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Evaluation of serum levels of heat shock protein 70 in patients with psoriasis in Basra, Iraq

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Abstract

Introduction: Psoriasis is a chronic, non-infectious skin disease that affects people of all ages and has no sex preference, which is caused by environmental stressors involving skin cells, immunocytes, and several biologic signaling molecules. Psoriasis has been linked to psychological, metabolic, arthritic, and cardiovascular complications. Heat shock protein 70 (HSP70) is considered the most protective member of the HSP family. HSP70 can regulate protein homeostasis, minimize stress-induced denaturation and aggregation of intracellular proteins and operate as a protective factor in tissue damage. This study aimed to investigate the serum level of HSP70 in patients with psoriasis to assess whether there is an association of HSP70 with psoriasis and to assess the effects of age, gender, body mass index (BMI), waist circumference, and disease duration on the serum level of HSP70.

Material and methods: This was a case-control study which recruited 98 patients with psoriasis and 81 apparently healthy age- and sex-matched individuals as controls. Blood samples were collected via venipuncture (5 ml) to estimate the HSP70, random blood sugar, liver enzymes, lipid profile, and complete blood count.

Results: The results revealed that the level of HSP70 was significantly higher in psoriasis patients compared to the control group (p-value < 0.05). The level of HSP70 showed a significant association with gender, but a non-significant positive correlation with duration of psoriasis. The level of HSP70 showed a non-significant negative correlation with age, BMI and waist circumference.

Conclusions: The study suggested that HSP70 may have a potential role in the pathophysiology of psoriasis and may help to explain the mechanisms behind the development and treatment of psoriatic lesions with different severity.

Key words: psoriasis, heat shock protein 70, heat shock proteins.

Introduction

Psoriasis is a long-term skin condition that is not infectious and can develop in people of all ages and genders [1]. The prevalence of psoriasis can range 0–1.8% in various populations [2]. Although psoriasis can impact individuals across all age groups, it is more frequently observed in people who are under 29 years old [3]. Psoriasis is believed to be attributable to a combination of genetic, epigenetic, and environmental factors. These factors contribute to abnormal interactions between immune cells, cytokines (proteins involved in cell signaling), and skin cells, leading to the development of psoriasis [4]. Heat shock proteins (HSPs) are ubiquitous and well-described proteins, with sizes varying from 10 to over 100 kDa, and these molecules can be found in various cellular compartments [5]. Heat shock proteins are categorized into six primary families: HSP100, HSP90, HSP70, HSP60, HSP40 and small HSP. These classifications are based on factors such as their molecular weight, function, and structure [6]. Heat shock proteins have an important function in safeguarding cells against inflammation, apoptosis, and oxidative stress. They also assist in protein refolding and maintaining proteostasis during challenging circumstances [7].

Their functions have recently been improved to involve immune response modulation, cell signaling control [8], and other chronic diseases such as psoriasis [9]. Heat shock protein 70 (HSP70) is the most protective member of the HSP family [10]. HSP70 can reduce stress, stimulate denaturation and aggregation of intracellular proteins, work as a protective factor in tissue damage, play essential roles in dendritic cell activation and maturation, and reflect systemic inflammation and oxidative stress [11, 12]. The effect of HSP70 on keratinocytes may possibly result in a decrease in HSP70 production, which may be associated with an increase in susceptibility to heat-induced death of old keratinocytes [13].

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This study aimed to investigate the serum level of HSP70 in patients with psoriasis to assess whether there is an association of HSP70 with psoriasis and to assess the effect of age, gender, body mass index (BMI), waist circumference (WC), and disease duration on the serum level of HSP70.

Materials and methods

Study population

A total of 179 subjects were included in this questionnaire-based retrospective study, which was conducted from December 2022 to March 2023 at Al-Basrah Teaching Hospital, after approval of the study protocol by the local Institutional Review Board. The study divided participants into two main groups: 98 patients with psoriasis as cases and 81 healthy individuals matched for both age and sex with cases. Psoriasis patients attended the dermatology clinic in Al-Basrah Teaching Hospital for medical consultation or routine check-ups. Exclusion criteria comprised diabetic mellitus, liver diseases, renal diseases, tumors and congestive heart failure. Each participant completed a thorough questionnaire comprising demographic data (age, gender, type of treatment, whether topical, systemic [methotrexate/biologic], or phototherapy, and duration of psoriasis).

Anthropometric parameters

During the morning, the researchers measured the body weight, height, and WC of each participant.

Sample collection

Five milliliters of venous blood were collected via venipuncture and divided into two parts: 2 ml were placed in an anticoagulant tube (K3EDTA) to be utilized in the analysis of complete blood count. The remaining blood was placed in a gel tube without any anticoagulant and containing a gel and clot stimulator. After centrifugation the sera were transferred into two separate Eppendorf tubes. One of these tubes was utilized for routine biochemical tests such as random blood glucose (RBS), blood urea, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total serum bilirubin (TSB), and direct bilirubin. The other Eppendorf tube was stored in a deep freezer at a temperature of –30°C for the subsequent estimation of HSP70.

Laboratory investigation

Random blood glucose, blood urea, TC, TG, HDL-C, AST, ALT, and TSB were measured by automated colorimetric methods using kits provided by Roche Diagnostics, Germany. Low-density lipoprotein cholesterol (LDL-C) was measured by Friedewald's equation. Complete blood count was measured by the Sysmex XT-1800i automatic hematological analyzer provided by Kokusan, Japan. To measure the level of HSP70 in the serum a sandwich enzyme-linked immunosorbent assay (ELISA) kit was used, based on the instructions of the manufacturer (Sunlong, China, REF SL0831Hu). Absorbance was measured at 450 nm, and a standard curve was constructed from the known dilution of HSP70. Results were compared with the standard curve, and the detection range was 0.8–40 ng/ml. The inter-assay precision was less than 12%, while intra-assay precision was less than 10%.

Statistical analysis

Taking the prevalence of psoriasis from a previous study [14], a sample size of 98 was reached (by using the formula Z2P (1 – P)/E2. Z is 1.96, P is 0.98, and E is allowable error) with absolute precision taken at 2%. In this study, the program SPSS Statistics version 23 was employed for data analysis. The data were presented using mean ±standard deviation and percentages. To compare continuous data between two groups we utilized the independent Student *t*-test, while to analyze categorical data we utilized the χ^2 test. Pearson correlation was used to assess the correlation coefficient (r). A p-value of less than 0.05 was considered to indicate statistical significance.

Results

The participants' demographic, clinical, and biochemical data are shown in Table 1. There were no significant differences between the patients and the controls regarding age, gender, BMI, WC, RBS, TC, TG, HDL, LDL, TSB, white blood cells, and platelets ($p > 0.05$). More than half of the participants were male (59.2% and 56.8% for patients and controls, respectively). There was a significant difference between the psoriasis patients and the controls in blood urea, ALT, AST, and hemoglobin ($p < 0.05$). The mean value of serum HSP70 was significantly higher in patients with psoriasis as compared controls (3.31 ±1.92 vs. 2.57 ±1.52 ng/ml; $p < 0.05$).

Table 2 presents the level of HSP70 among patients and controls with respect to age and sex. The results of this study revealed that the mean value of serum HSP70 decreased with the age of participants, although the association was not statistically significant. Additionally, the mean HSP70 levels in patients with psoriasis were higher in comparison to controls in similar age groups, being significantly higher among the age groups 26–40 and 41–55 years ($p < 0.05$).

With respect to sex we observed that the mean HSP70 level was significantly higher in female patients with

Table 1. Demographic, clinical, and biochemical data of the participants

Parameters	Controls, *n* = 81	Cases, *n* = 98	*p*-value*
Age (years)	32.62 ±10.64	34.62 ±12.71	NS**
Gender, *n* (%)			
Male	46 (56.8)	58 (59.2)	NS**
Female	35 (43.2)	40 (40.8)	
BMI [kg/m^2]	28.65 ±6.05	29.19 ±3.10	NS**
Duration of disease (years)	–	10.44 ±8.56	–
Random blood sugar [mg/dl]	103.20 ±12.01	101.90 ±16.87	NS**
Urea [mg/dl]	26.40 ±4.77	23.05 ±6.29	< 0.05**
Serum TC [mg/dl]	175.24 ±38.31	180.62 ±42.76	NS**
TG [mg/dl]	141.23 ±74.80	145.57 ±67.48	NS**
HDL-C [mg/dl]	50.77 ±12.81	54.14 ±20.15	NS**
LDL-C [mg/dl]	96.22 ±39.27	96.88 ±37.29	NS**
AST [U/l]	22.35 ±7.09	25.84 ±11.33	< 0.05**
ALT [U/l]	20.10 ±8.59	25.28 ±12.65	< 0.05**
TSB [mg/dl]	0.681 ±0.17	0.76 ±0.34	NS**
HSP70 [ng/ml]	2.57 ±1.52	3.31 ±1.92	< 0.05**
HGB [mg/dl]	14.13 ±1.67	12.97 ±1.77	< 0.05**
WBC [10^3/µl]	7.38 ±2.23	7.52 ±2.66	NS**
Platelets [10^3/µl]	297.23 ±53.65	321.32 ±39.08	NS**

ALT – alanine aminotransferase, AST – aspartate aminotransferase, BMI – body mass index, HDL-C – high-density lipoprotein cholesterol, HGB – hemoglobin, HSP70 – heat shock protein 70, LDL-C – low-density lipoprotein cholesterol, TC – total cholesterol, TG – triglyceride, TSB – total serum bilirubin, WBC – white blood cells
* *p* – level of significance of difference between cases and controls
** Student *t*-test
Data are presented as mean ±standard deviation or percent.

Table 2. Distribution of heat shock protein 70 of the study population according to age and sex

Parameters	HSP70 (mean±SD) [ng/ml]		*p*-value*
	Controls	Patients	
Age (years)			
10–25	3.39 ±1.44	3.53 ±2.39	NS
26–40	2.27 ±1.43	3.36 ±2.09	< 0.05
41–55	2.31 ±1.45	3.24 ±1.05	< 0.05
≥ 56	0.85 ±0.14	2.20 ±0.17	NS
Gender			
Male	2.61 ±1.60	2.93 ±1.25	NS
Female	2.53 ±1.41	3.86 ±2.51	< 0.05

HSP70 – heat shock protein 70, SD – standard deviation
* Level of significance of difference between cases and controls Student *t*-test

psoriasis as compared with controls (3.86 ±2.51 ng/ml and 2.53 ±1.41 ng/ml, respectively) ($p < 0.05$).

Also the results of this study revealed that the mean value of HSP70 was higher in patients with psoriasis than in the control group in overweight and obese subjects (Table 3), the difference only being statistically significant among overweight subjects ($p < 0.05$). Regarding WC, the mean value of HSP70 was higher in patients than controls, with no significant difference in males ($p > 0.05$), while in females, there was a significant difference among those with central obesity > 88 cm ($p < 0.05$).

With regard to duration of disease, the mean serum HSP70 level was higher in individuals with disease duration ≤ 5 years as compared with those with duration of more than 5 years but without statistical significance ($p > 0.05$) (Table 4).

There was a significant association between serum HSP70 and gender, while there were non-significant negative correlations of serum HSP70 with age, BMI, and WC in all studied populations (Table 5).

Discussion

Psoriasis, a skin disease caused by immune system dysfunction, is linked to various other conditions such as psoriatic arthritis, cardiovascular and metabolic diseases, and mental health issues. This makes it a global health concern and a major economic burden [15]. The results of the present study showed that more than 66% of the cases in this study were among the age groups 26–55 years; this is consistent with the finding of another study [16]. The study found that more than half of the patients were male (59.2%). The high proportion of males in this study could be attributed to social restrictions (for females) and the differences in health

Table 3. Distribution of heat shock protein 70 of the study population according to body mass index and white blood cells

Parameters	HSP70 (mean ±SD) [ng/ml]		*p*-value*
	Controls, *n* = 81	Patients, *n* = 98	
	BMI [kg/m^2]		
Normal weight 18.5–24.9	3.79 ±2.12	3.12 ±1.41	NS
Overweight 25–29.9	2.22 ±1.33	3.47 ±2.07	< 0.05
Obese ≥ 30	2.84 ±1.52	3.31 ±2.15	NS
	WC [cm]		
Male			
≤ 102	2.78 ±1.56	2.66 ±1.27	NS
> 102	2.54 ± 1.64	3.18 ±1.21	NS
Female			
≤ 88	3.95 ±2.43	3.45 ±1.37	NS
> 88	2.39 ±1.26	4.06 ±2.92	< 0.05

BMI – body mass index, HSP70 – heat shock protein 70, SD – standard deviation, WC – waist circumference
* Level of significance of difference between cases and controls
Student *t*-test

behaviors (e.g. diet, exercise, smoking or alcohol consumption) are among the reasons for the differences in the incidence and prevalence observed between the genders. Also this study revealed that the majority of the patients were obese or overweight. These observations may also support mechanistic research on the relationship between obesity and psoriasis, as well as the evaluation of the role of weight loss in the management of psoriasis [17].

The results of the current study showed that the mean value of serum HSP70 was significantly higher in patients with psoriasis than in controls ($p < 0.05$). Similar results have also been obtained by several other studies [18–21]. In contrast, Bayramgürler *et al*. [22] reported a lower HSP70 level in patients compared to controls. It was concluded that HSP70 may play an important role in the etiology of psoriasis; however, the possibility of its up-regulation secondary to inflammation could not be ignored [23]. Psoriasis is a genetically determined skin disease, probably initiated by hyperactivity of the triggered state of otherwise dormant cutaneous innate immunity [24]. In general, HSPs have an important role in safeguarding cells against inflammation, apoptosis, and oxidative stress [7]. Their functions have recently been proved to involve immune response modulation and cell signaling control [8] in chronic diseases such as psoriasis [9]. Recognition of the potential contribution of HSP70 in the pathophysiology of psoriasis may help explain the mechanisms behind the development and treatment of psoriatic lesions of different severity [25].

The strength of the study is that it took an age range of 13–71 years, and this covers most of the ages affected by psoriasis in both sexes. Among the limitations faced in the study were the expensive kits and the limited time for the study. It would be advisable for larger samples to be taken in the future.

Table 4. Distribution of HSP70 according to duration of psoriasis

Parameters	HSP70 (mean ±SD) [ng/ml]	*p*-value*
Duration of disease		
≤ 5 years	3.40 ±2.03	NS
> 5 years	3.24 ±1.85	

HSP70 – heat shock protein 70, SD – standard deviation
* Level of significance
Student *t*-test

Table 5. Pearson correlation of heat shock protein 70 levels with other variables of the study

Parameters	HSP70 [ng/ml]	
	Correlation coefficient	*p*-value
Age	–0.122	0.23
Gender	0.244*	< 0.05
Duration of psoriasis	0.108	0.29
BMI	–0.016	0.87
WC	–0.024	0.81

BMI – body mass index, HSP70 – heat shock protein 70, WC – waist circumference
* Correlation is significant at the 0.05 level (2-tailed).

Conclusions

The main finding of the current study was that the serum HSP70 concentration was significantly higher in patients with psoriasis than in apparently healthy controls. The results demonstrate that there was an increase in HSP70 in patients with psoriasis, which has a significant role in the development of psoriasis. A significant association of HSP70 levels with gender was observed in the present study. The HSP70 levels showed a non-significant negative correlation with age. The study found that in overweight and obese individuals, the level of HSP70 was higher and there was

a non-significant negative correlation with BMI. This might suggest that obesity with all its complications could be one of the causes of the elevation of HSP70.

Disclosures

1. Participants were included in this study after approval (No. 7/39/5231 dated 7.11.2022) from the Ethics Committee of Al-Basrah Medical University and after informed consent following the Helsinki Declaration from the participants themselves and their guardians.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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