УДК 616.5–003.87–02:618.173]:577.121.7.038

Features of oxidant-antioxidant homeostasis in women with climacteric keratoderma

Makurina H.I., Synakh O.K.
Zaporizhzhia State Medical and Pharmaceutical University

Abstract.

Objective: *to assess the features of oxidant-antioxidant homeostasis in women with climacteric keratoderma.*

Materials and methods. *On the basis of the Department of Dermatovenereology and Aesthetic Medicine of the Zaporizhzhia State Medical and Pharmaceutical University, 62 patients with manifestations of palmar-plantar keratoderma were examined. Laboratory studies were conducted based on the Educational and Scientific Medical Laboratory Center with a Vivarium of the Zaporizhzhia State Medical and Pharmaceutical University.*

Results. *When assessing early and late markers of spontaneous protein modification, there is a difference between the studied samples of APH and KPH of (1.76±0.24) a.u./g protein ($p<0.05$) and (1.75±0.28) a.u./g protein ($p<0.05$), respectively. While stimulated oxidation, according to the obtained data, demonstrates an increase and the presence of a difference for APH within (2.52±0.3) a.u./g protein ($p<0.05$), and KPH – (1.53±0.29) a.u./g protein ($p<0.05$). Numerically, the difference in the obtained data when comparing the indicators of the thiol-disulfide system of the main and control groups is (11.61±0.74) μg/ml ($p<0.05$) and (0.46±0.03) μg/ml ($p<0.05$) for GSH and GSSG, respectively. The indicator of their ratio demonstrates a difference within (6.7±0.42) a.u. ($p<0.05$), while superoxide dismutase differs between the studied samples at the level of (7.56±0.88) a.u./mg protein/min ($p<0.05$).*

Conclusions. *The results of the study indicate that in patients with climacteric keratoderma, a statistically significant predominance of both spontaneous and stimulated oxidative modification of protein indicators was established compared to the control group. Such changes occur against the background of a statistically significant decrease in the level of superoxide dismutase, as well as reduced glutathione, which indicate a disruption of adaptive mechanisms and are a manifestation of oxidative stress.*

Keywords: *climacteric changes, oxidative protein modification, antioxidant system, homeostasis, diagnostics*

DOI: 10.33743/2308-1066-2025-3-11-15

Introduction

The skin is the largest organ of the human body and performs important functions, one of the main of which is to protect the body from the external environment. Therefore, changes in skin homeostasis associated with aging increase susceptibility to skin diseases and injuries [4, 24]. Skin aging is a complex process that is attracting increasing attention because it mediates many molecular levels in our body [9]. The structure and function of women's skin are affected by low estrogen levels associated with menopause [6]. Declining estrogen levels during menopause contribute to structural and functional changes in the skin, including decreased collagen production, decreased elasticity, and loss of moisture, leading to dryness and wrinkles [23]. Many consider menopausal skin changes to be merely an aesthetic problem, but they can significantly impact a woman's quality of life [11].

The perimenopausal period and menopause can be associated with many clinical manifestations, such as vasomotor symptoms, genitourinary problems, and additional psychological disorders [10]. Menopause is a difficult period in a woman's life, during which the risk of developing both cardiovascular diseases and metabolic disorders increases, and almost all existing somatic diseases are exacerbated [17]. The increased cardiovascular risk after menopause is explained by the sharp decline in endogenous estrogen levels, suggesting its potential cardioprotective effect in premenopausal women [18,19,21]. Female (reproductive) aging is closely linked to both cardiovascular risk and oxidative stress [20]. Its development, which is an excessive production of reactive oxygen species, is associated with estrogen deficiency [14]. Free radicals can negatively affect various important classes of biological molecules, thereby altering the normal redox status [15]. Usually, the body's oxidation system and antioxidant defense system maintain a dynamic balance. However, when antioxidant and oxidative effects are out of balance, pathological damage occurs [16,18]. Although a healthy body system has its own plan of action to maintain a balance between pro-oxidants and antioxidants with an effective defense system to combat reactive oxygen species [5]. It is the imbalance caused by increased free radical formation and ineffective antioxidant capacity that leads to oxidative stress with subsequent damage to nucleic acids, lipids, and proteins [25]. Considering that the skin is the first to come into contact with the external environment, it is subjected to this pathological process caused by various factors, including psychological stress [3]. Recent studies confirm that women with depression, anxiety, and low self-esteem are in a state of oxidative stress, which may be associated with estrogen depletion [2].

Estrogens significantly influence skin physiology by affecting keratinocytes, fibroblasts, melanocytes, hair follicles, and sebaceous glands, as well as enhancing angiogenesis, wound healing, and immune response. Estrogen deficiency reduces protection against oxidative stress, leading to thinner skin,

decreased collagen levels, reduced elasticity, increased wrinkles, greater dryness, and diminished blood circulation [22]. Of all the organs, the skin most visibly shows signs of aging or dermal changes [8]. With aging, the response to oxidative stress and the detoxification capacity of keratinocytes, fibroblasts, macrophages, and vascular endothelial cells are significantly weakened [4]. Oxidative stress increases with the onset of menopause, as the decline in estrogen levels worsens the antioxidant status [2]. The consequences for the skin associated with low estrogen levels include both a reduction in collagen and elasticity, as well as the development of dermatoses [6]. Dermatoses observed as a result of estrogen deficiency include, in particular, climacteric keratoderma. It is characterized by palmar-plantar hyperkeratosis associated with menopause and more severely affects the feet [6, 12, 13]. This condition was first described by Haaksthausen back in 1934. Although the pathogenesis remains unclear, hormonal changes during menopause have a significant impact on the trophism and normal cellular function of the epidermis and dermis in the palmar-plantar region [7].

Thus, the analysis of literary sources indicates rather limited data on the study of pathogenetic links of climacteric keratoderma, in particular, the study of markers of oxidative stress. The action of multivector factors – endocrine, neurovegetative, and psychoemotional – can potentially have an impact on the shift of the equilibrium state of the organism, including towards the activity of destructive phenomena at the molecular and cellular level. However, a general understanding of the functional capacity of oxidative processes and the corresponding reaction of the antagonistic system of antioxidant protection does not provide a full-fledged extrapolation of the obtained data to narrow-profile nosological categories with a specific, often comorbid, pathogenetic nature. That is why an important stage of this study is the determination not only of markers of oxidative protein modification (OMP), as the most stable indicators of oxidative stress, but also of understanding their interaction with the protection system. Taking into account the obtained results, it may be justified to adjust the treatment strategy for climacteric keratoderma with an emphasis on optimizing antioxidant protection and reducing oxidative stress.

The **aim** of this study is to assess the characteristics of oxidant-antioxidant homeostasis in women with climacteric keratoderma.

Materials and methods

At the Department of Dermatovenereology and Aesthetic Medicine of Zaporizhzhia State Medical and Pharmaceutical University, 62 female patients with manifestations of palmar-plantar keratoderma were examined, forming the main study cohort. The age of the patients ranged from 41 to 67 years, with a mean ± standard error of the mean (M ± m) of (53.1 ± 0.88) years. The duration of menopause, as a key factor in the onset of the pathological skin process in this group, was (4.9 ± 0.5) years, and the mean age at manifestation of this condition was (48.1 ± 0.5) years. The control group consisted mainly of younger individuals, with a mean age of (33.17 ± 0.77) years, ranging from 23 to 39 years.

The levels of OPM were assessed using a spectrophotometric method based on the reaction of protein free radical oxidation products with 2,4-dinitrophenylhydrazine (2,4-DNPH), resulting in the formation of hydrazones. Spectrophotometric measurements were performed at 270 nm for aliphatic hydrazones (APH – aldehydphenylhydrazones) and at 363 nm for carbonyl hydrazones (KPH – ketophenylhydrazones). The values of oxidative protein modification were expressed in arbitrary units per gram of protein (a.u./g protein). Superoxide dismutase (SOD) activity was measured using the method of S. Chevari et al. and expressed in arbitrary units per mg of protein per minute (a.u./mg protein/min). Glutathione was quantified in both its reduced (GSH) and oxidized (GSSG) forms. Concentrations were calculated using a calibration curve and expressed in μg/mL [25]. Laboratory investigations were conducted at the Educational and Scientific Medical Laboratory Center with a Vivarium at Zaporizhzhia State Medical and Pharmaceutical University. All measurements were performed using certified equipment in accordance with validated laboratory protocols. The results were normalized to total protein content and presented in appropriate units of measurement.

The study complies with current ethical standards according to the ICH/GCP guidelines, the Declaration of Helsinki (1964), the Council of Europe's Convention on Human Rights and Biomedicine, as well as the applicable legislative acts of Ukraine. All women provided informed consent to participate in the study.

Statistical analysis of the obtained results was performed on a personal computer using the software. «Statistica® for Windows 13.0» (StatSoft Inc., license No JP Z804I382130ARCN10-J).

Results and Discussion

To assess the processes of oxidative protein modification, APH and KPH were analyzed as early and late markers of pathological imbalance, respectively. The assessment of the levels of spontaneous oxidative protein modification products reflects the body's capacity to renew its protein composition, indicating the overall basal oxidative potential, while stimulated modification reflects the level of adaptive reserves of the antioxidant system in response to stressors. An integrative analysis of spontaneous and stimulated oxidative protein modification provides a more accurate assessment of this balance, influencing the prognosis of the pathological process. In the study of both spontaneous and stimulated OPM, a general increase in levels was observed among patients with climacteric keratoderma belonging to the main group (Table 1). Analyzing the extent of this dynamic, it is important to focus on specific OPM markers as points of concentration of these changes, which may serve as potential targets for further therapeutic intervention. Thus, when assessing early and late markers of spontaneous protein modification, a difference between the studied samples of APH and KPH was observed at (1.76 ± 0.24) a.u./g protein ($p < 0.05$) and (1.75 ± 0.28) a.u./g protein ($p < 0.05$), respectively. Meanwhile, stimulated oxidation also, according to the obtained data, shows an increase and a significant difference for APH within the range of (2.52±0.3) a.u./g protein ($p<0,05$), and KPH –(1.53±0.29) a.u./g protein ($p<0,05$).

Figures 1 and 2 present a comparison of the results of spontaneous protein modification among individuals of reproductive age and patients with menopausal manifestations accompanied by the phenomenon of keratoderma. In percentage terms, the increase in spontaneous markers APH and KPH between the control and main groups was 72.4% ($p < 0.05$) and 89.7% ($p < 0.05$), respectively (Fig. 1). Meanwhile, the markers of stimulated OPM also showed an increase of 65.9% ($p < 0.05$) for APH and 53.7% ($p < 0.05$) for KPH (рис. 2).

Thus, the obtained result indicates an active imbalance in the direction of oxidative stress and the cascade of OMB markers, which indicate a disruption of adaptive mechanisms. It is also worth focusing on the degree of these changes. In general, both spontaneous and stimulated protein oxidation in patients of the

Table 1. Indicators of spontaneous and stimulated oxidative protein modification (OPM) processes in the studied groups (M ± m, 95% – confidence interval)

Indicator, unit of measurement	Main group (n=62)	Control group (n=35)
APH spontaneous, a.u./g protein	4.19±0.171* (3.86–4.52)	2.43±0.168 (2.1–2.76)
APH stimulated, a.u./g protein	6.34±0.251* (5.85–6.83)	3.82± 0.22 (3.39–4.25)
KPH spontaneous, a.u./g protein	3.7±0.262* (3.18–4.22)	1.95±0.114 (1.72–2.18)
KPH stimulated, a.u./g protein	4.38±0.275* (3.84–4.92)	2.85±0.098 (2.66–3.04)

Note: ** indicates a statistically significant difference between the control and main groups (p<0,05)*

Table 2. Indicators of components of antioxidant defense in patients of the main and control groups (M ± m, 95% – confidence interval)

Indicator, unit of measurement	Main group (n=62)	Control group (n=35)
GSH, μg/ml	6.59±0.5* (5.62–7.56)	18.2±0.54 (17.14–19.26)
GSSG, μg/ml	2.38±0.04* (2.3–2.46)	1.92±0.03 (1.85–1.99)
Ratio of reduced to oxidized forms (GSH/GSSG), arbitrary units	2.77± 0.21* (2.35–3.19)	9.47± 0.36 (8.77–10.17)
SOD, a.u./mg protein/min	7.92±0.37* (7.2–8.64)	15.48±0.8 (13.91–17.05)

Note: ** indicates a statistically significant difference between the control and main groups (p<0.05)*

main group, when compared with the control cohort, is represented by a significant increase in APH and KPH against the background of menopause with corresponding dermatological symptoms, which confirms the previous thesis. However, more active shifts occur precisely when analyzing the spontaneous process, which demonstrates a significant degree of oxidative destruction against the background of the constant action of reactive oxygen species, which can occur within a long-term, chronic process. When assessing the stimulated reaction, its reliable increase was also determined, but the trend indicates the exhaustion of the potential of the response to stimuli and the imbalance of adaptive and compensatory mechanisms. Therefore, the presented changes correspond to the profile of functional depletion of the compensatory system, with the subsequent need for a comprehensive assessment of this process

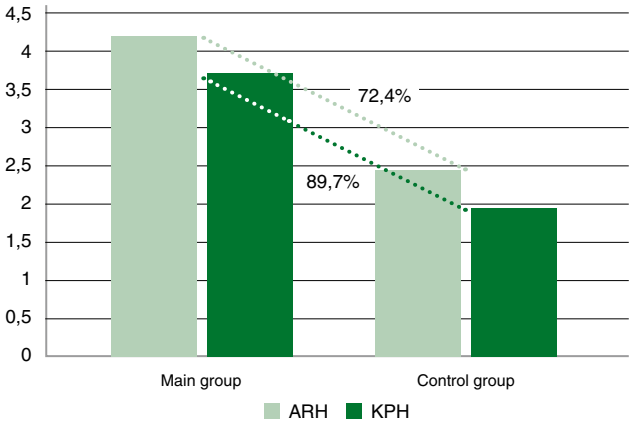

Fig.1. Features of spontaneous protein oxidation (a.u./g protein) and their ratio in the main and control study groups (%)

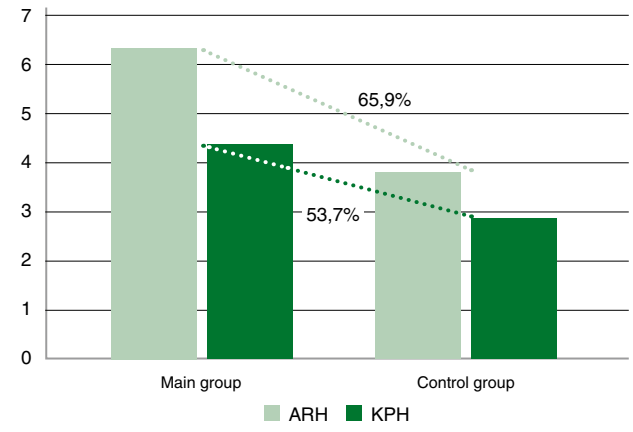

Fig.2. Features of stimulated protein oxidation (a.u./g protein) and their ratio in the main and control study groups (%).

and determination of the levels of markers in the context of analyzing the level of antioxidant protection.

Glutathione, in both its reduced and oxidized forms, along with superoxide dismutase, are key components in maintaining redox balance, providing protection against the effects of the free radical cascade. When assessing the level of the antioxidant barrier as a regulator of oxidative stress, quantitative indicators of this system were determined and are presented in Table 2. Numerically, the difference in the thiol-disulfide system parameters between the main and control groups was (11.61 ± 0.74) μg/ml ($p < 0.05$) and (0.46 ± 0.03) μg/ml ($p < 0.05$) for GSH and GSSG, respectively. The ratio between these parameters showed a difference of (6.7 ± 0.42) a.u. ($p < 0.05$), while SOD differed between the studied samples at the level of (7.56±0.88) a.u./mg protein/min (p<0,05).

However, the percentage difference in antioxidant defense marker levels between the studied groups, illustrated in Fig.3 and Fig. 4, is more indicative. According to the results, when comparing individuals with climacteric syndrome, including manifestations of keratoderma, to patients of reproductive age, GSH showed a decrease of 63.8% ($p < 0.05$), whereas GSSG demonstrated an increase of 23.96% ($p < 0.05$). The GSH/GSSG ratio in patients of the main group was significantly lower than that in the control group by 70.75% ($p < 0.05$).

The obtained indicators of the thiol-disulfide system also correlate with the overall decrease in SOD activity. Figure 4 visualizes the difference between the main and control groups, showing a decrease in the former, which reflects a difference of 48.84%.

Thus, the presence of oxidative stress, established through the analysis of OPM, confirms a shift in the antioxidant system balance towards its depletion, evidenced by a significant decrease in GSH and superoxide dismutase SOD, alongside an increase in oxidized glutathione GSSG. The obtained data objectify the severity of the pathological process, highlighting the need for further optimization of diagnostic and therapeutic algorithms aimed at antioxidant support for patients with clinical manifestations of climacteric keratoderma.

To understand the potential interaction between the clinical-anamnestic profile of the studied cohort and the features of biochemical homeostasis, it is important to emphasize their correlation. The analysis of menopause as the background of the overall imbalance, including the corresponding dermatological symptoms, becomes particularly relevant in this context. To objectify and systematize the obtained data regarding climacteric manifestations, the use of the Menopause Rating Scale (MRS) is appropriate. Interpreting the data, the median score for the main group

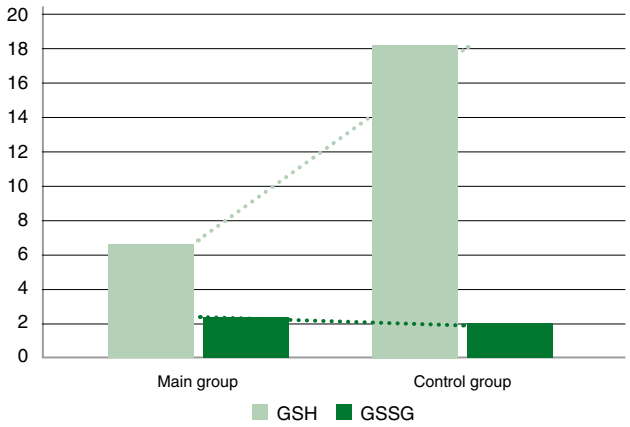

Fig.3 Characteristics of GSH and GSSG indicators (μg/ml) in the main and control study groups and their ratio (%)

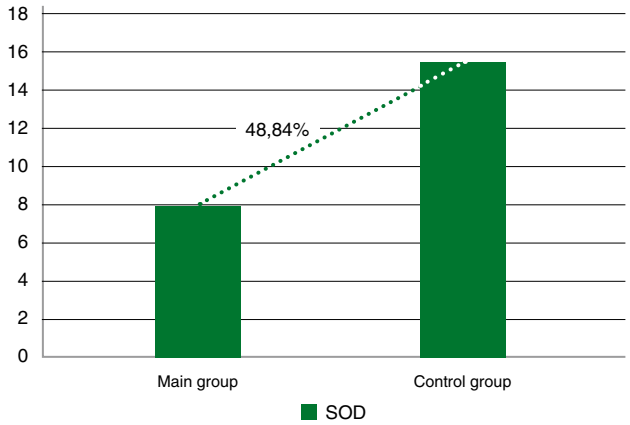

Fig.4. Characteristics of SOD (a.u./mg protein/min) in the main and control study groups and their ratio (%)

was 13 (9.25–16), indicating moderate menopausal symptoms in this cohort.

The next step is to determine the potential interaction with climacteric activity, taking into account the MRS scores. A direct moderate correlation was observed between the level of spontaneous APH (+0.69, r=0.69; p<0.05), KPH (+0.67, r=0.67; p<0.05), and stimulated APH (+0.63, r=0.63; p<0.05), KPH (+0.65, r=0.65; p<0.05). Conversely, an inverse correlation was found between SOD levels (–0.75, r= –0.75; p<0.05) and the GSH/GSSG ratio (–0.67, r= –0.67; p<0.05). These data indicate the presence of an imbalance in the antioxidant defense system, demonstrating statistically significant moderate correlations (OPM markers and GSH/GSSG ratio) and a strong correlation (SOD) with the severity of menopausal symptoms. The results not only emphasize the importance of collecting anamnesis and using questionnaires as research tools but also highlight the need to implement OPM and antioxidant defense system indicators into clinical practice.

Considering that the results of SOD in patients of the main group demonstrate a high level of correlation, in the

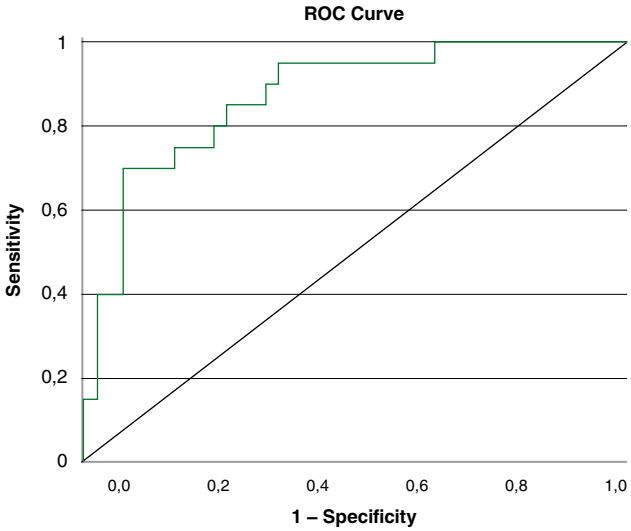

Fig 5. ROC curve based on SOD level assessment and severity of climacteric symptoms according to MRS

course of the research work, it was decided to focus on this parameter with the transfer of its analytical role to the sphere of practical use. The results of the ROC analysis are presented in Figure 5.

According to the ROC analysis algorithm, the MRS scale was dichotomously stratified to classify menopausal symptoms into mild-moderate and severe categories. The area under the ROC curve (AUC), representing the relationship between the severity of the pathological process and SOD levels, was 0.87 with a 95% confidence interval (CI) of 0.78–0.96. The cut-off value for SOD was determined to be 8.2 a.u./mg protein/min. At SOD levels below this threshold, an MRS score of 16 or higher is predicted. For this cut-off, sensitivity and specificity were 85% and 74%, respectively. The results of this analysis demonstrate the clinical significance of SOD as a predictor in assessing the level of antioxidant imbalance in patients from the main group. Thus, the aforementioned data in the studied cohort not only contribute to understanding the biochemical basis of climacteric keratoderma but also provide a practically oriented model for developing a personalized therapeutic algorithm.

Conclusions

The results of the study indicate that patients with climacteric keratoderma exhibit a statistically significant predominance of both spontaneous and stimulated oxidative protein modification markers compared to the control group. These changes occur against the background of a statistically significant decrease in the levels of superoxide dismutase, as well as reduced glutathione, indicating a breakdown of adaptive mechanisms and reflecting oxidative stress. Translating these findings into clinical practice supports the development of new therapeutic approaches aimed at correcting the oxidative-antioxidant imbalance.

Список літератури

1. Доклінічне вивчення специфічної активності потенційних лікарських засобів первинної та вторинної нейропротекції: методичні рекомендації/ І.С. Чекман, І.Ф. Беленічев, О.О. Нагорна та ін. Київ, 2016. С. 93.
2. Chandankhede M., Gupta M., Pakhmode S. Assessment of Psychological Status and Oxidative Stress in Postmenopausal Women: A Cross-Sectional Study. *J Menopausal Med*. 2021. Vol.27(3).P.155–161. doi: 10.6118/jmm.20035.
3. Chen J., Liu Y., Zhao Z., Qiu J. Oxidative stress in the skin: Impact and related protection. *Int J Cosmet Sci*. 2021.Vol.43(5).P.495–509. doi: 10.1111/ics.12728.
4. Decreased oxidative stress response and oxidant detoxification of skin during aging/ X. Dai, Y. Hu, L. Jiang et al. *Mech Ageing Dev*. 2023. Vol. 216.P.111878. doi: 10.1016/j.mad.2023.111878.
5. Goutami L., Jena S.R., Swain A., Samanta L. Pathological Role of Reactive Oxygen Species on Female Reproduction. *Adv Exp Med Biol*. 2022.Vol.1391.P.201–220. doi: 10.1007/978–3–031–12966–7_12

References

1. Chekman I.S, Bielenichev I.F., Nahorna O.O. et al. Doklinichne vyvchennia spetsyfichnoi aktyvnosti potentsiinykh likarskykh zasobiv pervynnoi ta vtorynnoi neiroprotektsii: metodychni rekomendatsii [Preclinical study of specific activity of potential drugs for primary and secondary neuroprotection: methodological recommendations]. Kyiv; 2016. 93 p. Ukrainian
2. Chandankhede M., Gupta M., Pakhmode S. Assessment of Psychological Status and Oxidative Stress in Postmenopausal Women: A Cross-Sectional Study. J Menopausal Med. 2021;27(3):155–161. doi: 10.6118/jmm.20035.
3. Chen J., Liu Y., Zhao Z., Qiu J. Oxidative stress in the skin: Impact and related protection. Int J Cosmet Sci. 2021;43(5):495–509. doi: 10.1111/ics.12728.
4. Dai X., Hu Y., Jiang L. et al. Decreased oxidative stress response and oxidant detoxification of skin during aging. Mech Ageing Dev. 2023;216:111878. doi: 10.1016/j.mad.2023.111878.
5. Goutami L., Jena S.R., Swain A., Samanta L. Pathological Role of Reactive Oxygen Species on Female Reproduction. Adv Exp Med Biol. 2022;1391:201–220. doi: 10.1007/978–3–031–12966–7_12

6. Kamp E., Ashraf M., Musbahi E., DeGiovanni C. Menopause, skin and common dermatoses. Part 2: skin disorders. *Clin Exp Dermatol*. 2022. Vol. 47(12).P.2117–2122. doi: 10.1111/ced.15308.
7. Keratoderma climactericum: an under-reported condition successfully treated with an estriol cream/ A. Tatti, B. Conti, M. Corbeddu, M. Uda et al.. *Journal of Applied Cosmetology*. 2024. Vol.42(1).P.40–44. doi: 10.56609/jac.v42i1.329.
8. Lephart E.D., Naftolin F. Factors Influencing Skin Aging and the Important Role of Estrogens and Selective Estrogen Receptor Modulators (SERMs). *Clin Cosmet Investig Dermatol*. 2022. Vol.15.P.1695–1709. doi: 10.2147/CCID.S333663.
9. Letsiou S. Tracing skin aging process: a mini- review of in vitro approaches. *Biogerontology*. 2021. № 22(3). P. 261–272. doi: 10.1007/s10522–021–09916-z.
10. Management of menopausal disorders in women at risk: potential and advantages of transdermal estrogen: Literature review/ V.H. Siusiuka, M. Yu. Sergienko, M.I. Pavliuchenko et. al. *Reproductive endocrinology*. 2024.Vol.74. P.39–46. doi: 10.18370/2309–4117.2024.74.39–46
11. Merzel abović E.K., Kocjan T., Zalaudek I. Treatment of menopausal skin – A narrative review of existing treatments, controversies, and future perspectives. *Post Reprod Health*. 2024. Vol.30(2).P.85–94. doi: 10.1177/20533691241233440.
12. Nair P.A. Dermatosis associated with menopause. *J Midlife Health*. 2014. Vol.5(4).P.168–75. doi: 10.4103/0976–7800.145152.
13. Norman T., Obed O., Chen A., Worswick S. Palmoplantar keratoderma climactericum successfully treated with topical oestrogen. *Jeadv Clinical Practice*. 2024.Vol.3(1).P.309–312. doi: 10.1002/jvc2.277.
14. Oxidative Stress: The Role of Estrogen and Progesterone/ A Cagnacci., I. Gazzo, S. Stigliani et al. *J Clin Med*. 2023.Vol.12(23).P.7304. doi: 10.3390/jcm12237304.
15. Phaniendra A., Jestadi D.B., Periyasamy L. Free radicals: properties, sources, targets, and their implication in various diseases. *Indian J Clin Biochem*. 2015.Vol. 30(1).P.11–26. doi: 10.1007/s12291–014–0446–0.
16. Pignatelli P., Menichelli D., Pastori D., Violi F. Oxidative stress and cardiovascular disease: new insights. *Kardiol Pol*. 2018.Vol. 76(4).P.713–722. doi: 10.5603/KP.a2018.0071.
17. Perimenopause period and menopause: cardiovascular and metabolic risks/ V.H. Siusiuka, V.A. Vizir, M. Yu. Serhienko et al. *Zaporozhye Medical Journal*. 2024.№ 26(5).P.424–429. doi: 10.14739/2310–1210.2024.5.303438
18. Protective Effects of Estrogen on Cardiovascular Disease Mediated by Oxidative Stress/ D. Xiang, Y. Liu., S. Zhou et al. *Oxid Med Cell Longev*. 2021 Jun 28;2021:5523516.. doi: 10.1155/2021/5523516
19. Short- and long-term impact by vasomotor symptoms in menopause and modern approaches to their correction/ V.G. Siusiuka, M. Yu. Serhiienko, M.I. Pavliuchenko et al. *Reproductive health of woman*. 2024.Vol. 4 (75).P.63–69. doi: 10.30841/2708–8731.4.2024.306540
20. Systemic Oxidative Stress, Aging and the Risk of Cardiovascular Events in the General Female Population/ M.F Bourgonje, A.R. Bourgonje, A.E. Abdulle et al. *Front Cardiovasc Med*. 2021.Vol..8.630543. doi: 10.3389/fcvm.2021.630543.
21. The benefits and risks of menopause hormone therapy for the cardiovascular system in postmenopausal women: a systematic review and meta-analysis/ Y. Gu, F. Han, M. Xue et al. *BMC Womens Health*. 2024.Vol. 24(1).P.60. doi:10.1186/s12905–023–02788–0
22. Thornton M.J. Estrogens and aging skin. *Dermatoendocrinol*. 2013.Vol.5(2).P.264–270.
23. Viscomi B., Muniz M., Sattler S. Managing Menopausal Skin Changes: A Narrative Review of Skin Quality Changes, Their Aesthetic Impact, and the Actual Role of Hormone Replacement Therapy in Improvement. *J Cosmet Dermatol*. 2025;(Suppl 4).P.e70393. doi: 10.1111/jocd.70393.
24. Wilkinson H.N., Hardman M.J. A role for estrogen in skin ageing and dermal biomechanics. *Mech Ageing Dev*. 2021.Vol.197.P.111513. doi: 10.1016/j.mad.2021.111513.
25. Zejnullahu V.A., Zejnullahu V.A., Kosumi E. The role of oxidative stress in patients with recurrent pregnancy loss: a review. *Reprod Health*. 2021.Vol.18(1).P.207. doi: 10.1186/s12978–021–01257-x.

6. Kamp E., Ashraf M., Musbahi E., DeGiovanni C. Menopause, skin and common dermatoses. Part 2: skin disorders. Clin Exp Dermatol. 2022;47(12):2117–2122. doi: 10.1111/ced.15308.
7. Tatti A., Conti B., Corbeddu M., Uda M., et al.Keratoderma climactericum: an under-reported condition successfully treated with an estriol cream. Journal of Applied Cosmetology. 2024;42(1):40–44. doi: 10.56609/jac.v42i1.329.
8. Lephart E.D., Naftolin F. Factors Influencing Skin Aging and the Important Role of Estrogens and Selective Estrogen Receptor Modulators (SERMs). Clin Cosmet Investig Dermatol. 2022;15:1695–1709. doi: 10.2147/CCID.S333663.
9. Letsiou S. Tracing skin aging process: a mini- review of in vitro approaches. Biogerontology. 2021;22(3):261–272. doi: 10.1007/s10522–021–09916-z.
10. Siusiuka V.H., Sergienko M. Yu., Pavliuchenko M.I. et. al. Management of menopausal disorders in women at risk: potential and advantages of transdermal estrogen: Literature review. Reproductive endocrinology. 2024;74:39–46. doi: 10.18370/2309–4117.2024.74.39–46
11. Merzel abović E.K., Kocjan T., Zalaudek I. Treatment of menopausal skin – A narrative review of existing treatments, controversies, and future perspectives. Post Reprod Health. 2024;30(2):85–94. doi: 10.1177/20533691241233440.
12. Nair P.A. Dermatosis associated with menopause. J Midlife Health. 2014;5(4):168–75. doi: 10.4103/0976–7800.145152.
13. Norman T., Obed O., Chen A., Worswick S. Palmoplantar keratoderma climactericum successfully treated with topical oestrogen. Jeadv Clinical Practice. 2024;3(1):309–312. doi: 10.1002/jvc2.277.
14. Cagnacci A., Gazzo I., Stigliani S. at al. Oxidative Stress: The Role of Estrogen and Progesterone. J Clin Med. 2023;12(23):7304. doi: 10.3390/jcm12237304.
15.Phaniendra A., Jestadi D.B., Periyasamy L. Free radicals: properties, sources, targets, and their implication in various diseases. Indian J Clin Biochem. 2015;30(1):11–26. doi: 10.1007/s12291–014–0446–0.
16. Pignatelli P., Menichelli D., Pastori D., Violi F. Oxidative stress and cardiovascular disease: new insights. Kardiol Pol. 2018;76(4):713–722. doi: 10.5603/KP.a2018.0071.
17. Siusiuka V.H., Vizir V.A., Serhienko M. Yu. et al. Perimenopause period and menopause: cardiovascular and metabolic risks. Zaporozhye Medical Journal. 2024;26(5):424–429. doi: 10.14739/2310–1210.2024.5.303438
18. Xiang D., Liu Y., Zhou S., et al. Protective Effects of Estrogen on Cardiovascular Disease Mediated by Oxidative Stress. Oxid Med Cell Longev. 2021;2021:5523516. doi: 10.1155/2021/5523516
19. Siusiuka V.G., Serhiienko M. Yu., Pavliuchenko M.I. et al. Short- and long-term impact by vasomotor symptoms in menopause and modern approaches to their correction. Reproductive health of woman. 2024;4 (75):63–69. doi: 10.30841/2708–8731.4.2024.306540
20. Bourgonje M.F., Bourgonje A.R., Abdulle A.E., et al. Systemic Oxidative Stress, Aging and the Risk of Cardiovascular Events in the General Female Population. Front Cardiovasc Med. 2021;8:630543. doi: 10.3389/fcvm.2021.630543.
21. Gu Y., Han F., Xue M. et al. The benefits and risks of menopause hormone therapy for the cardiovascular system in postmenopausal women: a systematic review and meta-analysis. BMC Womens Health. 2024;24(1):60. doi:10.1186/s12905–023–02788–0
22. Thornton M.J. Estrogens and aging skin. Dermatoendocrinol. 2013;5(2):264–270.
23. Viscomi B., Muniz M., Sattler S. Managing Menopausal Skin Changes: A Narrative Review of Skin Quality Changes, Their Aesthetic Impact, and the Actual Role of Hormone Replacement Therapy in Improvement. J Cosmet Dermatol. 2025;24 Suppl 4(Suppl 4): e70393. doi: 10.1111/jocd.70393.
24. Wilkinson H.N., Hardman M.J. A role for estrogen in skin ageing and dermal biomechanics. Mech Ageing Dev. 2021;197:111513. doi: 10.1016/j.mad.2021.111513.
25. Zejnullahu V.A., Zejnullahu V.A., Kosumi E. The role of oxidative stress in patients with recurrent pregnancy loss: a review. Reprod Health. 2021;18(1):207. doi: 10.1186/s12978–021–01257-x.

Конфлікт інтересів: відсутній.

ОСОБЛИВОСТІ ОКСИДАНТНО-АНТИОКСИДАНТНОГО ГОМЕОСТАЗУ У ЖІНОК З КЛІМАКТЕРИЧНОЮ КЕРАТОДЕРМІЄЮ

Г.І. Макуріна, О.К. Синах
Запорізький державний медико-фармацевтичний університет

Резюме.

Мета: *оцінити особливості оксидантно-антиоксидантного гомеостазу у жінок з клімактеричною кератодермією.*

Матеріали і методи. *На базі кафедри дерматовенерології та естетичної медицини Запорізького державного медико-фармацевтичного університету обстежено 62 пацієнтки з проявами долонно-підошовної кератодермії. Лабораторні дослідження проводились на базі Навчально-наукового медико-лабораторного центру з віварієм Запорізького державного медико-фармацевтичного університету.*

Результати. *При оцінці ранніх та пізніх маркерів спонтанної модифікації білка, спостерігається різниця між досліджуваними вибірками АФГ та КФГ на (1.76±0.24) умов. од./г білка (p<0.05) та (1.75±0.28) умов.од./г білка (p<0.05) відповідно. Тоді як стимульоване окислення також згідно отриманих даних демонструє підвищення та наявність різниці для АФГ в межах (2.52±0.3) умов. од./г білка (p<0.05), а КФГ – (1.53±0.29) умов. од./г білка (p<0.05). Чисельно різниця отриманих даних при порівнянні показників тіол-дисульфідної системи основної та контрольної групи складає (11.61±0.74) мкг/мл (p<0.05) та (0,46±0,03) мкг/мл (p<0.05) для глутатіону відновленого та окисленого відповідно. Показник їх співвідношення демонструє різницю в межах (6.7±0.42) умов.од. (p<0.05), тоді як показники супероксиддисмутази відрізняються між досліджуваними вибірками на рівні (7.56±0.88) у.о./мг білка/хв (p<0.05).*

Висновки. *Результати проведеного дослідження свідчать, що у пацієнток з клімактеричною кератодермією встановлено статистично достовірне переважання показників як спонтанної, так і стимульованої окисної модифікації білка у порівнянні з контрольною групою. Такі зміни відбуваються на тлі статистично достовірного зниження рівня супероксиддисмутази, а також відновлюваного глутатіону, що свідчать про зрив адаптаційних механізмів та є проявом оксидативного стресу.*

Ключові слова: *клімактеричні зміни, окисна модифікація білка, антиоксидантна система, гомеостаз, діагностика.*

Відомості про авторів:

Макуріна Галина Іванівна – *д-р мед. наук, професор, зав. кафедри дерматовенерології та естетичної медицини, Запорізький державний медико-фармацевтичний університет, м. Запоріжжя.*
ORCID ID: ***0000-0002-3293-2748***

Синах Ольга Костянтинівна – *аспірант кафедри дерматовенерології та естетичної медицини, Запорізький державний медико-фармацевтичний університет, Запоріжжя.*
ORCID ID: ***0000-0002-6626-7723***