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Assessment a Novel Iron Status Biomarker (Hepcidin) among Patients with Psoriasis

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Abstract

Background : Psoriasis is a skin disease caused by an overactive immune system, affecting up to 3% of the population. It is characterized by chronic inflammation and excessive growth of skin cells due to interactions between immune cells and skin cells. Recently, researchers have observed connections between psoriasis and other systemic diseases, suggesting that skin inflammation may be related to inflammation throughout the body. Hepcidin is a peptide hormone transcription in the hepatocytes, is a significant iron homeostasis regulator that was just recently identified. The interaction between positive and negative stimulation is crucial in defining the net levels of Hepcidin, even though the iron store and inflammatory regulation activate Hepcidin and hypoxia, anemia, excessive iron load, and enhanced erythropoiesis all adversely control Hepcidin expression.

Methods : In a case-control study, 120 psoriasis patients and 120 seemingly healthy controls matched for age and sex were included., ages ranging from 18-60 years, who attended Al-Nasiriya-Teaching Hospital specialized dermatology and venereology consultant from December 2023 to June 2024. five milliliters of blood were drawn via venin puncture. According to the manufacturer's instructions, Hepcidin in serum will be measured using a sandwich enzyme-linked immunosorbent assay (ELISA) kit (Sunlong, China, REF SL0868Hu). and serum hs CRP using routine standard method.

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Results :The results indicate that the level of serum Hepcidin significantly decreased (P<0.05).), and higher significantly increase in hs-CRP (P<0.001) in psoriatic patients as compared to the control subjects, also indicate that the mean hsCRP value is statistically significantly higher (P<0.001), in patients with moderate to severe psoriasis than in patients with mild psoriasis.

Conclusions Psoriasis was associated with significantly decreased serum hepcidin levels compared to control subjects, suggesting that Hepcidin may be involved in the disturbed iron status reflecting the influence of psoriasis etiologies on Hepcidin expression. And also proposed that serum hsCRP was an effective psoriasis severity marker that might be applied to monitor the disease's progression and, used together with PASI, as a worldwide measure of disease severity.

Keywords: Hepcidin, High sensitive CRP, Psoriasis

Introduction : Psoriasis is an inflammatory dermatosis that is immune-mediated, constantly, and is characterized by the development of erythematous plaques that are coated in white scales, occasionally causing pruritus, and primarily found on the extensor areas (chest, elbows, knees, and scalp). [1]

Hepcidin is a peptide hormone made up of 25 amino acids. It was first discovered in urine and plasma in 2000 and 2001, respectively [2] [3]. The hepcidin gene (HAMP; OMIM 606464) found on chromosome 19q13.12 encodes an 84 amino acid precursor protein. Through enzymatic cleavage, the full-length pre-prohepcidin is exported from the cytoplasm, releasing a 64-amino prohepcidin peptide into the extracellular space [4].

Next, it seems that a protein convertase similar to furin may remove the 39 aa proregion peptide after translation [3]. According to research, the 20aa iso-form of hepcidin-25 can be found in human serum and urine, while the 22 aa iso-form is only detected in urine [5].

It is interesting to note that hepcidin, a crucial regulator of iron status, is predominantly synthesized by hepatocytes. Hepcidin is a substance that prevents iron from entering the plasma through three different pathways. These pathways are: 1) through the intestines, 2) from the liver's stored iron, and 3) via the release of macrophages that recycle iron from aged red blood cells. [6]

The assay for high-sensitivity C-reactive protein (hsCRP) quantifies very low levels of CRP. The blood's cutoff threshold was less than 10 mg/L. Low amounts of C-reactive protein can be precisely measured by the high-sensitivity CRP (hsCRP) test to determine low, prolonged levels of inflammation. Previous research has linked CRP to psoriasis as a predictive disease marker in psoriasis. [7][8]

suggested to be indicators of inflammation in several conditions, including psoriasis. [9] Elevated CRP levels are additionally associated with more rapid disease development and a greater symptom burden in patients. [10].

Methodology : This questionnaire-based retrospective study was carried out at Al-Nasiriya Teaching Hospital from December 2023 to June 2024, with 240 subjects in total, following the local Institutional Review Board's approval of the study protocol. The participants were separated into two distinct groups: 120 patients with psoriasis as cases and 120 healthy persons matched for both age and sex with cases. The same investigator used the Psoriasis Area and Severity Index (PASI) score to determine the severity of psoriasis in each of the 120 cases. A disease with a PASI < 7 was deemed mild, a PASI 7–12 was regarded intermediate, and a PASI > 12 was deemed severe.

Psoriatic patients were presented to the dermatology and venereology consultant at Al-Nasiriya Teaching Hospital for medical examination. In order to measure the serum, blood samples were obtained to measure C-reactive protein (CRP) measurement using the standard routine method and serum hepcidin level, using an enzyme-linked immunosorbent assay (ELISA) kit, according to the manufacturer's instructions (Sunlong, China, REF SL0868Hu).

Statistical Analysis: The means ± standard deviation (SD) of the data are displayed. The t-test and the chi-square test were used to compare the means of the groups. Additionally, correlations between the variables were identified. A P-value of less than 0.05 was deemed significant in statistical terms. SPSS for Windows (version 26, USA) was used for all statistical analyses.

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Results:

Table (3-1) shows no significant differences in sex, age, BMI and residence in the two studied groups ($p > 0.05$).

Table (1) Socio-demographic characteristics of the population study

Parameters		Control Group (N=120) Mean ± SD	Patients Group (N=120) Mean ± SD	P. Value
Age (Years)		33.27 ± 11.40	33.22 ± 11.61	0.97 NS*
BMI (Kg/M^2)		22.97 ± 1.56	23.03 ± 1.70	0.77 NS*
Sex	Male	67 (55.8%)	67 (55.8%)	1.00 NS**
	Female	53 (44.2%)	53 (44.2%)	
Geographic Area	Urban	74 (61.7%)	74 (61.7%)	1.00 NS**
	Rural	46 (38.3 %)	46 (38.3 %)	

* t- test. ** Chi-square test. NS: Non-significant at P>0.05; BMI: Body mass index

In **Table (2)** there were statistically highly significant increase in the level of hs CRP ($P < 0.001$), significant decrease in the level of Hepcidin ($P < 0.01$) in patients group related to the control subjects.

Table (2) Comparison of Study parameters among control and patients with psoriasis

Parameters	Control Group (N=120) Mean ± SD	Patients Group (N=120) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	29.01 ± 10.62	24.49 ± 9.83	<0.01
Hscrp (Mg/Dl)	0.99 ± 0.63	7.06 ± 5.48	<0.001

High significance P<0.001, significance P<0.05

Table (3), reveals that the level of hs CRP was highly significantly increase (P<0.001), Hepcidin was non- significance decrease (P>0.05) in patient's male compared to healthy males.

Also, the table shows serum CRP was high significantly increase(P<0.001), Hepcidin were significance decrease (P<0.05) in patients female compared to healthy females.

Table (3) Comparison of parameters studied in male and female in patients and control subjects.

Parameters		Control Group (N=120) Mean ± SD	Patients Group (N=120) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	M N=67	26.50 ± 9.88	23.51 ± 9.36	0.07
	F N =53	32.20 ± 10.77	25.75 ± 10.35	<0.01
Hscrp (Mg/Dl)	M N=67	1.19 ± 0.60	7.43 ± 5.51	<0.001
	F N =53	0.98 ± 0.61	6.68 ± 5.48	<0.001

M=male, **F**= female, High significance P<0.001, significance P<0.05, non-significance P>0.05

Table (4) display non-significant changes in each of hs CRP and Hepcidin in male and female psoriatic patients (P>0.05)

Table (4) the comparison of all parameters studied in psoriatic male and female.

Parameters	Male(N=67) Mean ± SD	Female (N=53) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	23.51 ± 9.36	25.75 ± 10.35	0.22
Hscrp (Mg/Dl)	7.43 ± 5.51	6.68 ± 5.48	0.54

Non- Significant P>0.05

Table (5) shows highly significantly increase in hs CRP (P<0.001) in 3 age group in patient compared to control subjects.

Hepcidin was significantly decrease in age group (18-35) and non-significantly change in age groups (>52) and (36-52) (P>0.05), in patient compared to the control subjects.

Table (5) Study parameters among control and patients with psoriasis according to age groups.

Parameters		Control Group (N=120) Mean ± SD	Patients Group (N=120) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	18-35 N =74	28.47 ± 10.98	23.22 ± 9.70	<0.01
	36-52 N=36	29.14 ± 10.18	25.97 ± 10.01	0.17
	>52 N= 10	33.82 ± 9.31	29.63 ± 8.62	0.38
Hscrp (Mg/Dl)	18-35 N =74	0.97 ± 0.62	6.79 ± 5.40	<0.001
	36-52 N =36	1.27 ± 0.60	7.22 ± 5.74	<0.001
	>52 N= 10	1.21 ± 0.29	8.35 ± 5.66	<0.001

High significance P<0.001, significance P<0.05, non-significance P>0.05

Table (6) showed non- significant changes (P > 0.05) in levels hs CRP and Hepcidin in negative and positive family history psoriatic patients.

Table (6) Study the effect of family history in studied group.

Parameters	Negative (N= 80) Mean ± SD	Positive (N=40) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	23.97 ± 9.96	25.40 ± 9.68	0.46
Hscrp (Mg/Dl)	7.02 ± 5.36	7.01 ± 5.96	0.99

Non-significant P> 0.05

Table (7) showed non- significant changes in each of hs CRP and Hepcidin in 3 duration disease groups (P >0.05).

Table (7) The effect of duration disease groups among patient's parameters

Parameters	(1-10) Years (N=69) Mean ± SD	(11-20) Years (N=41) Mean ± SD	(>21) (N=10) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	23.37 ± 10.04	25.42 ± 9.77	28.78 ± 7.51	0.22
Hscrp (Mg/Dl)	6.85 ± 5.58	7.22 ± 5.28	8.06 ± 6.32	0.86

Non-Significant P> 0.05

Table (8) showed highly significant changes in the level hsCRP (P <0.001), the table also showed non- significant changes in level Hepcidin in 3 classes of disease severity groups (P >0.05).

Table (8) The effect severity groups among patient's parameters.

Parameters	Mild (N=53) Mean ± SD	Moderate (N=26) Mean ± SD	Severe (N=41) Mean ± SD	P. Value
Hepcidin (Ng/Ml)	22.47 ± 9.89	24.38 ± 10.70	27.13 ± 8.76	0.07
Hscrp (Mg/Dl)	3.99 ± 2.70	6.48 ± 3.73	10.21 ± 6.36	<0.001

Highly significant P <0.001, non-Significant P> 0.05

Table (9) showed non-significant changes in each of the levels of hsCRP and Hepcidin in the types of the disease (P >0.05).

Table (9) Comparison parameters among patients with psoriasis according to type of the disease.

Parameters	Plaque(n=92) Mean ± SD	Guttate (n=28) Mean ± SD	P. value
Hepcidin (ng/ml)	23.59 ± 10.44	27.56 ± 6.67	0.06
hsCRP (mg/dl)	6.37 ± 5.13	8.91 ± 6.06	0.06

Non-Significant P> 0.05

Table (10) showed non-significant positive correlation of Hepcidin with hs CRP (P >0.05).

Table (10) The correlation of biomarker in the study

Parameter		hsCRP
Hepcidin	Pearson Correlation	.177
	P. value	.117

Non-Significant P> 0.05

Discussion : Psoriasis is a dermatological affliction that is characterized by abnormalities in the proliferation of epidermal keratinocytes. The disorder is predominantly immune-mediated with other factors, although vascular perturbations, environmental triggers, genetic predispositions, and others all play significant etiological and prognostic roles. [11]

Regarding socio-demographic characteristics of study groups Shows non-statistically significant differences in gender, age, and body mass index in psoriatic patients compared to the healthy control (P>0.05). More than half of the patients were males (55.8 %).

Different health behaviors, such as nutrition, exercise, smoking, or alcohol intake, and social limitations for women can account for the observed discrepancies in incidence and prevalence between genders.

The results show a significant decrease in Hepcidin in the patients group compared to the healthy control subjects ($P < 0.05$). In agreement with the study conducted by El-Rifaie, A. et al [12] A study conducted by Arafat, E. S. et al [13], found a statistically highly significant increase ($P < 0.001$) in serum Hepcidin levels in patients with psoriatic compared with the control subjects, dis-agreement with our results.

The study shows, a non-significant changes ($P>0.05$) in serum Hepcidin levels about family history of the disease, and duration of the, according to research done

by El-Rifaie, A. et al [12]. in agreement with our study.

A study by Ponikowska, M. et al [14], reveled a significant decrease in Hepcidin in the patient's group compared to the control groups, in agreement with our study ($P < 0.05$).

The signal transduction pathway that IL-6 employs to regulate Hepcidin has been the subject of multiple recent articles. Numerous investigations have shown that interleukin (IL-6) is a major activator of Hepcidin production during inflammation. [15] The explanation for this observation might be the ability of biological therapy tumor necrosis factor (TNF) inhibitions to reduce IL-6, which may be caused in partly by a reduction in IL6 production, TNF-α inhibitors' suppression of serum Hepcidin in psoriatic patients may be indirectly brought about by a decrease in IL-6 production. [16]

The data indicate, a higher significant hs CRP ($P < 0.001$). Agreement with Kural, B. V., et al [17] who showed that the patients with psoriasis have significantly higher hsCRP in psoriatic patient compared to the healthy control subjects ($P < 0.001$).
Also, the results indicate that the mean hs CRP value is statistically highly significant increase in patients with moderate to severe psoriasis than in patients with mild psoriasis ($P<0.001$), in agreement with the study, Jain, K., et al [18], and Agravatt et al [19].

This might be explained by the fact that the C-reactive protein is the most sensitive indicator of inflammation. The degree and severity of tissue damage are correlated with an increase in inflammatory intensity. [20] Moreover higher CRP levels are linked to patients undergoing more symptoms and accelerated disease progress. [10]

The data indicate non –significant correlation positively Hepcidin with hs CRP ($P>0.05$). This explain may be CRP is activated by IL-6 and participates in the acute-phase response, it can be used as a stand-in indicator of inflammation. Hepcidin is regarded as an acute-phase reactant as well, though. The levels of IL-6, although strongly linked with both clinical activation and Hepcidin levels, we did not find a relationship between CRP and these levels. [21]

Conclusion: We can conclude from the result that the significant decrease in serum Hepcidin concentration($P<0.05$), may be due to the effect of psoriasis pathogenesis and biological therapy on Hepcidin expression in patients, hsCRP a significant increase ($P<0.001$) This was observed in

psoriatic patient compared with healthy control subjects. Along with PASI, hsCRP is a helpful indicator of the severity of psoriasis that can be employed to monitor the disease's progression.

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