groups and bivariate findings (n=204)

Variables	Psoriasis+ NAFLD (N=103)	Neither Psoriasis nor NAFLD (N=101)	p-value
Age (mean ± SD)	32.5 (± 16.2)	31.5 (± 14.3)	0.720
Gender: (Male-(N%)	58(56.3)	51(50.5)	0.061
: (Female-N%)	45(43.7)	50(49.5)	0.235
ALT (U/L) (Mean ± SD)	61 ± 29	33 ± 17	<0.0001
AST (U/L) (Mean ± SD)	55 ± 27	25 ± 15	<0.0001
GGT (U/L) (Mean ± SD)	63 ± 25	31 ± 19	<0.0001
BMI (kg/m^2) (Mean ± SD)	28.3 ± 4.7	24.5 ± 3.6	0.0007
IL-6 levels (pg/mL) (Mean ± SD)	3.56± 2.3	1.82± 1.7	0.0003
Waist circumference (cm) (Mean ± SD)	97 ± 14.5	85 ± 12.8	0.0005
Fasting blood sugar (mg/dL) (Mean ± SD)	131 ± 36.1	91 ± 11.2	<0.0001
Triglycerides (mg/dL) Mean ± SD)	225 ± 112	119 ± 79	<0.0001
Total Cholesterol (mg/dL) Mean ± SD)	221 ± 55.2	185 ± 47.5	0.0002

NAFLD = Non-Alcoholic Fatty Liver Disease; p = p-value (Mann-Whitney U-test for continuous variables. Chi-square (X2) test and independent sample t-test for categorical variables); ALT = Alanine Transaminase; AST = Aspartate Transaminase; GGT = Gamma-Glutamyl-Transferase; BMI = body mass index.

Discussion

Psoriasis is a persistent inflammatory-immunologic condition, exhibiting a prevalence of 2.0% in Diyala province [11], 2.3% among the Iraqi population [12], and varying prevalence worldwide 13]. Earlier studies have documented an elevated incidence of nonalcoholic fatty liver disease (NAFLD) in individuals with psoriasis [14,15,16]. In line with the present investigation, it is noteworthy that over two-thirds (74.1%) of individuals diagnosed with psoriasis in this study exhibited a fatty liver index score of 60 and above. This prevalence falls within the range reported internationally, which spans from 44.3% to 65.6% [14,15,16,17,18]. Beyond the association with nonalcoholic fatty liver disease (NAFLD), individuals with psoriasis face an increased susceptibility to liver abnormalities, including various types of hepatitis and neutrophilic cholangitis, in comparison to the general population. Moreover, aberrations in liver function tests are frequently observed in patients with psoriasis [19]. Likewise, the current study identified a notable rise in all employed liver function tests in individuals with psoriasis when contrasted with those without psoriasis. Elevated serum IL-6 levels were observed in this study, demonstrating statistical significance (P = 0.0003) when juxtaposed with the healthy control group. These findings align with a study conducted in the Iraqi (city of Baghdad), where patients exhibited significantly higher IL-6 levels than controls (P = 0.01) [20]. Elevated concentrations of IL-6 have been detected in both the skin lesions of individuals with psoriasis and the synovial tissue of patients diagnosed with psoriatic arthritis [[21]. Additionally, a noteworthy association has been observed between serum IL-6 levels and the Disease Activity Score-28, specifically based on CRP level, among psoriatic arthritis [22]. These discoveries highlight the potential of IL-6 as a promising target for therapeutic intervention in the context of psoriatic arthritis. Within our investigation, we observed no notable distinctions in age and gender distribution between the two cohorts. Nevertheless, we did identify a higher body mass index (BMI) among individuals with psoriasis and non-alcoholic fatty liver disease (NAFLD) when compared to their counterparts (28.3 ± 4.7 versus 24.5 ± 3.6, p=0.0007). In contrast, the findings of Narayanasamy et al [17] suggested a different trend, reporting that psoriasis patients with NAFLD were younger than those with psoriasis alone. Furthermore, the former group exhibited greater obesity compared to non-NAFLD patients with psoriasis, a higher likelihood of being male, and elevated BMI levels. This study complains of certain limitations that warrant acknowledgment. Firstly, owing to the inherent case-control design, establishing a definitive temporal association between psoriasis and non-alcoholic fatty liver disease (NAFLD) proved challenging. Additionally, while liver biopsy stands as the gold standard for diagnosing NAFLD, its impracticality in the context of a population-based study led us to rely on the Fatty Liver Index (FLI) for diagnosis. It is imperative to note that the data collection exclusively took place at a single tertiary hospital in Diyala province, located in the northwest region of Iraq. Consequently, the generalizability of these findings to the entire country may be subject to scrutiny.

Conclusion

Within the scope of this study, a comparative analysis was conducted between individuals afflicted with both psoriasis and non-alcoholic fatty liver disease (NAFLD) and those devoid of either condition. The diagnosis of NAFLD was confirmed through the application of the "Fatty Liver Index" (FLI). Notably, the levels of IL-6 and liver function tests demonstrated significant elevation in the group affected by psoriasis and NAFLD in comparison to their counterparts without these conditions. Interestingly, sociodemographic factors such as age and gender exhibited no significant variations between the two groups. An intriguing observation emerged in our investigation, revealing that individuals with psoriasis whose BMI surpassed 28 displayed a heightened susceptibility to developing NAFLD. This underscores the potential role of obesity, as reflected by BMI, as a contributing factor in the association between psoriasis and NAFLD. The findings suggest a novel perspective on the diagnostic landscape, proposing that both liver function tests and IL-6 may serve as early predictive markers for identifying non-alcoholic fatty liver disease in individuals with psoriasis. This insight opens avenues for further research and underscores the importance of considering a multifaceted approach when assessing the health implications of psoriasis.

Abbreviation

NAFLD: Nonalcoholic Fatty Liver Disease; FLI: Fatty Liver Index; IL-6: Interleukin 6; BMI: Body Mass Index; ALT: Alanine Transaminase; AST: Aspartate Transaminase; GGT: Gamma-Glutamyl-Transferase; ELISA: Enzyme-Linked Immunosorbent Assay; SD: Standard Deviation

Declaration

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Availability of data and materials

Data will be available by emailing tadhmun.h@oudiyala.edu.iq

Authors' contributions

All authors are equality conceived and designed the study, analyzed and interpreted the data; drafted the manuscript; revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the declaration of Helsinki. The ethical approval was obtained from the Ethics Review Committee, College of Medicine, University of Diyala, Iraq (Ref No: 17-2023). Informed consent was obtained from the participants before filling out the survey questionnaire

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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References

1. Bu J, Ding R, Zhou L, Chen X, Shen E. Epidemiology of Psoriasis and Comorbid Diseases: A Narrative Review. Front Immunol. 2022 Jun 10; 13:880201. doi: 10.3389/fimmu.2022.880201.
2. Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. Hippokratia. 2009 Jan;13(1):9-19.
3. Ganzetti G, Campanati A, Offidani A. Non-alcoholic fatty liver disease and psoriasis: So far, so near. World J Hepatol. 2015 Mar 27;7(3):315-26. doi: 10.4254/wjh.v7.i3.315.
4. Klujszo EH, Parcheta P, Witkowska AB, Krecisz B. Non-alcoholic fatty liver disease in patients with psoriasis: therapeutic implications. Postepy Dermatol Alergol. 2020 Aug;37(4):468-474. doi: 10.5114/ada.2019.83983.
5. Mantovani A, Gisondi P, Lonardo A, Targher G. Relationship between Non-Alcoholic Fatty Liver Disease and Psoriasis: A Novel Hepato-Dermal Axis? Int J Mol Sci. 2016 Feb 5;17(2):217. doi: 10.3390/ijms17020217.
6. Barros G, Duran P, Vera I, Bermúdez V. Exploring the Links between Obesity and Psoriasis: A Comprehensive Review. International Journal of Molecular Sciences. 2022; 23(14):7499. https://doi.org/10.3390/ijms23147499.
7. Prussick R, Prussick L, Nussbaum D. Nonalcoholic Fatty liver disease and psoriasis: what a dermatologist needs to know. J Clin Aesthet Dermatol. 2015 Mar;8(3):43-5.
8. Gau SY, Huang KH, Lee CH, Kuan YH, Tsai TH, Lee CY. Bidirectional Association Between Psoriasis and Nonalcoholic Fatty Liver Disease: Real-World Evidence From Two Longitudinal Cohort Studies. Front Immunol. 2022 Feb 16;13:840106. doi: 10.3389/fimmu.2022.840106.
9. Barnes TC, Anderson ME, Moots RJ. The many faces of interleukin-6: the role of IL-6 in inflammation, vasculopathy, and fibrosis in systemic sclerosis. Int J Rheumatol. 2011;2011:721608. doi: 10.1155/2011/721608.
10. Bedogni G, Bellentani S, Miglioli L, et al. The fatty liver index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol. 2006;6(1):33.
11. Murad AAK, Hussien WM. Incidence of psoriasis in patients with different skin diseases in Baquba City. Diyala Journal of Medicine 2017; 12(1): 25-28.
12. Al Samarai AG. Prevalence of skin diseases in Iraq: a community based study. Int J Dermatol. 2009 Jul;48(7):734-9. doi: 10.1111/j.1365-4632.2009.03812.x.
13. Torres T, Bettencourt N. Psoriasis: the visible killer. Rev Port Cardiol. 2014 Feb;33(2):95-9. doi: 10.1016/j.repc.2013.06.017.
14. Ruan Z, Lu T, Chen Y, Yuan M, Yu H, Liu R, Xie X. Association Between Psoriasis and Nonalcoholic Fatty Liver Disease Among Outpatient US Adults. JAMA Dermatol. 2022 Jul 1;158(7):745-753. doi: 10.1001/jamadermatol.2022.1609.
15. Abedini R, Salehi M, Lajevardi V, Beygi S. Patients with psoriasis are at a higher risk of developing nonalcoholic fatty liver disease. Clin Exp Dermatol. 2015;40(7):722-727. doi: 10.1111/ced.12672.
16. Gisondi P, Targher G, Zoppini G, Girolomoni G. Non-alcoholic fatty liver disease in patients with chronic plaque psoriasis. J Hepatol. 2009;51(4):758-764. doi: 10.1016/j.jhep.2009.04.020.
17. Narayanasamy K, Sanmarkan AD, Rajendran K, Annasamy C, Ramalingam S. Relationship between psoriasis and non-alcoholic fatty liver disease. Prz Gastroenterol. 2016;11(4):263-269. doi: 10.5114/pg.2015.53376.
18. van der Voort EAM, Koehler EM, Dowlatshahi EA, 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(3):517-524. doi: 10.1016/j.jaad.2013.10.044.
19. Dhurgham A. Mahmood, et al. Evalution of Liver Function Tests in Patients with Psoriasis. Revista Latinoamericana de Hipertensión 2022;17(6):397-403. DOI: https://doi.org/10.5281/zenodo.7406087.
20. Iqbal U, Perumpail BJ, Akhtar D, Kim D, Ahmed A. The Epidemiology, Risk Profiling and Diagnostic Challenges of Nonalcoholic Fatty Liver Disease. Medicines (Basel). 2019 Mar 18;6(1):41. doi: 10.3390/medicines6010041.
21. Atzeni F, Ventura D, Batticciotto A, Boccassini L, Sarzi-Puttini P. Interleukin 6 blockade: tocilizumab in psoriatic arthritis. J Rheumatol Suppl. 2012;89:97–9. https://doi.org/10.3899/jrheum.120256.
22. Muramatsu S, Kubo R, Nishida E, Morita A. Serum interleukin-6 levels in response to biologic treatment in patients with psoriasis. Mod Rheumatol. 2017;27:137–41. https://doi.org/10.3109/14397595.2016.117432