Ann. For. Res. 66(1): 3845-3856, 2023
ISSN: 18448135, 20652445

ANNALS OF FOREST RESEARCH
www.e-afr.org

DETERMINATION THE RELATIONSHIP BETWEEN IL-38 AND IL-17 IN REDUCING THE SEVERITY OF PSORIASIS IN SAMPLES OF IRAQI PATIENTS

Amna E. Fawzi[1*], Researcher Prof. Ghada M. AL-Quraishi[2]
[1,2] Dept. of Biology, Collage of Science, University of Baghdad, Iraq.
*Corresponding author E-mail: amna.emad1202a@sc.uobaghdad.edu.iq

Abstract
This study was aimed to determine the relationship between level of Interleukin-38 and Interleukin-17 in psoriasis, one hundred-five patients, twenty-five of them suffering from psoriasis and twenty-two of them suffering from psoriasis and *Helicobacter pylori* who attended at Dermatological Clinic and fifty-eight patients who infected with *Helicobacter pylori* take from Al-kindi Hospital, Kadhimiya Teaching Hospital, AL-Yarmouk Teaching Hospital and AL-Zahra Hospital. Aged (≤ 35, >35) years have been investigated and compared to Twenty-five samples of apparently healthy individuals were studied as control group. All the studied groups were subjected to measurement level of IL-38 and IL-17 by Enzyme linked immunosorbent assay (ELISA). The results of current study revealed that there was a highly significant elevation (P<0.0001) between level of IL-38 and IL-17 in sera of patients. Conclusion, IL-17 play critical role in the pathogenesis of psoriasis. The highest level of IL-17 in patients' serum was in patients whose infected with psoriasis and *Helicobacter pylori* together, IL-38 act as protective factor in psoriasis and there was a negative relationship between level of IL-17 and IL-38.
Keywords: Psoriasis, Interleukin-38, interleukin-17, *Helicobacter pylori*, ELISA.

1.Introduction

psoriasis is a chronic inflammatory, immune mediated disease of the skin which is characterized by the presence of erythematous scaly plaques. Around 2-3% of people worldwide are affected by the persistent skin condition psoriasis [1]. Skin cells normally develop about 10 times more quickly than usual when psoriasis is present. Moreover, other organ systems, particularly the joints, may be impacted [2]. There are several types of psoriasis some is common such as plaque psoriasis (psoriasis vulgaris), scalp psoriasis, nail psoriasis, guttate psoriasis, inverse psoriasis [3] and another which less common types such as pustular psoriasis, erythrodermic psoriasis, and there's also psoriatic arthritis, a combo of psoriasis and arthritis [4]. Genetics, a hyperactive immune system, and triggers like bacterial infection, skin damage, smoking, medicines, and obesity all contribute to the development of psoriasis [5]. Adaptive and innate immune responses, as well as genetic and environmental variables, interact in a complicated way to develop psoriasis. Its pathophysiology is primarily characterized by dysregulated inflammation, keratinocyte proliferation mediated by T cells, and abnormal epidermal differentiation [6]. Interleukin-17A (IL-17A), one of the inflammatory cytokines secreted by T helper 17 (Th17) cells, encourages keratinocyte growth and angiogenesis within lesions. Cluster of differentiation 4 (CD4+) T lymphocytes that produce IL-17 have a variety of helper activities that boost the humoral immune

response, the cytotoxic activity of cluster of differentiation 8 (CD8+) T lymphocytes, and the phagocytic capacities of macrophages [7]. IL-38, IL-1 receptor antagonist (IL-1Ra), and IL-36Ra have structural similarities [8]. The particular receptor for IL-38, a partially receptor antagonist of IL-36, is called IL-36R [9]. The synthesis of the T-cell cytokines IL-17 and IL-22 is inhibited by IL-38 [10]. Study show that skin and circulation IL-38 levels are lower in psoriatic patients and in other skin illnesses marked by neutrophilic infiltration. The function of IL-38 antagonists in psoriasis is still unknown [11]. In some areas, the prevalence of *Helicobacter pylori* (*H.pylori*), a gram-negative, flagellated, helix-shaped bacterium with a microaerophilic metabolism, can surpass 80%, impacting more than 50% of the world's population [12]. Some studies have shown that *H. pylori* infection triggers the inflammatory response by releasing interleukins uncontrollably. Nonetheless, investigations on the connection between *H. pylori* infection and dermatological conditions such as rosacea, chronic urticaria, alopecia areata, and psoriasis have also been documented [13]. Infections may potentially cause the onset of psoriasis due to the binding of superantigens to the T-cell receptor and the major histocompatibility complex, which is expressed on antigen-presenting cells and ultimately activates CD4+ T cells, one of the microbial infections that could aggravate psoriasis through the aforementioned processes is the *H. pylori* infection. Despite this, publications regarding the relationship are contradictory [14]. The research aimed to determine the association between IL-38 and IL-17 in the pathogenesis of psoriasis patients.

2.Materials and Methods

2.1 Study Samples

A case study was conducted during December 2021–june 2022 to determine the levels of Interleukin-38 and Interleukin-17 in samples of Iraqi psoriasis Patients. The study was conducted on a group infected with psoriasis, a group infected with *H.pylori* and a group who's infected with psoriasis and *H.pylori* together and apparently healthy controls group. The Ethics Committee at the Department of Biology (University of Baghdad) approved the study protocol by (Reference: CSEC/0921/0048) In September 25,2021.

2.1.1 Patients

Consecutive 105 cases (59 males and 46 females) of Iraqi patients (25 patients infected with psoriasis, 58 patients infected with *H.pylori* and 22 patients infected with both psoriasis and *H.pylori)* were randomly selected and recruited from Al-kindi Hospital, Kadhimiya Teaching Hospital, AL-Yarmouk Teaching Hospital and AL-Zahra Hospital that were diagnosed by doctor. most of patients as well as all cases were selected without any chronic disease, not smoking and with the ideal BMI.

2.1.2 Healthy Control Group:

twenty-five healthy individuals, (13 males and 12 females), without apparent diseases, not smoking and with ideal BMI were randomly selected as the healthy control groups during the period of this study.

2.2 Laboratory methods

The Enzyme-linked Immunosorbent Assay (ELISA) kits were used for quantitative assessments of IL-38 and IL-17 in sera of patients and control the kits were products of My BioSource Company (USA) and was based on a competitive and sandwich ELISA technique. Standard procedures recommended by the manufacturers were followed in these assessments.

2.2.1 The Statistical Analysis

to managed and analyzed using the statistical package (SSPS), variables presented as median with interquartile range (IQR).The Chi-square test was used to assess the association between categorical variables, as a Fisher's exact test was used when chi-square was inapplicable. The Kruskal-Wallis test and the Mann-Whitney U test probability were used to compare nonparametric variables (not normally distributed). They were expressed as the median and interquartile range (IQR). A probability (p) value < 0.05 was taken as statistically significant. Receiver operating characteristics curve (ROC) analysis was used to estimate the area under the curve (AUC), 95% confidence interval (CI), cut-off value, sensitivity and specificity to assess the validity of the significantly different. Logistic regression analysis was applied to calculate odds ratio (OR) and 95% CI. Spearman's rank-order correlation was performed to analyze the correlation coefficient.

3. Results and Discussion:

3.1 Median levels of IL17 among studied groups.

Median levels of IL-17 were highly significantly increase (p-value < 0.001) in patients with psoriasis and patients with psoriasis and *H. pylori* (660.92 and 949.37 pg/mL, respectively) compared to patients with *H. pylori* and controls (327.57 and 194.92pg/mL; p-value < 0.001), also there was a highly significant differences (p-value < 0.001) in the levels of IL17 between patients with psoriasis and *H. pylori* and patients whose only infected with *H. pylori,* and a high significant difference (p-value < 0.001) was indicated between patients with *H. pylori* and healthy controls (p-value< 0.001) as shown in figure 3-1, table 3-1. The highest median IL17 of [949.37 (773 – 1022.2)] (pg/ml) was recorded in patients with psoriasis and *H.pylori* followed by the median of patients with psoriasis [660.92 (487.4 – 683)] (pg/ml) then median of patients with *H.pylori* [327.57 (247.1 – 372.4)] (pg/ml) and finally the lowest median in healthy control was [194.92(187.48-199.18)] (pg/ml) as shown in Table 3-1.

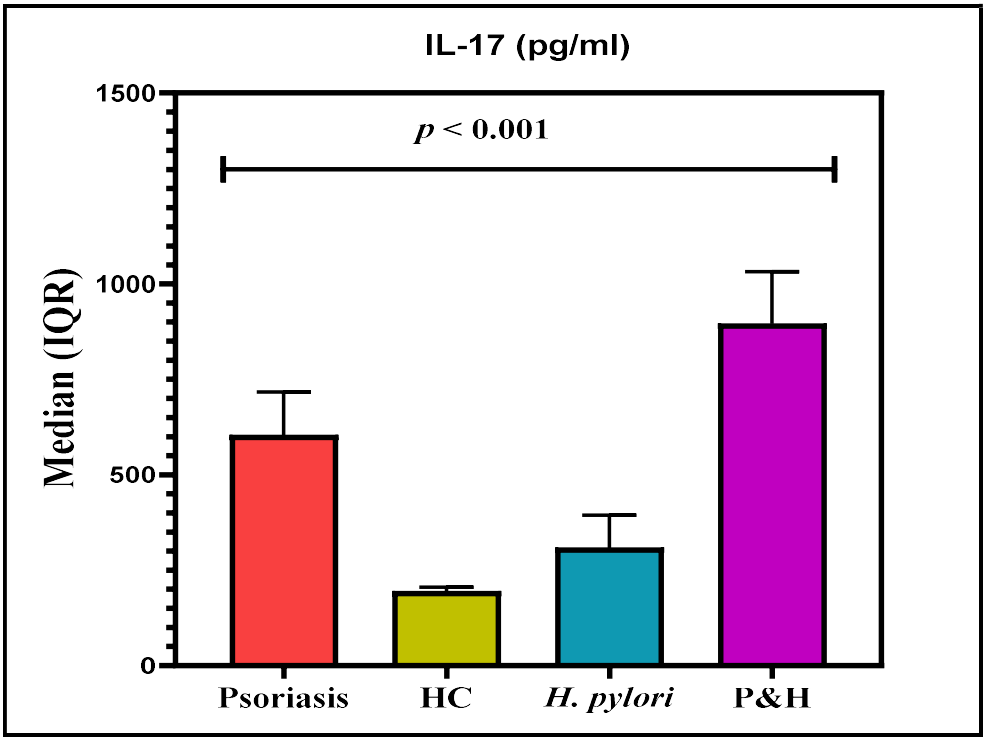

Figure 3-1: Median level of Interleukin 17 in psoriasis, *H.pylori* and psoriasis with *H.pylori* patients group and healthy controls.

P&H: psoriasis and *Helicobacter pylori*

H.pylori*: Helicobacter pylori*

Table 3-1: Median of IL-17 among studied groups compared with heathy control

Groups	Median (IQR) of IL-17 pg/ml	Probability (Mann-Whitney Test)
Psoriasis	660.92 (487.4 – 683)	< 0.001
H. pylori	327.57 (247.1 – 372.4)	< 0.001
Psoriasis and *H. pylori*	949.37 (773 – 1022.2)	< 0.001
control	194.92(187.48-199.18)	< 0.001
Probability (Kruskal-Wallis Test)	< 0.001	---

3.1.2 Logistic regression analysis of IL17 in studied groups.

Logistic regression revel the OR of unadjusted patients was 1.14 (95% CI: 1.06-1.23; *p*-value < 0.001) followed by age adjusted 1.4 (95% CI:0.86-2.28; *p*-value=0.176) then sex adjusted 7.84 (95% CI:0.58-105.38; *p*-value=0.120) and BMI adjusted 0.08 (95% CI:0.01-3.82; *p*-value=0.197).

These values mean IL17 was increase severity of disease and increases the possibility of infection, act as effective factor in psoriasis as shown in Table 3-2.

Table 3-2: Logistic regression analysis of IL-17 level in total patients *versus* healthy control group.

Analysis Model†	OR	95% CI	*p*-value
I (unadjusted)	**1.14**	**1.06 – 1.23**	**0.001**
II (age adjusted)	**1.4**	**0.86 – 2.28**	**0.176**
III (sex adjusted)	**7.84**	**0.58 – 105.38**	**0.120**
IV (BMI adjusted)	**0.08**	**0.01 – 3.82**	**0.197**

†: The reference category is healthy control; BMI: body mass index; OR: Odds ratio; CI: Confidence interval; *p*: Probability (significant *p*-value is indicated in bold).

3.1.3 ROC curve of IL17 with total patients

The Receiver Operating Characteristic (ROC)curve analysis revealed that the levels of IL17 was a excellent predictor of psoriasis severity. The AUC was 1 (95% CI = 84.5 – 100; p < 0.001). At a cut-off value of >218.2 pg/ml in patients with psoriasis and patients with psoriasis and *H. pylori* together, the sensitivity and specificity of IL17 was 100% and 95.3%, respectively Figure 3-2

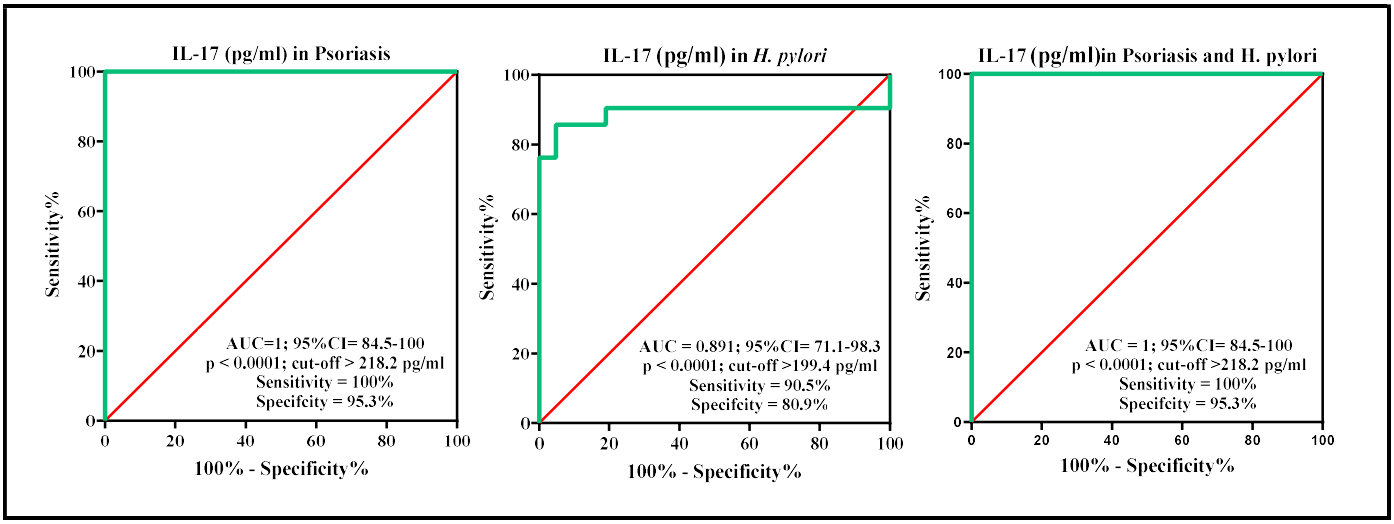

Figure 3-2: ROC curve analysis of IL-17 in total studied patients *versus* healthy controls (HC).

Tables 3-1, 3-2 and figure 3-2 shows that interleukin-17 elevated in patients with psoriasis compared to healthy controls as shown in the results, also there is the first epidemiological study in Iraq have showed that patients with psoriasis and *H. pylori* had a very high level of IL17 than those patients with *H. pylori* only. The present study also shows that patients infection with *H. pylori* had a rise of IL17 levels and that's approved by [15] who showed, Immune-sensitive cells including T-helper 1 (Th1), T-helper 2 (Th2), T-helper 17 (Th17), and T-regulatory (Treg) cells inside the gastric milieu release a variety of cytokines in response to H. pylori infection, including IL17, IL6, and transforming growth factor- (TFG-).

Consistent with our findings, most studies indicated that interleukin IL17 pathway plays a critically important role in the pathogenesis of psoriasis. The IL-17 effectors (IL-17A, IL-17C, IL-17E, and IL-17F) drive epidermal hyperplasia and the pro-inflammatory feed-forward loop seen in plaque psoriasis by acting on keratinocytes, endothelial cells, and immune cells. [16]. Compared to healthy individuals, those with psoriasis have greater plasma levels of IL17 and more circulating IL-17-producing cells. [17]. Serum IL-17 was significantly increasing among psoriatic patients as compared to healthy controls (895.066 pg/ml and 364.334 pg/ml) respectively. Additionally, there was a highly significant difference between groups' psoriasis severity and higher IL17 serum levels. Conclusion: (IL-17) should be a target for biological therapy in patients with psoriasis in Iraq because it has a significant role in the activity of the disease. [18].
Agreement the present study with [19] The findings showed that patients with psoriasis had significantly higher serum levels of IL-17A, IL-18, and IL-22 when compared to healthy controls (P 0.01). These findings are consistent with the hypothesis that blood levels of IL-17A, IL-18, and IL-22 contribute to the pathogenesis of psoriasis, presumably by causing and maintaining psoriatic lesions.

Another study by [20] approve that, Patients with psoriasis have higher levels of IL17 and TNF in their serum. As [21] proved that Potential involvement of H. pylori in the etiology of psoriasis. The role of *H.pylori* lies in the immune response that occurs during infection, and this was confirmed by [22] NF-B and JNK, chemokines, and other proinflammatory cytokines can all be activated by IL17. The interplay of IL-17, IL-21, and IL-23 affects the extracellular matrix (ECM), draws neutrophil migration, and changes the defensive mechanisms of the mucosa. In addition, precancerous gastric lesions are associated with variant polymorphisms in IL-17, IL-21, and IL-23.

3.2 Interleukin 38

3.2.1 Median levels of IL38 in total among studied groups.

Median levels of IL38 was highly significantly decreased (; *p*-value < 0.001) in patients with psoriasis and patients infected with psoriasis and *H.pylori* together (305.71 and 233.83 pg/mL, respectively) compared to patients with *H. pylori* and controls (422.25 and 438.93 pg/ml respectively; *p*-value < 0.001), while there was no significant difference between patients with psoriasis and patients infected with psoriasis and *H. pylori,* Also no significant difference between patients with *H. pylori* and controls (*p*-value = 0.521) Table 3-3, Figure 3-3. The lowest median

IL38 of [233.83 (218.9 – 237.2)] (pg/ml) was recorded in patients with psoriasis and *H. pylori* followed by the median of patients with psoriasis [305.71 (246.3 – 328.3)] (pg/ml) then median of patients with *H. pylori* [422.25 (350.8 – 496.9)] (pg/ml) and finally the highest median in healthy control was [438.93(382.67-484.93)] (pg/ml) as shown in table 3-3.

Table 3-3: Median of IL-38 among studied groups compared with heathy control

Groups	Median (IQR) of IL-38 pg/ml	Probability (Mann-Whitney Test)
Psoriasis	**305.71 (246.3 – 328.3)**	**< 0.001**
H. pylori	**422.25 (350.8 – 496.9)**	**0.521 (NS)**
Psoriasis and *H. pylori*	**233.83 (218.9 – 237.2)**	**< 0.001**
controls	**438.93(382.67-484.93)**	**< 0.001**
Probability (Kruskal-Wallis Test)	**< 0.001**	

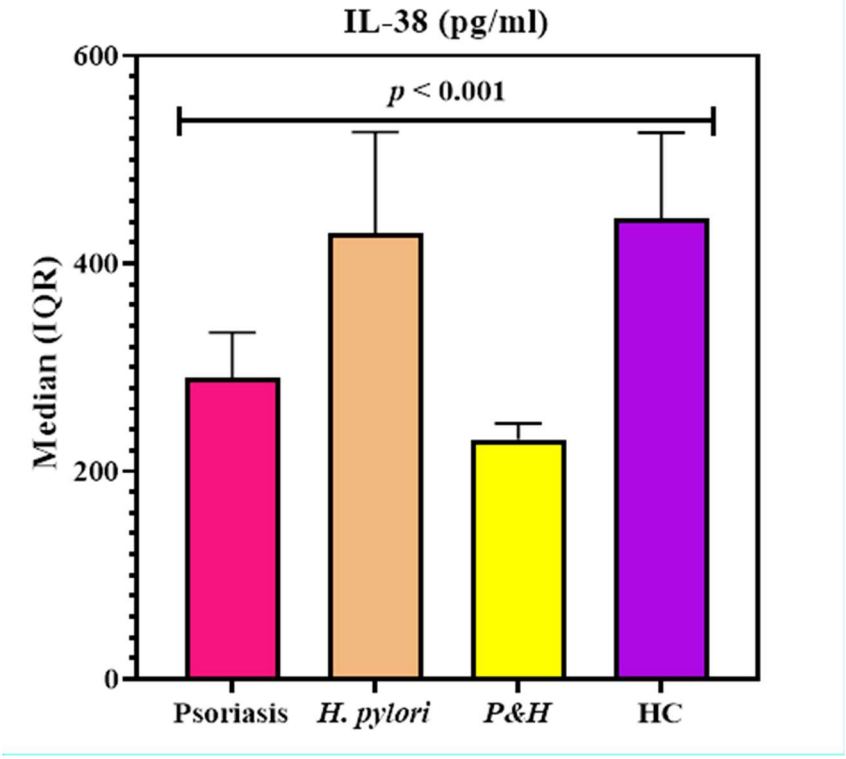

Figure 3-3: Median level of Interleukin 18 in psoriasis, *H.pylori* and psoriasis with *H.pylori* patients group and healthy controls.

P&H: psoriasis and *Helicobacter pylori*

H.pylori*: Helicobacter pylori*

3.2.1 Logistic regression analysis of IL38 in total patients

Logistic regression revel the OR of unadjusted patients was 0.89 (95% CI: 0.86 – 0.94; *p*-value < 0.001), followed by age adjusted 1.33 (95% CI:1.08-1.64; p-value=0.007) then sex adjusted 0.98 (95% CI:0.12-8.03; *p*-value=0.987) and BMI adjusted 0.25 (95% CI:0.07-0.89; p-value=0.034). These values mean IL38 was decrease severity of disease and act as protective factor from psoriasis as shown in Table 3-4.

Table 3-4: Logistic regression analysis of IL-38 level in total patients *versus* healthy control group.

Analysis Model†	OR	95% CI	*p*-value
I (unadjusted)	**0.89**	**0.86 – 0.94**	**0.001**
II (age adjusted)	**1.33**	**1.08 – 1.64**	**0.007**
III (sex adjusted)	**0.98**	**0.12 – 8.03**	**0.987**
IV (BMI adjusted)	**0.25**	**0.07 – 0.89**	**0.034**

†: The reference category is healthy control; BMI: body mass index; OR: Odds ratio; CI: Confidence interval; *p*: Probability (significant *p*-value is indicated in bold).

3.2.2 ROC curve of IL38 with total patients

The Receiver Operating Characteristic (ROC) curve analysis revealed that the level of IL38 was a good predictor of psoriasis severity. The AUC was 0.97 (95% CI = 71.1 – 98.3; p < 0.001). At a cut-off value of <344.4 pg/ml in patients with psoriasis and AUC was 1 (95% CI = 84.5 – 100; p < 0.001). At a cut-off value of <292.6 pg/ml in patients with psoriasis and *H. pylori* together, the sensitivity and specificity of IL38 was 90.5% and 85.7%, respectively in patients with psoriasis and the sensitivity and specificity of IL38 was 100% and 100%, respectively in patients with psoriasis and *H. pylori* together as shown in Figure 3-4.

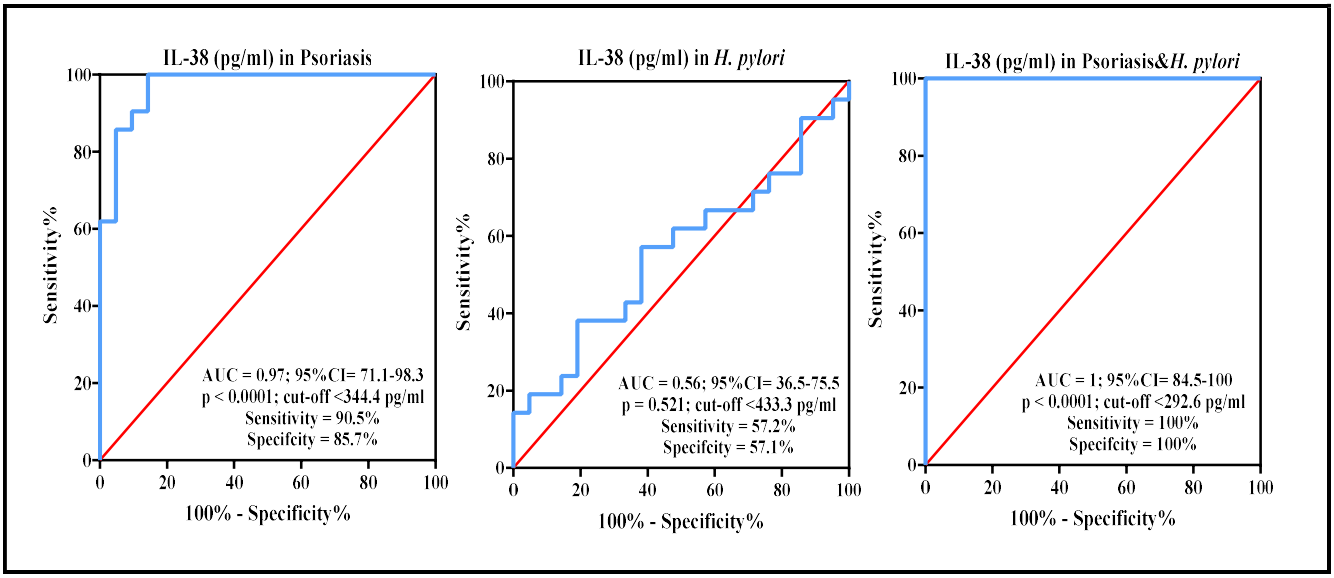

Figure 3-4: ROC curve analysis of IL-38 in total studied patients *versus* healthy controls (HC).

Explanation of the tables 3-3, 3-4 and figure 3-4 patients with psoriasis and patients with psoriasis and *H. pylori* together have the lowest level of interleukin 38 compared to patients infected with *H. pylori* only and healthy controls, also patients with psoriasis and *H. pylori* compared to patients infected with only *H. pylori* had a high significant difference p-value<0.001). Some studies had support that such as in the research of [23] Undefined is the function of IL-38 antagonist in psoriasis. Here, we show that patients with psoriasis and other skin conditions marked by neutrophilic infiltration had lower levels of circulating and skin IL-38. The balance of IL-36 agonist/IL-38 antagonist serum levels in psoriasis is in favor of agonists and is closely related to the degree of the condition. According to a different study, psoriatic patients' IL-38 expression is clearly lowered in both their skin and peripheral blood, while being strongly expressed in their skin [24].

Based on the mentioned before results that indicate that interleukin-38 becomes lower in patients with psoriasis and that due to the rise of interleukin-17, as these interleukins are opposite to each other, when one of them increases, the other decreases, and vice versa. That was proven by in fact, IL-17 and IL-22 cytokines significantly contribute to the defective differentiation processes that take place in the afflicted skin, which are connected with the loss of IL-38 in the super basal layers of the psoriatic epidermis [25].

A recent study found that low concentrations of IL-38 were more effective than higher concentrations in inhibiting the production of IL-17 and IL-22 from peripheral blood mononuclear cells (PBMCs) because higher concentrations only mildly increased IL-22. IL-38 reduced the expression of C. albicans-induced IL-17 and IL-22 from PBMCs by reducing the stimulation of proinflammatory cytokines in the tissues [26].

3.3 Correlation IL-17and IL-38 and between studied groups patients

Correlation between IL-17 and IL-38 were highly significant difference ($p < 0.001$). The figure 3-5 demonstrates the increasing in IL-38 levels lead to decrease in IL-17 level with (rs= - 0.85), which indicate that IL-17 are negatively correlated with IL-38. The result of current study approved that IL-38 act as biomarkers to prevent or reduce of psoriasis severity. However, IL-17 may be a good marker to progression of disease.

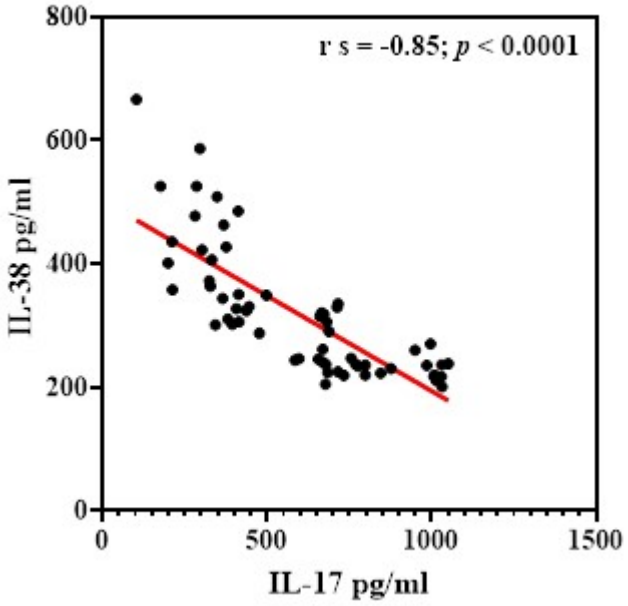

Figure 3-4: Spearman's rank correlation coefficient (rs) between IL-17 and IL-38 in total studied patients' groups.

4. Conclusion:

IL-17 play critical role in the pathogenesis of psoriasis. The highest level of IL-17 in patients' serum was in patients whose infected with psoriasis and *Helicobacter pylori* together, IL-38 act as protective factor in psoriasis and there was a negative relationship between level of IL-17 and IL-38.

References

1. Orlando, G., Molon, B., Viola, A., Alaibac, M., Angioni, R., & Piaserico, S. (2022). Psoriasis and cardiovascular diseases: an immune-mediated cross talk?. *Frontiers in Immunology*, *13*, 868277.
2. Ji, C., Wang, H., Bao, C., Zhang, L., Ruan, S., Zhang, J., ... & Cheng, B. (2021). Challenge of nail psoriasis: an update review. *Clinical Reviews in Allergy & Immunology*, 1-26.
3. Gisondi, P., Bellinato, F., & Girolomoni, G. (2020). Topographic differential diagnosis of chronic plaque psoriasis: challenges and tricks. Journal of Clinical Medicine, 9(11), 3594.
4. Gisondi, P., Bellinato, F., Targher, G., Idolazzi, L., & Girolomoni, G. (2022). Biological disease-modifying antirheumatic drugs may mitigate the risk of psoriatic arthritis in patients with chronic plaque psoriasis. Annals of the Rheumatic Diseases, 81(1), 68-73.

5. Mahajan, T., Singh, N., Goyal, K., Jindal, S., Pandit, V., & Ashawat, M. S. (2022). Recent Updates on Psoriasis: A Review. *Asian Journal of Pharmaceutical Research*, *12*(1), 76-83.
6. Chhabra, S., Dogra, S., Sharma, K., Raychaudhuri, S. K., & Raychaudhuri, S. P. (2022). Recent update on immunopathogenesis of psoriasis. *Indian Journal of Dermatology*, *67*(4), 360.
7. Ahmed, A. S., Al-Najjar, A. H., Alshalahi, H., Altowayan, W. M., & Elgharabawy, R. M. (2021). Clinical Significance of Helicobacter Pylori Infection on Psoriasis Severity. *Journal of Interferon & Cytokine Research*, *41*(2), 44-51.
8. Xia, H. S., Liu, Y., Fu, Y., Li, M., & Wu, Y. Q. (2021). Biology of interleukin-38 and its role in chronic inflammatory diseases. International immunopharmacology, 95, 107528.
9. Ngo, V. L., Kuczma, M., Maxim, E., & Denning, T. L. (2021). IL-36 cytokines and gut immunity. Immunology, 163(2), 145-154.
10. Han, Y., Mora, J., Huard, A., da Silva, P., Wiechmann, S., Putyrski, M., ... & Weigert, A. (2019). IL-38 ameliorates skin inflammation and limits IL-17 production from γδ T cells. Cell reports, 27(3), 835-846.
11. Mercurio, L., Morelli, M., Scarponi, C., Eisenmesser, E. Z., Doti, N., Pagnanelli, G., ... & Madonna, S. (2018). IL-38 has an anti-inflammatory action in psoriasis and its expression correlates with disease severity and therapeutic response to anti-IL-17A treatment. Cell death & disease, 9(11), 1104.
12. Silva, C. S., da Silva Júnior, R. T., de Sá Santos, L. K., Apolonio, J. S., da Costa, B. T., Cuzzuol, B. R., ... & de Melo, F. F. (2021). Extragastric Manifestations of Helicobacter pylori Infection: A Commentary. Archives of Gastroenterology Research, 2(3), 102-109.
13. Teng, Y., Xie, W., Tao, X., Liu, N., Yu, Y., Huang, Y., ... & Fan, Y. (2021). Infection provoked psoriasis: Induced or aggravated. Experimental and therapeutic medicine, 21(6), 1-9.
14. Zhou, S., & Yao, Z. (2022). Roles of infection in psoriasis. International Journal of Molecular Sciences, 23(13), 6955.
15. Jan, I., Rather, R. A., Mushtaq, I., Malik, A. A., Besina, S., Baba, A. B., ... & Afroze, D. (2021). Helicobacter pylori subdues cytokine signaling to alter mucosal inflammation via hypermethylation of suppressor of cytokine signaling 1 gene during gastric carcinogenesis. Frontiers in Oncology, 10, 604747.
16. Mosca, M., Hong, J., Hadeler, E., Hakimi, M., Liao, W., & Bhutani, T. (2021). The role of IL-17 cytokines in psoriasis. ImmunoTargets and Therapy, 409-418.
17. Pușcaș, A. D., Cătană, A., Pușcaș, C., Roman, I. I., Vornicescu, C., Șomlea, M., & Orăsan, R. I. (2019). Psoriasis: Association of interleukin-17 gene polymorphisms with severity and response to treatment. Experimental and Therapeutic Medicine, 18(2), 875-880.
18. Mousa, H. M., & Hassan, A. G. (2020). Interleukin-17 serum levels as a vital indicator of psoriatic Iraqi patients in Thi-Qar Province. EurAsian Journal of BioSciences, 14, 1101-1104.

19. Al-Thwani, A. N. (2021). Evaluation of IL-17, IL-18 and IL-22 as Vital indicators of Iraqi Patients with Psoriasis. Iraqi journal of biotechnology, 1(20).
20. Schön, M. P., & Erpenbeck, L. (2018). The interleukin-23/interleukin-17 axis links adaptive and innate immunity in psoriasis. Frontiers in immunology, 9, 1323.
21. Ahmed, A. S., Al-Najjar, A. H., Alshalahi, H., Altowayan, W. M., & Elgharabawy, R. M. (2021). Clinical Significance of Helicobacter Pylori Infection on Psoriasis Severity. Journal of Interferon & Cytokine Research, 41(2), 44-51.
22. Dewayani, A., Fauzia, K. A., Alfaray, R. I., Waskito, L. A., Doohan, D., Rezkitha, Y. A. A., ... & Miftahussurur, M. (2021). The roles of IL-17, IL-21, and IL-23 in the Helicobacter pylori infection and gastrointestinal inflammation: a review. Toxins, 13(5), 315.
23. Mercurio, L., Morelli, M., Scarponi, C., Eisenmesser, E. Z., Doti, N., Pagnanelli, G., ... & Madonna, S. (2018). IL-38 has an anti-inflammatory action in psoriasis and its expression correlates with disease severity and therapeutic response to anti-IL-17A treatment. Cell death & disease, 9(11), 1104.
24. Han, Y., Mora, J., Huard, A., da Silva, P., Wiechmann, S., Putyrski, M., ... & Weigert, A. (2019). IL-38 ameliorates skin inflammation and limits IL-17 production from γδ T cells. Cell reports, 27(3), 835-846.
25. Lowes, M. A., Suarez-Farinas, M., & Krueger, J. G. (2014). Immunology of psoriasis. Annual review of immunology, 32, 227-255.
26. Xie, L., Huang, Z., Li, H., Liu, X., Zheng, S. G., & Su, W. (2019). IL-38: a new player in inflammatory autoimmune disorders. Biomolecules, 9(8), 345.