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Original Article

Correlation between Serum Heat Shock Protein–27 (HSP–27) Levels with Facial Skin Aging

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Abstract

Background Facial skin aging is influenced by intrinsic and extrinsic factors, particularly ultraviolet (UV) radiation, which increases oxidative stress and cellular damage. Heat Shock Protein-27 (HSP-27) helps protect cells from oxidative damage. However, studies examining the relationship between serum HSP-27 levels and facial skin aging remain limited in this population.

Objective This study aimed to analyze the relationship between serum HSP-27 levels and facial skin aging.

Methods Eighty subjects were included, consisting of 40 subjects aged 20-40 years with facial skin aging and 40 control subjects aged 18-25 years without signs of facial skin aging. Subjects were selected using consecutive sampling. Facial skin aging was assessed using the Dermoscopic Photoaging Scale (DPAS), while serum HSP-27 levels were measured using the Enzyme-Linked Immunosorbent Assay (ELISA).

Results Mean serum HSP-27 levels were lower in the facial skin aging group than in the control group (17.26±2.79 ng/mL vs. 52.72±24.50 ng/mL). The Mann-Whitney test showed a significant difference between groups (P<.001).

Conclusion Serum HSP-27 levels were significantly associated with facial skin aging, with lower levels observed in subjects with facial skin aging. HSP-27 may serve as a supporting biomarker and warrants further investigation with larger samples and robust study designs.

Keywords HSP-27; Facial skin aging; Photoaging; Serum, DPAS.

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Introduction

Aging is a physiological process characterized by declining body functions, with the skin being one of its most visible effects.[1,2] Skin aging affects both older and younger individuals, as youthful appearance is considered important for self-confidence and social relationships.[3,4]

Indonesia's equatorial location causes intense year-round sunlight exposure, increasing the risk of UV-induced skin aging.[5] Studies have reported sign of early aging in 18-21 years in Jakarta,[6] while Jusuf *et al*. found that in Medan was most common in 30-39 years of age.[7]

Skin aging occurs through intrinsic and extrinsic mechanisms.[8] Intrinsic aging is influenced by genetic, hormonal, and biochemical factors, causing wrinkles, reduced elasticity, and sagging.[9] Extrinsic aging or photoaging is associated with UV exposure,

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smoking, alcohol consumption, malnutrition, and pollution, resulting in roughness, wrinkles, telangiectasis, mottled pigmentation, and skin lesions. Unlike intrinsic aging, extrinsic aging is potentially preventable.[10]

Skin aging can be assessed using Glogau and Fitzpatrick classifications. Glogau classifies photoaging into four severity types, while Fitzpatrick classifies skin into six types based on UV sensitivity and skin tone.[7]

Isik *et al*. developed Dermoscopic Photoaging Scale (DPAS) as an objective method for evaluating photoaging.[11] Jusuf *et al*. reported strong correlations between DPAS and Glogau, and moderate significant correlations between DPAS and Fitzpatrick Skin Type in Medan.[7]

The theory of oxidative stress is considered as the main cause of aging in the skin, as well as the most widely accepted theory.[12,13] Oxidative stress is a widely accepted mechanism of skin aging.[12,13] Reactive Oxygen Species (ROS)-induced damage to deoxyribonucleic acid (DNA) and proteins accumulates with age.[14] UV-induced ROS increases Activator Protein-1 (AP-1) and Matrix Metalloproteinase (MMP) activity, accelerating collagen degradation and skin aging.[15]

The body's cells activate various defense mechanisms to maintain cellular stability and function, including Heat Shock Protein (HSP). HSP–27 acts as a protein "chaperone" that helps maintain protein structure, refold and stabilize proteins, and prevent protein breakdown.[16,17] Aging cells show decreased HSP-27 expression, making them more susceptible to environmental damage and contributing to the aging process.[17]

Studies have shown that HSP-27 expression increases after long-term UVB exposure, reduces oxidative stress caused by free radicals, and plays an important role in immune responses and cellular aging. Therefore, HSP-27 is suspected to play a role in the pathophysiology of skin aging, particularly in relation to facial skin aging.[14,16,18]

The novelty of this study lies in evaluating the relationship between serum HSP-27 levels and facial skin aging in the Indonesian population. Unlike previous studies that mainly examined HSP-27 in inflammation, malignancy, or skin tissue, this study evaluates serum HSP-27 as a systemic biomarker with potential clinical applications. If confirmed by larger and stronger studies, HSP-27 could potentially serve as a noninvasive biomarker for premature skin aging, monitoring anti-aging therapy, and developing targeted therapeutic strategies.

This study has several limitations. The cross-sectional design cannot establish causality and only shows an association between serum HSP-27 levels and facial skin aging. The single-center setting and limited sample size also restrict generalizability. Furthermore, only HSP-27 was evaluated without comparison with other skin-aging biomarkers, such as MMPs, transforming growth factor- β (TGF-β), collagen, elastin, and oxidative stress biomarkers, so the underlying biological mechanisms remain incompletely elucidated.

Methods

This study was an analytical observational study with a cross-sectional design to analyze the relationship or difference between serum HSP-27 levels and facial skin aging status. Variables were measured during one observation period without intervention. Consecutive sampling was used to recruit eligible subjects sequentially until the required sample size was reached. The study included 80 subjects, consisting of 40 subjects with facial skin aging and 40 control subjects, to assess differences in serum HSP-27 levels between the two groups.

The sample size was 80 subjects, consisting of 40 subjects per group. Statistical calculations with α=5%, β=20%, and r=0.49 resulted in a minimum of

30 subjects per group; therefore, 80 subjects were recruited to provide adequate data and anticipate incomplete data.[14] Inclusion criteria were subjects aged 18-40 years, willing to participate, providing informed consent, and categorized as facial skin aging based on DPAS or healthy controls. Exclusion criteria included pregnancy or breastfeeding, active skin inflammation, chronic skin disease, malignancy, systemic inflammatory disease, and autoimmune disease.

Dermoscopy was performed on both cheeks, forehead, and chin under standardized conditions by one trained dermatologist. Consecutive sampling facilitated sequential recruitment but, as a non-probability technique, may limit population representation. DPAS is a validated objective dermoscopic photoaging assessment tool.[11] The study was approved by the Health Research Ethics Committee of Universitas Sumatera Utara (No. 840/KEPK/USU/2025 dated 07.08.2025).

The sample size was determined based on α=5%, β=20%, and a correlation value of r=0.49, resulting in a minimum of 30 subjects per group. To ensure adequate data and anticipate incomplete or unusable data, the sample was increased to 40 subjects per group. Thus, a total of 80 subjects were included, consisting of 40 case subjects and 40 control subjects. This addition was expected to provide more adequate data and maintain the statistical strength of the study.

Discussion

Clinical examination was performed after informed consent under standardized conditions. The face was cleaned and hair secured for clear visualization. Blood sampling procedures, including venipuncture, blood volume, tube type, centrifugation, storage, and transportation, were standardized to maintain sample quality and HSP-27 measurement validity.

Facial skin aging was assessed using DPAS based on 11 binary criteria (0=absent, 1=present) across the left cheek, right cheek, forehead, and chin, with a maximum score of 44. Dermoscopy was performed using the ILLUCO® IDS-1100 Dermoscope, with higher DPAS scores indicating greater facial skin aging.

Serum HSP-27 levels were measured using the ELISA method with HSP-27 ELISA KIT (Cat. No. E7307Hu). Standardized procedures, strict inclusion and exclusion criteria, consecutive sampling, and a control group were used to improve reliability and minimize confounding factors.

The minimum sample size was 30 subjects per group and was increased to 40 subjects in each group (80 total). The case group included subjects aged 20-40 years, while the control group included subjects aged 18-25 years without facial skin aging to obtain a relatively homogeneous population and reduce biological variation due to physiological aging. Conditions potentially affecting HSP-27 or skin aging, including pregnancy, lactation, inflammatory or chronic skin diseases, malignancy, systemic inflammation, infection, and autoimmune diseases, were excluded. Consecutive sampling facilitated sequential recruitment but may limit generalizability.

Extrinsic aging, or photoaging, is caused by external factors that accelerate the aging process of the skin.[19] Exposure to UV rays is the main cause of extrinsic skin aging and contributes as much as 80% to the aging process in the facial area.[15]

Extrinsic aging is a biochemical process influenced by external factors, primarily UV exposure, air pollution, mechanical factors such as muscle tension, and lifestyle changes including diet, sleep habits, and smoking. A typical sign of UV-induced skin aging is the appearance of darker brown spots. Extrinsic aging also increases the risk of developing benign or malignant tumors.[1]

Photoaging is mainly caused by UVA and UVB exposure. UVA penetrates the dermis, while UVB affects the epidermis. UV exposure produces ROS that damage cells and DNA and disrupt TGF-β and

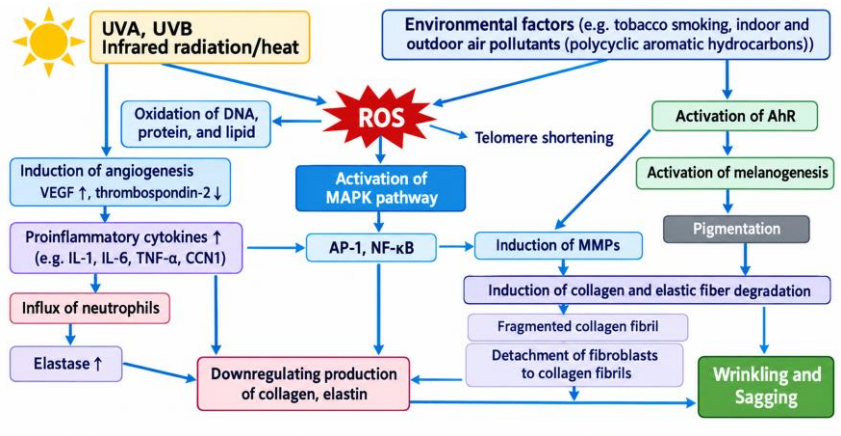


Figure 1 Ultraviolet radiation and external factors affect ROS.[15]



Figure 2 Clinical symptoms of extrinsic aging are characterized by fine and rough wrinkles, yellowish-brown macula, uneven pigmentation, telangiectasia, decreased skin elasticity, xerosis, and dull-looking skin tone.[25]

AP-1, leading to increased MMP expression and collagen breakdown. Prolonged UV exposure causes wrinkles and skin aging **(Figure 1)**.[20]

Clinical symptoms of photoaging include epidermal thickening or atrophy, solar elastosis, irregular collagen structure, dispigmentation, and moderate to severe wrinkles, particularly in the elderly and individuals frequently exposed to UV rays **(Figure 2)**.[21] Research by Jusuf *et al*. found that the most common clinical signs of facial skin aging among various ethnic groups in Medan include yellowish skin discoloration, ephelids/ lentigos, telangiectasis, and superficial wrinkles.[7] Skin aging, especially on the face, affects not only appearance but also psychosocial well-being and self-confidence, while increasing skin care costs and potentially reduces quality of life.[22]

Research shows that occupation, education level, marital status, and number of children can affect facial skin aging through environmental exposure, skin care behavior, parenting burden, stress, and related hormonal and biological mechanisms.[21,23]

Diet and nutrient intake play an important role in skin repair and aging. A healthy and balanced diet provides essential nutrients, oxygen, and water needed for cell regeneration and repair, while nutritional status can influence skin health and the aging process. The ideal diet should meet daily nutritional needs and limit additives such as preservatives, pesticides, food coloring, and artificial flavorings.[24]

This study involved 40 subjects with aging facial skin and 40 subjects without facial skin aging at the Dermatology and Venereology Polyclinic of Prof. Chairuddin Panusunan Lubis Hospital USU Medan, conducted from August to December 2025. All subjects underwent anamnesis, dermatological examination, and blood sampling. The collected data were then statistically analyzed as follows. The characteristics of the research subjects by age in this study are shown in **Table 1**.

As shown in **Table 1**, subjects aged 34-40 years constituted the largest proportion of the facial skin aging group (50%). Facial skin aging at younger ages (18-24 years) is referred to as pre-ageing,

Table 1 Age distribution of subjects in the facial skin aging and control groups

Age	*Aging*	*%*	*Control*	*%*
18 - 25 yrs.	6	15	40	100
26 - 33 yrs.	14	35	0	0
34 - 40 yrs.	20	50	0	0
Total	40	100	40	100

Table 2 Characteristics of facial skin aging subjects and controls by sex.

Gender	*Aging*	*%*	*Control*	*%*
Male	3	7.5	13	32.5
Female	37	92.5	27	67.5
Total	40	100	40	100

Table 3 Relationship between serum HSP–27 levels and facial skin aging.

HSP–27 Serum (ng/mL)	*Group*		*P value*
	Facial Skin Aging	*Control*	
Average ± SD	17.26±2.79	52.72±24.50	
Median	17.45	50.65	<.001*
(Min–Max)	(10-22)	(24.5-97.4)	

which may begin from age 18. Studies report that approximately 10% of women aged 18-24 years develop fine lines, increasing to 37% among women aged 25-34 years.[26] Signs of pre-ageing in Asian populations are generally not visible at age 18 but may emerge in the early 20s due to extrinsic factors such as sleep deprivation, psychological stress, smoking, and unbalanced nutrition. Intrinsic factors begin to appear in the mid-20s and gradually progress into the mid-30s.[26]

The characteristics of the research subjects by gender in this study are shown in **Table 2**.

The results of the study in table 1.2 show that most of the subjects with facial skin aging are females as many as 37 people (92.5%) and males as many as 3 people (7.5%).

Table 3 presents the results of the analysis of the relationship between serum HSP-27 levels and facial skin aging. The figures obtained from the examination of serum HSP-27 levels in the facial skin aging group and the control group were obtained, both of which showed higher serum HSP–27 levels in the control group compared to the facial skin aging group.

The study found a very significant difference in serum HSP–27 levels between the facial skin aging and control groups. The facial skin aging group had lower HSP–27 levels (17.26±2.79 ng/mL; median 17.45 ng/mL) than the control group (52.72±24.5 ng/mL; median 50.65 ng/mL). The Mann-Whitney test showed $p < 0.001$, confirming a statistically significant difference. Thus, lower serum HSP-27 levels are closely associated with facial skin aging.

The results of the data analysis are presented in the form of Box and Whisker plots graphs where the graph describes the form of data distribution, the size of the central tendency and the size of the data distribution **(Figure 3)**.

Overall, aging skin is associated with decreased HSP-27 levels. HSP-27 protects skin cells by stabilizing structural proteins, controlling oxidative stress, and regulating apoptosis and tissue regeneration. Its decline with age contributes to degenerative changes in the skin.[27] Decreased HSP-27 expression in aging skin reduces the ability of cells to counteract oxidative stress, leading to DNA damage, lipid peroxidation, and structural protein degradation, which result in loss of skin suppleness and elasticity.[28] Decreased HSP-27 expression makes skin cells more susceptible to damage and premature death, reducing epidermal regeneration. Consequently, the skin becomes thinner, drier, and more prone to irritation, with decreased collagen density and elasticity that contribute to wrinkles and sagging.[27]

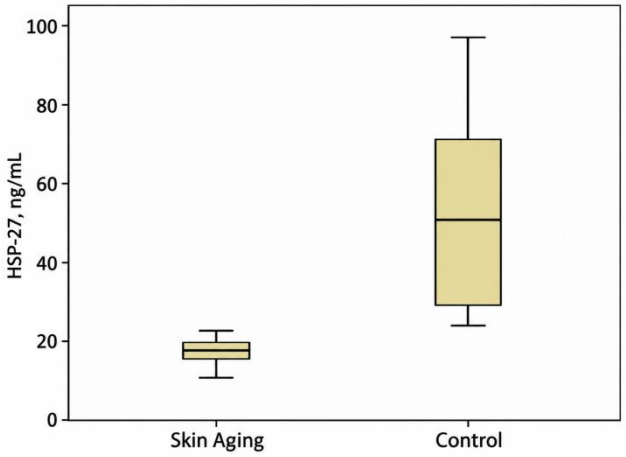


Figure 3 Box and Whisker Plots Graph of HSP–27 Levels in Subject Groups with Facial Skin Aging and Control.

The results showed lower serum HSP-27 levels in the facial skin aging group, with a negative correlation indicating that lower HSP-27 levels were associated with higher facial skin aging scores. This supports HSP-27's role as a cytoprotective protein involved in oxidative stress, inflammation, and apoptosis. However, the weak to moderate correlation suggests that HSP-27 is not the only factor influencing facial skin aging. Despite statistical significance not necessarily indicating a large clinical effect, HSP-27 may have potential as a supporting biomarker for assessing and monitoring skin aging if the association is strong and consistent.

However, the results of this study cannot be generalized directly to the entire community. This is related to the relatively specific characteristics of the research population. The facial skin aging group in the study consisted of subjects aged 20-40 years, while the control group had an age range of 18-25 years. The difference in age range needs to be considered in interpreting the results of the study because age characteristics can be related to the physiological condition of the skin and the aging process.

Although statistical significance does not necessarily indicate a large clinical effect, HSP-27 may have potential as a supporting biomarker for assessing and monitoring skin aging if the association is strong and consistent.

These findings contribute scientific information regarding the relationship between serum HSP-27 and facial skin aging and its potential as a dermatological biomarker. However, generalizability is limited by the specific population, different age ranges, single-center setting, consecutive sampling, and predominance of women in the aging group (92.5%). Therefore, the findings represent empirical evidence within the studied population rather than the wider community. Future studies should use larger and more diverse samples, wider age ranges, multiple centers, and more proportionate demographic characteristics.

Conclusion

Based on the results, there was a significant relationship between serum HSP–27 levels and facial skin aging (P<.001). Subjects with facial skin aging had lower serum HSP-27 levels (17.26±2.79 ng/mL) than the control group (52.72±24.50 ng/mL). Facial skin aging was most commonly found in subjects aged 34-40 years and females.

These findings support the potential role of decreased HSP-27 in the skin aging process and its potential as a supporting biomarker. However, due to the cross-sectional design, single-center setting, consecutive sampling, and limited sample characteristics, causality and broad generalization cannot be established. Further studies with larger samples, multiple research centers, and stronger study designs are needed.

Declaration of patient consent Authors certify that they have obtained all appropriate patient consent.

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Author's contribution

MKM: Substantial contributions to conception and design, acquisition of data, analysis & interpretation of data, drafting the article and revising it critically.

KN, IBP: Substantial contributions to conception and design, acquisition of data, analysis & interpretation of data, drafting the article and revising it critically, and final approval of the version to be published.

Every author has given final approval of the manuscript version to be published and agreed to be accountable for all aspects of the work.

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