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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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საქართველოს სამედიცინო სიახლენი

**GEORGIAN MEDICAL NEWS**

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**GMN: Georgian Medical News** is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

**GMN: Медицинские новости Грузии -** ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

**GMN: Georgian Medical News –** საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

**WEBSITE**

www.geomednews.com

## К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

**При нарушении указанных правил статьи не рассматриваются**.

## REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.**

## ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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# ECZEMA AND TRANSEPIDERMAL MOISTURE LOSS: A SYSTEMATIC REVIEW AND META-ANALYSIS (REVIEW)

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## Abstract.

**Introduction:** Eczema is a chronic, recurrent, inflammatory skin disease. Its main symptom is intermittent pruritus, as well as xerosis of the skin and eczematous lesions caused by the interaction of genetic and environmental factors. Risk factors for development are also associated with skin barrier defects that reduce skin hydration (capacity) and increase transepidermal water loss (TEWL). There are many studies and, in our analysis, we aimed to determine how TEWL scores differed significantly between patients with skin diseases, including eczema.

**Aim:** The specific aims of our systematic review and meta-analysis were:

• To determine, by analyzing studies, the change in the level of the epidermal barrier in skin diseases, namely eczema.

• To study the effect of changes in transepidermal moisture loss in patients with eczema, taking into account gender characteristics.

**Methodology:** By conducting a systematic review and meta-analysis, we synthesized data from various studies that evaluated the association between TEWL scores and clinical severity of disease. Fifteen articles describing 1355 cases of eczema were included in our study.

**Results:** We found that the difference in TEWL levels between men and women was statistically significant. In the studies included in this meta-analysis, TEWL elevation in eczema patients ranged from 13.3% to 76.7%. Among the age group 19 to 44 years - 59.8% of eczema cases had TEWL elevation in contrast to other age groups.

**Conclusions:** Disruption of epidermal barrier permeability in eczematous conditions may also occur in other skin diseases. We have found that improvement in TEWL levels can prevent and alleviate the clinical severity of inflammatory dermatoses.

**Key words.** Skin, eczema, epidermal barrier, transepidermal moisture loss, systematic review, meta-analysis.

## Introduction.

Eczema is an inflammatory skin disease caused by the interaction of both exogenous and endogenous risk factors, with a significant burden on the patient in terms of psychosocial and economic consequences. The prevalence of eczema differs between developing and industrialized countries [1]. Over the past three decades, prevalence rates in industrialized countries have increased to 15-30% in children and 2-10% in adults [2]. For example, among the statistical studies conducted in developing countries such as Mexico, Chile, Kenya and South-East Asia [2], there has been an increase in the prevalence of eczema in adults. However, rates are also increasing in children (6-7 years) with 84% of participating centers, especially in Western Europe, Canada, South America, Australasia and the Far East [2], older adults (13-14 years) with 58% of participating centers reporting eczema prevalence [3,4]. According to the sources studied, authors state that in 60% of cases eczema manifests itself in a child from birth in the first months of life [2]. Therefore, the development of eczema is divided into 3 periods (infancy, childhood and adolescence/adulthood) [2].

Eczema has many causes, ranging from psychological disorders to permanent mechanical damage [2]. Eczema is one of the most common skin diseases, but despite this, the exact etiology is not known. Although treatment is available, it is not always successful, and well-being and activities are limited due to the severe pain and irritation of the skin. Considering the pathomechanism of inflammation of eczema disease it is known that having a history of atopic dermatitis is an endogenous risk factor, whereas working in a humid environment, exposure to irritants and contact sensitization are exogenous risk factors.

There are no precise diagnostic criteria for eczema, so we studied the indicators that change in eczema. The upper epidermal layer of the human skin functions as a physical and chemical barrier consisting of a brick and mortar-like structure called the stratum corneum [2,5] There is abundant evidence in the literature supporting the role of skin barrier dysfunction in eczema [2,6]. Transepidermal moisture loss (TEWL) assessment is one of the methods used to quantify the barrier function of the skin. Changes in epidermal lipids caused by water loss allow cracks to form in the stratum corneum, allowing the penetration of external antigens, irritants and microbial pathogens, which can provoke further inflammation [2,7,8].

Non-invasive tools that assess the level of hydration and the integrity of the skin barrier function have been found to be most informative for determining the severity and monitoring disease progression using various criteria, for diagnosis and follow-up of patients with eczema as medical examinations to obtain objective and reproducible results of skin barrier measurements. Thus, increased TEWL and decreased skin elasticity are characteristic features of epidermal barrier disruption in atopic eczema [9]. Atopic dermatitis and eczema are characterised by impaired skin barrier function, allergic inflammation, water imbalance (low skin hydration and increased transepidermal water loss, TEWL), itching and dry skin, and reduced quality of life. In both diseases, a mutation in the filaggrin gene plays an important role. Filaggrin is the main protein that forms the epidermal barrier, and its deficiency leads to a weakening of

the skin barrier and the development of eczematous reactions. Therefore, we consider atopic dermatitis to be a type of eczema or its atopic form. In the course of our study, we were exposed to a variety of data that supported our hypotheses.

**Aim.** The specific aims of our systematic review and meta-analysis were:

· To determine, by analyzing studies, the change in the level of the epidermal barrier in skin diseases, namely eczema;

· To study the effect of changes in transepidermal moisture loss in patients with eczema, taking into account gender characteristics.

Patients with eczema, taking into account gender characteristics.

## Materials and Methods.

We conducted this systematic review and meta-analysis in accordance with the statement of preferred reporting elements for systematic reviews and meta-analyses (PRISMA) (Figure 1). Before proceeding with the quantitative and systematic synthesis, we analyzed all studies that aimed to assess the association between eczema and measures of transepidermal moisture loss.

In certain segments of the analysis where primary studies did not provide granular data for specific subtypes, atopic Dermatitis and other forms of eczema were pooled into a single category labeled TEWL. This decision was based on the shared pathophysiological hallmark of these conditions: a significant disruption of the epidermal barrier and a resultant increase in TEWL. For these combined cohorts, the diagnosis was accepted as defined by the original authors, provided the clinical presentation included chronic or relapsing inflammatory skin lesions.

### Search Strategy.

A comprehensive search was conducted using PubMed, Cochrane Library, MEDLINE, Embase, Up ToDate, Research Gate, Google Scholar, and eLibrary databases. The following search criteria were applied: ["Eczema" (MeSH)] OR ["Eczema, Dyshidrotic" (MeSH) OR "Dermatitis, Atopic" (MeSH)]. This search was restricted to English language studies published from inception to 15 April 2024. Subsequently, we analysed the abstracts of all identified papers to determine whether they met the inclusion criteria. Finally, we reviewed the reference lists of all eligible papers to find additional relevant articles.

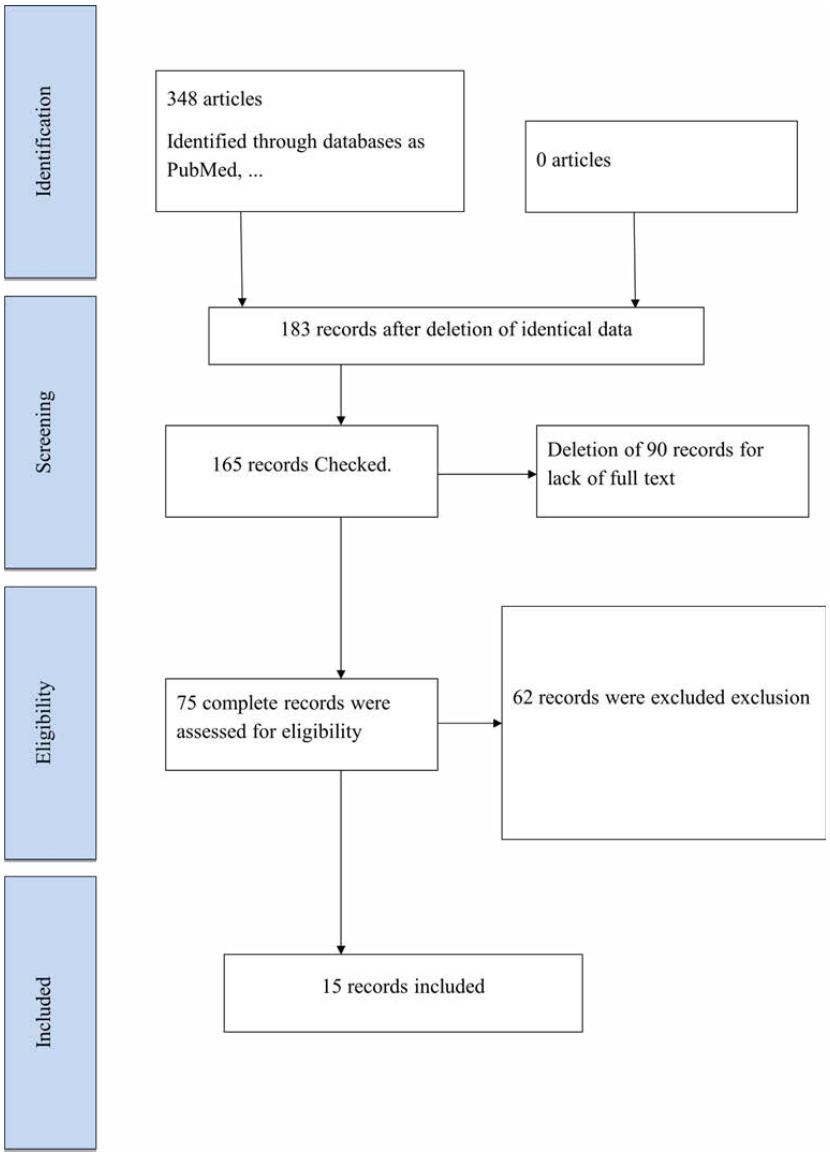


***Figure 1.*** *Flow diagram PRISMA.*

Our inclusion criteria were studies that included patients with eczema, studies that assessed transepidermal moisture loss, studies that assessed transepidermal moisture loss based on standardised and validated instruments/questionnaires, and studies published in English. Our exclusion criteria were studies that did not report the rate of transepidermal moisture loss among patients with eczema or provided insufficient data to calculate the rate of transepidermal moisture loss, lack of full text for the full review, studies with poor methodological quality, i.e. case reports, case series and commentaries, and studies published in languages other than English. Studies in other languages were excluded because inaccurate translations into English led to misinterpretation of the research.

The initial search and selection of articles was conducted independently by the author (T.I.), who checked titles and abstracts and excluded all articles that did not fulfil the inclusion criteria. As a next step, we collected the full text of articles that were deemed suitable for publication and assessed all studies based on their design. All disagreements about the eligibility of studies were resolved through discussions. The selection process according to PRISMA guidelines is summarized in Figure 1. The PRISMA checklist can be found on many platforms. We used the PRISMA checklist from the website https://www.prisma-statement.org/.

Studies should have provided sufficient data, such as odds ratio (OR) and 95% confidence interval (CI), so that the corresponding standard errors (SES) could be calculated. If such information was not available, we looked for crude data with the number of cases.

**Data Extraction and Study Evaluation.**

The reviewer (T.I.) extracted data from the screened articles. All selected data were presented in a standardized form that included (i) first author's surname and year of publication, (ii) country of study origin, (iii) sample size in groups with and without eczema, if any, (iv) prevalence of TEWL scores in patients with eczema and controls, if any, (v) TEWL assessment tool, (vi) proportion of female and male patients with eczema, if any, (vii) age category. The quality of included articles was assessed using the Newcastle-Ottawa scale for non-randomized studies [10]. Studies scoring ≥7 on the Newcastle-Ottawa scale were considered high quality, 4-6 met the criteria of medium quality studies, and less than 4 were considered low quality studies. Each article was evaluated independently by a reviewer (T.I.). All differences in scores were confirmed in the AI discussion. As we did not perform any patient interventions and all information was recycled from previous scientific studies, ethical committee approval was not required.

**Statistical Analysis:**

We performed statistical analyses using Review Manager (RevMan) software version 5.3 (Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration, 2014). Then, using a random-effects model, we calculated the prevalence and frequency of changes in TEWL levels in eczema patients and in the general population of study participants. An i2 value was processed to assess study heterogeneity. We used a random-effects model (DerSimonian-Laird method) when the heterogeneity of studies was large ($i2 > 60\%$, $p < 0.05$) and a fixed-effects meta-analysis when heterogeneity was small ($i2 < 60\%$, $p < 0.05$).

**Subgroup Analysis:**

Subgroup analysis was performed to examine the influence of sex, age, localization, severity of skin manifestations, continence and skin disease on the prevalence of changes in TEWL levels among eczema patients. Data from the World Health Organization were used to classify all included studies by age category [11]. The countries considered for incidence information by publication were China, Germany, Malaysia, UK, Belgium, Denmark, USA, Sweden, South Korea, Brazil [11]. By continentally, European and American countries were covered, China and South Korea were allocated to the East Asia continent subgroup, and Malaysia was allocated to South-east Asia. Controlled studies have compared the prevalence of TEWL changes in groups of patients with and without eczema (or in remission). Regarding the type of skin disease, some studies contained data on the prevalence of TEWL changes among patients with eczema and atopic dermatitis, while other studies contained data on different skin diseases. The control group was most often comprised of patients with eczema.

## Ethical Statement:

Our analysis is based on studies previously conducted by other authors; therefore, no ethical committee approval or patient informed consent was required for this review.

## Results.

**Identification, Screening, Eligibility:**

A search using PubMed, Cochrane Library, MEDLINE, Embase, Up ToDate, Research Gate, Google Scholar, eLibrary identified 348 studies (Table 1). There were no studies that met the inclusion criteria in the Cochrane Library. One hundred and eighty-three studies were removed as duplicate studies. The titles and abstracts of the remaining 165 articles were selected. The full texts of 165 studies were analyzed and 90 of them were excluded for the following reasons: irrelevant results; review articles; not in English/non-Russian language. Finally, 15 articles describing 1355 cases of eczema were included in our study.

**Demographic Data of the Studies:**

All articles presented data on TEWL levels in patients with eczema. When analyzing the reviewed publications, the authors assessed the prevalence of changes in TEWL levels, where scientific studies using modern non-invasive ways of studying skin structures were examined. Thus, our meta-analysis included 15 studies involving 1355 patients with eczema, with sample sizes ranging from 18 to 650 participants. The vast majority of studies included participants whose age was >18 years, some articles were older than 60 years, and one study did not include the age of the participants. Participants aged 0 to 70 years, whose mean age was available in the articles, were included. We categorized by age group: 0-18 "Children"; 19-44 "Adults"; 45-59 "Middle age"; 60-74 "Older age". The number of patients with eczema ranged from 13 to 103, in one study the sex ratio was not specified.

Almost all studies were designed as cohort studies. Assessing the quality of included studies using the Newcastle-Ottawa

scale, we found that eight studies met the criteria for acceptable quality, the same numbers of studies were considered of good quality, and two studies were of poor quality. Study countries, geographical regions, sample size, TEWL rates among eczema patients, screening tools, study design and quality of included publications are summarized in Table 1.

**Analysis of random effects models:**

Table 2 summarizes the incidence of elevation in the total sample and in patients with eczema. The sample size in the fifteen studies ranged from 18 to 650 participants. The number of patients with eczema in the included studies ranged from 18 to 60. TEWL elevation in patients with eczema ranged from 9.8 % to 67.0 %, thus the minimum and maximum case rate values were 0.09 and 0.67 respectively.

Analysis of TEWL levels among eczema patients using random effects models showed that the prevalence was 77 % (P < 0.00001). The pooled Mean Difference for change in TEWL levels among eczema patients was 22.89 [19.62, 26.16] (Figure 2). There was high heterogeneity between studies ($I^2$ = 99% (P < 0.00001). The increase in TEWL was 39.5 % in patients with eczema versus 31.7 % in patients with atopic dermatitis and this result was statistically significant (P=0.04). The increase in TEWL in patients with atopic dermatitis was 24.4 % compared to 29.3 % in patients with eczema. TEWL was frequently observed in patients with eczema compared to patients with atopic dermatitis. A statistically significant detail was also observed: The age group "adults" (19-44 years) had more cases of eczema with TEWL elevation and the percentage was 59.8 % in favor of this category out of 15 articles as compared to other age groups.

Subgroup Analysis by Gender The meta-analysis of TEWL levels among gender-specific subgroups was performed using a random effects model (DerSimonian-Laird method) due to the presence of extreme heterogeneity (I^2 = 99/%, P < 0.00001). The pooled mean difference in TEWL levels between female and male patients with eczema was 28.16 [95% CI: 1.27, 55.05] (Figure 2). This result indicates a statistically significant elevation of TEWL in the female subgroup compared to the male subgroup (Z = 2.05, P = 0.04). However, the wide confidence interval reflects the substantial variability among the 15 included studies, particularly influenced by outliers with significant measurement deviations.

We demonstrated that patients with eczema had higher levels of TEWL scores. About one third of patients with eczema had elevated TEWL levels. We found that the difference in TEWL scores between men and women was statistically significant. In the studies included in this meta-analysis, TEWL elevation in eczema patients ranged from 13.3 % to 76.7 %.

## Discussion.

This meta-analysis aimed to assess changes in TEWL levels among eczema patients from different countries and to elucidate associated risk factors. In addition, we searched for publications on the incidence from early infancy and childhood, where a chronic recurrent skin disease like atopic dermatitis was most commonly encountered. There was no single distinguishing sign or diagnostic laboratory test; therefore, the diagnosis was based on the totality of clinical findings. As a result of the different clinical features, the term "atopic eczema/dermatitis syndrome" was used, which was consistent with the study of our problem.

In the studies included in this systematic review, a comparison of TEWL levels in eczema patients according to age category showed that people in the "adult" category had higher TEWL levels. TEWL scores were positively correlated with disease severity regardless of age category, both adult and infant [12-14]. In addition, infants with higher TEWL scores during the

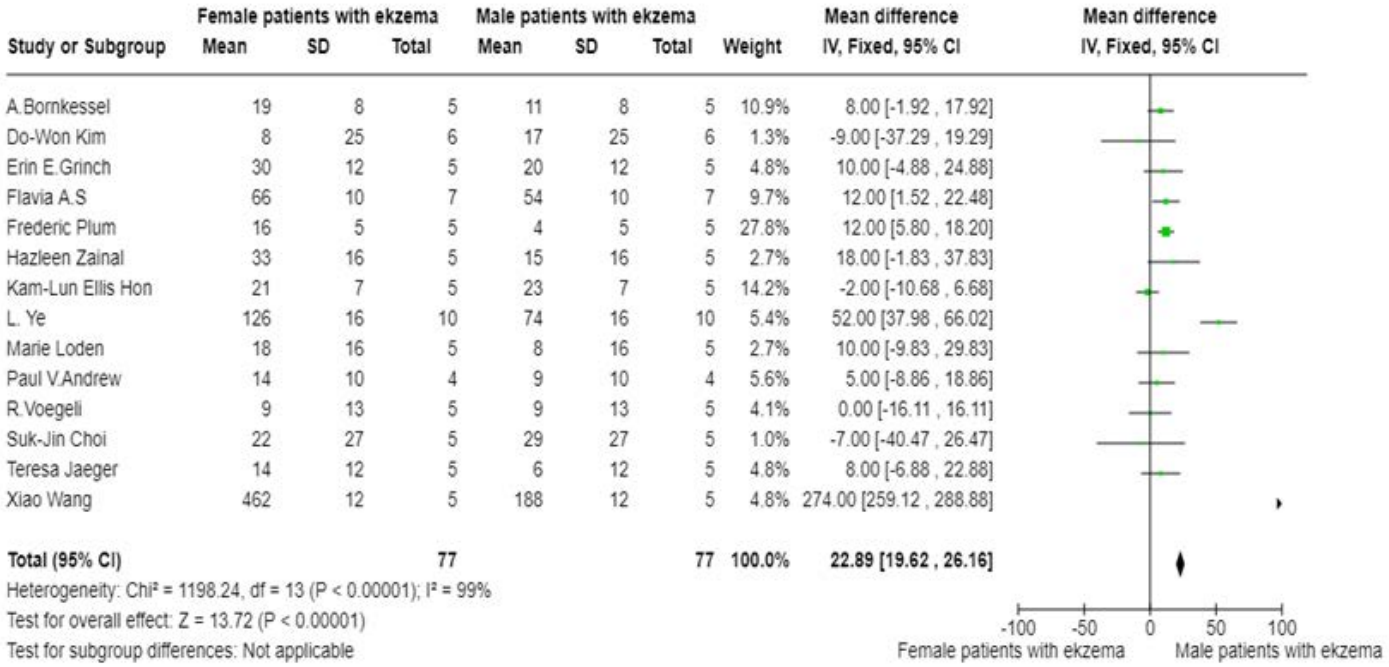


***Figure 2.*** *Comparison analysis of TEWL levels between male and female patients with eczema.*

***Table 1.*** *Characteristics of included studies, TEWL rates among eczema patients, and quality assessment of publication.*

| First autor, year | Country | Continent | Instrument Used | Study Design |
|---|---|---|---|---|
| 1. Xiaohua Wang, 2020 | China | East Asia | 1. GPskin Barrier® (GPower Inc., Seoul, South Korea), portable skin pH meter | cross-sectional |
| 2. Ben Wang, 2018 | China | East Asia | 2. pH value, decreased water content, elevated TEWL, and impaired integrity of the stratum corneum | cohort |
| 3. R. Voegeli, 2009 | Germany | Europe | 3. CR 300, PH 905, CM825, Standard D-Squame, SquameScanTM 850A | cohort |
| 4. Kam-lun Ellis Hon, 2008 | China | East Asia | 4. CM 825, TM 210, NESS, SCORAD index, CDLQI | cohort |
| 5. Hazleen Zainal, 2019 | Malaysia | SouthEast Asia | 5. Hanna Instruments H199181 pH meter, TEWL was measured using Tewameter TM300, and hydration measured using DermaLab Combo | cross-sectional |
| 6. L. Ye, 2018 | China | East Asia | 6. Corneometer® CM 825 and Tewameter® TM300, VapoMeter SWL4001TJ | cross-sectional |
| A. Bornkessel, 2005 | Germany | Europe | Corneometer CM 825, skin-pH-meter PH 900, e Tewameter TM 300, thermometer, D-Squames | cohort |
| 7. Paul V. Andrew, 2024 | UK | Europe | 7. Corneometer CM825, AquaFlux AF200, Skin-pH-Meter 905, D-Squame scan 850A, Mexameter MK18 | cohort |
| 8. Teresa Jaeger, 2015 | Belgium | Europe | 8. Corneometer (Courage and Khazaka electronic GmbH, Cologne, Germany), vapometer (Delfin Technologies, Kuopio, Finland), pH meter (Courage and Khazaka electronic GmbH, Cologne, Germany) | cohort |
| 9. Frederik Plum, 2020 | Denmark | Europe | 9. H-18049625, VD-2019-15, DermaLab Combo | cross-sectional |
| 10. Erin E. Grinich, 2021 | USA | America | 10. Corneometer CM 825, F 200 Evaporimeter | cohort |
| 11. Marie Loden, 1992 | Sweden | Europe | 11. Corneometer SM H20, Evaporlmeter EP1 | cohort |
| 12. Suk-Jin Choi, 2003 | South Korea | East Asia | 12. Tewameter TM210, CM 820 | cohort |
| 13. Do-Won Kim, 2006 | South Korea | East Asia | 13. SM810, CM825, pH900 | cohort |
| 14. Flavia A.S, 2012 | Brazil | South America | 14. Corneometer MPA 580, Tewameter TM300 | cohort |

***Table 2.*** *Information about the studies included in the meta-analysis.*

| Study year | Number of patients | Female patients with eczema | Male patients with eczema | Age categories | Average age | Average TEWL g/(m2h) | Average Ph |
|---|---|---|---|---|---|---|---|
| Xiaohua Wang, 2020 | 650 | 462 | 188 | Adult | 36.7 ± 0.46 | 12.4±1.3 | 5.0±0.5 |
| Ben Wang, 2018 | 30 | 19 | 11 | Middle age | 50 | 28.82±7.52 | 5.80±0.41 |
| R.Voegeli, 2009 | 18 | - | - | Adult | 23-31.2 | 12.48 ± 3.74 | 5.32 ± 0.68 |
| Kam-lun Ellis Hon, 2008 | 44 | 21 | 23 | Children | 11.5 ± 4.6 | 7.4 ± 2.9 | 5.1 ± 2.4 |
| Hazleen Zainal, 2019 | 48 | 33 | 15 | Adult | 28.46 ± 12.07 | 16.34 | 5.33 |
| L.Ye, 2018 | 200 | 126 | 74 | Middle age | 45.24 | 16.35 | 9.5 |
| A.Bornkessel, 2005 | 30 | 19 | 11 | Adult | 29.13 | 8.11±1.2 | 4.82 |
| Paul.V.Andrew, 2024 | 23 | 14 | 9 | Adult | 38 ± 15 | 10.44 ± 3.18 | 4.49 ± 0.38 |
| Teresa Jaeger, 2015 | 20 | 14 | 6 | Adult | 36.85 | 12.23 | 5.42 |
| Frederik Plum, 2020 | 20 | 16 | 4 | Adult | 25.9 | 4.90 | 5.25 |
| Erin E.Grinch, 2021 | 50 | 30 | 20 | Adult | 29.1 | 12 | 5.25 |
| Marie Loden, 1992 | 26 | 9 | 2 | Adult | 29 ± 8 | 16.3±0.8 | 5.1±1.3 |
| Suk-Jin Choi, 2003 | 51 | 22 | 29 | Children | 8.877 | 26.7 | 5.2 |
| Do-Won Kim, 2006 | 25 | 8 | 17 | Adult | 20.5 | 25.14 | 5.568 |
| Flavia A.S, 2012 | 120 | 66 | 54 | Adult | 22.1 | 10.2 | 7.0±0.6 |

first week of life predicted a higher risk of atopic dermatitis later in life [15]. Similarly, TEWL scores predicted psoriasis recurrence, i.e., psoriasis may recur earlier in subjects with higher TEWL scores [12,16]. TEWL was measured using a standardised method with non-invasive devices, such as the Vapo Meter, SW-4002 or Tewameter TM300®.

We also surmise from most of the publications studied that the role of epidermal permeability dysfunction could serve as an indirect indicator in predicting the risk of developing eczema, as TEWL scores were higher in measurements performed on affected or adjacent areas and on unaffected skin areas in subjects with eczema. Studies demonstrating a significant increase in TEWL on intact skin of eczema patients have been attributed to impaired maturation of lamellar cells associated with a genetic predisposition to high protease production, leading to early destruction of stratum corneum desmosomes and subsequent disruption of the epidermal barrier [17]. Disruption of barrier function promotes exposure to antigens and other environmental stimuli, so that interleukins and cytokines are activated, leading to increased. In addition, studies have identified the importance of measuring the barrier function of epidermal permeability in the effectiveness of therapeutic action not only for eczema but also for some skin diseases such as atopic dermatitis, psoriasis [18-22].

In atopic dermatitis (AD), TEWL was elevated in both normal-looking skin and in affected or dry skin. In dermatitis in the active phase, TEWL values increased and gradually decreased during clinical improvement [23]. Assessing skin barrier function in longitudinal dimension during therapy, measuring TEWL and percutaneous absorption of hydrocortisone, found that there was rapid improvement during treatment. The water content of the stratum corneum is also important for maintaining skin barrier function. The minimum water content of the stratum corneum to maintain intact skin is about 10%. The water content of normal skin is 15-40% [24,25]. Dry skin in AD showed reduced water content in the stratum corneum, in contrast to normal skin or normal looking skin in AD [26]. Barrier restoration strategies delay relapses or improve eczema and other skin diseases, such as atopic dermatitis, with defective permeability barrier being risk factors for eczema [12,27]. The difference in eczema prevalence between male and female patients was statistically significant as females had higher TEWL [12].

Analyses of the studies included in our meta-analysis showed that changes in TEWL levels are most often work-related. In some observational studies on gender differences in TEWL rates, differences in eczema prevalence between men and women are likely because they tend to have different occupations that may influence the development of eczema [12]. Neither prior personal nor family history of allergy was associated with the prevalence of eczema, but certain occupations and frequent contact with disinfectants were independently associated with the incidence of hand eczema. Both skin surface pH and TEWL scores differed significantly between normal control groups and subjects with active hand eczema or a prior history of hand eczema [12]. In addition, when comparing the prevalence of eczema in both sexes, female patients had a statistically higher risk of developing eczema. We hypothesize that the higher TEWL observed in patients with eczema may be explained by hormonal imbalances and the fact that eczema affects adolescents and young adults at a time when they are more likely to be concerned about their health and body and more susceptible to public opinion.

When comparing patients between male and female sexes, TEWL levels and pH showed a small correlation of eczema prevalence per level higher in females than in males [28-30]. The higher prevalence of elevated TEWL levels in patients with eczema may be explained by the fact that most of the studies included in this meta-analysis were conducted in Asian and European countries. Comparison of the incidence in patients according to their continent of residence showed that hand eczema is a common dermatosis in the United States and Europe, information on the prevalence of hand eczema in China is limited. The lifetime prevalence of hand eczema was 9.7%, while the point prevalence was 5.4% [12,31].

Also, aqueous capacitance is a widely used method that assesses stratum corneum and skin barrier function, and skin pH is a useful method for assessing skin barrier function [32,33]. Skin has an acidic pH, which is important for maintaining skin barrier homeostasis, and an alkaline pH causes or exacerbates disease. Recovery of skin barrier function after disruption is normal at acidic pH, but recovery is difficult at neutral or alkaline pH. Skin pH is known to be elevated in AD, eczema, although no statistical correlation with clinical severity has been described, but skin pH is above normal, and alkaline pH may be an exacerbating factor [34]. Since skin pH can be influenced by many endogenous factors such as skin moisture, age and genetic predisposition, as well as exogenous factors such as detergents and cosmetics, the pH value can be both a cause and a result of epidermal abnormalities [35,36]. Given the important role of pH in the regulation of skin barrier function [36,37] and the likely involvement of skin barrier dysfunction in the pathogenesis of CE, we hypothesize that elevated skin pH contributes to skin barrier dysfunction in patients with CE.

This meta-analysis included 15 publications involving 1441 patients, and the authors found that approximately one in three people with eczema had elevated TEWL levels. In the pathophysiology of this disease, a defect in the skin barrier is associated with decreased ceramide levels and profilaggrin production, leading to greater TEWL and increased susceptibility to aggression, causing inflammation.

Among the publications studied, biophysical properties of non-eczematous skin in atopic and non-atopic people were characterized by localization in specific areas using non-invasive physical methods with different instruments [38,39].

The areas studied included the widespread localization of the back of the hand, the palm surface of the forearm and the lower back, TEWL was significantly increased in all areas in atopic patients. Higher TEWL was found in the hands than in the other areas studied. This could be due to frequent exposure to water and detergents, which may have disrupted the skin barrier. In addition, in some areas of normal skin, TEWL tended to increase with increasing capacitance. A possible reason for this could be that an increase in skin moisture caused, for example, by occlusion reduced the diffusion resistance of the stratum corneum [40,41].

In the reviewed studies, the authors repeatedly emphasized the heterogeneity of the study groups and instruments used and reported that the overall prevalence of TEWL ranged from 23% to 56%. There are several differences between these studies and our work, which are mainly related to the main objective. While we focused exclusively on the level of TEWL, Second, we included more studies in our meta-analysis due to the two-year interval between the two studies, during which a number of additional publications appeared.

Our study has several strengths and limitations. First, we tried to minimize publication bias by strictly adhering to the rules for selecting studies for systematic reviews. Second, our meta-analysis includes studies using different non-invasive physical methods instruments from different countries and regions of the world. Third, our study focuses on assessing the prevalence of TEWL levels among eczema patients. However, there are limitations and the main one is moderate heterogeneity as a result of broad inclusion criteria. Therefore, the results of our study should be generalized with caution. Secondly, the wide range of measuring instruments may have affected the results of the study. Finally, we took into account age and sex characteristics, localization of the skin process, course or severity of the disease, occupational gender differences and sociocultural characteristics, which may also have contributed to the heterogeneity of our meta-analysis.

## Conclusion.

Defects in the epidermal permeable barrier can cause cutaneous inflammation. Conversely, improvement of the epidermal permeable barrier may prevent and alleviate some inflammatory dermatoses. We found that the prevalence of TEWL elevation among eczema patients was 67.7%. The lack of statistical significance may be due to the wide range of screening tools, suggesting the need for their validation in the field of dermatology. In addition, more qualitative observational studies would be desirable to establish clearer associations between different aspects of TEWL levels in patients with eczema. In addition, dermatologists working with eczema patients should be aware of their TEWL changes and be able to envisage corrective interventions to alleviate the burden of their disease.

## Author Contributions.

Conceptualization, T.I., T.A. and G.B.; methodology, D.A. and G.T.; investigation, T.I. and A.I.; writing—original draft preparation, I.E.A and A.S.; writing— review and editing, T.I., T.A, G.B., D.A., G.T. and I.E.A.; visualization, A.I., and A.S.; supervision, T.I. and A.S. All authors have read and agreed to the published version of the manuscript.


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## Conflicts of Interest.

The authors declare that there are no conflicts of interest.

## Search Strategy.

Standardized search strategy for Review of the Literature on Anxiety in patients with vitiligo. Search fields: Title and Abstract only Search terms: ["Vitiligo"(MeSH)] AND ["Anxiety"(MeSH) OR "Anxiety Disorder" (MeSH) OR Anx* (title/abstract;TIAB)].

## Abbreviations.

The following abbreviations are used in this manuscript:

**TEWL:** Transepidermal Water Loss

**PRISMA:** Reporting Elements for Systematic Reviews and Meta-Analyses

**OR:** Odds Ratio

**CI:** Confidence Interval

**SES:** Corresponding Standard Errors.

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