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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

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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Содержание:

DETERMINANTS OF SPINAL ANKYLOSIS IN KAZAKH PATIENTS WITH ANKYLOSING SPONDYLITIS: A CROSS-SECTIONAL STUDY

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Abstract.

Background: Progressive spinal ankylosis is the leading cause of disability in ankylosing spondylitis (AS), resulting in severe restriction and eventual loss of spinal mobility.

Objective: To develop and evaluate predictive models for lumbar spine ankylosis in Kazakh patients with AS.

Methods: This observational cross-sectional study included 70 patients with confirmed AS. Clinical assessment included disease history and standardized indices (BASDAI, BASFI, BASMI, ASDAS). Laboratory tests comprised complete blood count, biochemistry, CRP, and HLA-B27 genotyping. Predictive modeling was performed using multivariate binary logistic regression and MANOVA.

Results: Lumbar spine ankylosis was present in 51.4% of patients. Multivariate logistic regression identified three independent predictors: occupational hazard exposure, longer disease duration, and history of spinal trauma. The model showed excellent predictive performance (AUC = 0.917, 95% CI 0.856–0.978; sensitivity 80%, specificity 87%). Significant interactions for cervical involvement were found between smoking and peripheral arthritis, and between family history of AS and psoriasis.

Conclusion: Occupational hazards, disease duration, and spinal trauma are key independent predictors of lumbar ankylosis in Kazakh AS patients. The developed model demonstrates high predictive accuracy and supports the importance of modifiable environmental factors in structural progression of AS.

Key words. Ankylosing spondylitis, spinal ankylosis, predictors, occupational hazards, logistic regression.

Introduction.

Ankylosing spondylitis (AS) is a chronic autoimmune inflammatory disease of the spine that results in high rates of disability and dysfunction. Due to the early disability of patients and the significant financial burden that AS imposes on the healthcare system and the economy - not only in Kazakhstan, but around the world - it is an important issue for modern public health. According to a systematic review and meta-analysis by Malinowski KP et al, average annual indirect costs per AS patient vary from $661 to $45,954 in different regions of the world, averaging $6455 per patient per year worldwide [1].

Several authors claim that the prevalence of AS is currently increasing, especially in young adults [2,3]. Due to the chronic nature of the disease, the preservation of the patient's ability to work is a key point in order to maintain the patient's quality of life at an adequate level. As a result, regardless of country of residence, people with AS have very high levels of disability, according to the literature review by Nikiphorou E et al [4]. Patients' quality of life and ability to work are significantly reduced by conditions such as osteoporosis, cardiovascular pathology, infections, oncology, fibromyalgia and depression [5-11]. However, the primary pathogenetic component contributing to the impairment of AS patients is undoubtedly the increasing ankylosis of the spine, which significantly reduces the mobility of the back to the point of complete immobility. Many studies have shown that these changes are a major indicator of a potentially hazardous decrease in well-being and loss of ability to care for oneself [12-17].

To date, methods for predicting this condition have only been described in rare situations in the literature. Some studies have used laboratory markers, while others have used indicators of disease activity such as smoking history, gender and the presence of initial lesions. However, the authors point out the limitations of their research and the heterogeneity of the data obtained. It has been suggested that this may be due to the ethnic nature of the disease [18-22]. In this context, the aim of our study was to investigate multivariable associations with spine ankylosis in individuals with ankylosing spondylitis (AS) in the Kazakh population.

Materials and Methods.

We conducted a single-stage, cross-sectional, observational, analytical study in accordance with the Declaration of Helsinki, and approved by Ethics Committee of Medical University Astana (protocol #1 of 26.01.2023). Between 02.01.2023 and 01.12.2023, we continuously studied all 132 patients registered in the of Astana City Hospital №2 with a confirmed diagnosis of ankylosing spondylitis according to the modified New York criteria for ankylosing spondylitis. Sixty-two individuals were excluded from the study sample based on the following exclusion criteria: age under 18 and over 62, serious comorbid somatic and/or psychiatric illness, breastfeeding or pregnancy.

After an interview explaining the aims and design of the study, the remaining 70 participants in the sample were asked to sign an informed consent form to participate in the research study factors.

All participants were seen by a rheumatologist. During the examination, we collected complaints and medical history to identify risk factors for the development of the disease and potential triggers. When the medical history was taken, data on hereditary aggravation of AS and other diseases - psoriasis, inflammatory bowel disease - were taken into account. The following were also taken into account: infectious diseases, spinal contusions, including falls from a height of one's own height or more onto one's back (falls from a horse, from a stepladder, while skiing) and surgical interventions, the presence of allergic aggravations. Data on bad habits and occupational hazards (physical labour in conditions of low temperature for more than

one year) were recorded in individual cards. Information on the onset of the disease was taken into account when collecting the medical history. This included the type of joint syndrome lesion at disease onset, the patient's age at the time of AS manifestation, the duration of the disease, the patient's subjective association of the disease with any endogenous or exogenous trigger, and the interval between disease onset and AS diagnosis.

Clinical data were obtained through objective examination by a rheumatologist. Spinal and joint function was assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI). Occiput-to-wall distance, a component of the BASMI, was measured as a continuous variable to evaluate cervical spine mobility and forward posture. This simple clinical measure was used as a surrogate marker for cervical ankylosis because it is easily performed during routine physical examination without the need for imaging, reflects functional impairment due to reduced mobility, and is part of the validated BASMI score [23,24].

Extra-articular manifestations and complications were recorded. Disease activity was assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS). All patients underwent standard laboratory testing, including complete blood count (hemoglobin, erythrocytes, platelets, leukocytes, ESR by Westergren method), blood biochemistry (ALT, AST, total protein, creatinine, cholesterol, glucose, CRP), serology for brucellosis (IgG and IgM), and HLA-B27 genotyping.

Stages of ankylosis were classified according to the Kellgren system using MRI scans of the spine and sacroiliac joints performed within the last year.

Statistical analysis of the measurements was performed using IBM SPSS Statistics 21 software. As the distribution of quantitative characteristics was non-Gaussian, quantiles (25; 75) and median (Me) are used to represent these variables. Qualitative data are presented as absolute numbers and percentages. Confidence interval analysis software was used to obtain the 95% confidence interval (CI) for frequencies and fractions. The non-parametric Mann-Whitney test was used to assess the significance of differences in means. Nominal data were compared using conjugated tables for four-way tables with calculation of Pearson's chi-squared test, Fisher's two-sided exact test. Multivariate analysis was also performed by constructing binary logistic regression with calculation of constants and B regression coefficient. Sensitivity and specificity of diagnostic methods were assessed by constructing characteristic ROC curves, with calculation of the AUC area. In addition, a decision tree was constructed using the diagnostic accuracy, specificity and sensitivity calculations.

Results.

Demographic and clinical characteristics by HLA-B27 status:

To explore potential differences in disease presentation and progression, a comparative analysis was performed between HLA-B27-positive (n = 57) and HLA-B27-negative (n = 13) patients with ankylosing spondylitis (AS). The HLA-B27-positive group represented the majority of the cohort (81.4%), consistent with the well-established predominance of HLA-B27 positivity in most AS populations.

No statistically significant differences were observed between the two groups with respect to key demographic variables, including gender distribution, mean age at study inclusion, ethnicity (predominantly Kazakh in both groups), body mass index (BMI), or height-weight indices. Likewise, lifestyle factors such as current or past alcohol consumption and smoking habits did not differ significantly between HLA-B27-positive and HLA-B27-negative patients. Family history of AS or related HLA-B27-associated conditions (psoriasis and inflammatory bowel disease [IBD]) was also comparable across groups, as documented from detailed medical records. Furthermore, history of spinal trauma or prior spinal surgery did not contribute to observable differences in disease progression patterns between the subgroups.

However, a notable and statistically significant difference emerged in exposure to occupational hazards ($\chi^2 = 4.463$, df = 1, p = 0.035; $\varphi = 0.252$, OR = 4.950, 95% CI 1.006–24.367). Patients in the HLA-B27-positive group reported occupational hazard exposure (primarily heavy physical labor in low-temperature conditions for more than one year) substantially more frequently than those in the HLA-B27-negative group.

Age at disease onset was markedly lower in HLA-B27-positive patients (median 23 years, interquartile range [IQR] 19–31) compared to HLA-B27-negative patients (median 30 years, IQR 25–37; Mann-Whitney U = 230, Z = -2.125, p = 0.034). Disease duration at the time of study inclusion was also significantly longer in the HLA-B27-positive group (median 14 years, IQR 7.5–21.5) than in the HLA-B27-negative group (median 10 years, IQR 1.5–10.5; U = 196.5, Z = -2.631, p = 0.009). Time from symptom onset to confirmed AS diagnosis showed a tendency toward being shorter in HLA-B27-positive patients (median 1 year, IQR 1–3.5 vs. 3 years, IQR 1–10; p = 0.075), although this difference did not reach statistical significance. A detailed comparative overview of demographic, anamnestic, and selected clinical characteristics is provided in Table 1.

Differences were also apparent in the history of infectious diseases. Intestinal infections were significantly more common in the HLA-B27-negative group ($\chi^2 = 11.430$, df = 1, p = 0.003; $\varphi = -0.404$, OR = 4.385, 95% CI 1.861–10.332). Similarly, a history of Epstein-Barr virus infection was reported exclusively in the HLA-B27-negative subgroup (Fisher's exact test, two-tailed p = 0.089). Other infections (herpes, cytomegalovirus, viral hepatitis, tuberculosis, Helicobacter pylori, urogenital infections) showed no significant between-group differences.

No significant differences were detected between the HLA-B27-positive and HLA-B27-negative subgroups in terms of clinical disease stages, presence or severity of peripheral arthritis, extra-articular manifestations (e.g., uveitis, enthesitis), disease activity indices (BASDAI and ASDAS), functional impairment assessed by BASFI, or spinal and hip mobility evaluated by BASMI. These findings are summarized in Table 2.

In the overall study cohort, several rare but serious complications of AS were absent, including secondary systemic amyloidosis, aortic coarctation, cardiac arrhythmias, syndesmophyte fractures, atlantoaxial subluxation, and temporomandibular joint ankylosis. However, lumbar spine

Table 1. *Demographic, anamnestic and clinical characteristics of patients with ankylosing spondylitis according to HLA-B27 status.*

Characteristic	HLA-B27+ (n=57)	HLA-B27– (n=13)	p-value
Age, years	40 [32–54]	38 [34.5–42]	0.634
BMI, kg/m²	25.3 [21.7–30.0]	26.1 [24.3–27.3]	0.786
Smoking index	6.1 [2.5–12.0]	4.2 [1.8–9.5]	0.942
Duration of AS, years	14 [7.5–21.5]	10 [1.5–10.5]	0.009*
Age at onset of AS, years	23 [19–31]	30 [25–37]	0.034*
Time from onset to diagnosis, years	1 [1–3.5]	3 [1–10]	0.075
Nationality, n (%)			
Kazakhs	48 (84.2)	11 (84.6)	1.000
Not Kazakhs	9 (15.8)	2 (15.4)	
Gender, n (%)			
Male	47 (82.5)	9 (69.2)	0.227
Female	10 (17.5)	4 (30.8)	
Smoking, n (%)	24 (42.1)	5 (38.5)	0.810
Alcohol consumption, n (%)	29 (50.9)	9 (69.2)	0.231
Occupational hazard exposure, n (%)	27 (47.4)	2 (15.4)	0.035*
History of spinal trauma, n (%)	32 (56.1)	9 (69.2)	0.387
History of operations, n (%)	35 (61.4)	9 (69.2)	0.754
AS hereditary burden, n (%)	12 (21.1)	2 (15.4)	1.000
Psoriasis hereditary burden, n (%)	6 (10.5)	2 (15.4)	0.636
IBD hereditary burden, n (%)	1 (1.8)	0 (0)	1.000
History of infectious diseases, n (%)			
Herpes	6 (10.5)	4 (30.8)	0.081
Cytomegalovirus (CMV)	1 (1.8)	1 (7.7)	0.339
Epstein-Barr virus	0 (0)	2 (15.4)	0.089†
Viral hepatitis	7 (12.3)	2 (15.4)	0.493
Tuberculosis	2 (3.5)	0 (0)	1.000
Helicobacter pylori	4 (7.0)	1 (7.7)	1.000
Urogenital infection	7 (12.3)	2 (15.4)	1.000
Intestinal infection	6 (10.5)	4 (30.8)	0.003*

BMI — Body Mass Index, IBD — Inflammatory Bowel Disease, Quantitative data are presented as median [Q1–Q3]. Categorical data are presented as n (%). p-values were calculated using Mann–Whitney U test (for quantitative variables) or chi-square / †Fisher's exact test (for categorical variables). *$p < 0.05$ (statistically significant).

ankylosis emerged as a highly prevalent complication, affecting 36 patients (51.4% of the cohort), underscoring its clinical importance in this population.

Multivariate logistic regression analysis for lumbar spine ankylosis:

To identify independent factors associated with an increased likelihood of lumbar spine ankylosis, multivariate binary logistic regression analysis was conducted. The following candidate variables were entered into the model development process: age at study inclusion, HLA-B27 status, family history of AS, psoriasis and/or IBD, smoking status, occupational hazard exposure, history of infections, prior spinal contusions/trauma, disease duration, and diagnostic delay (defined as the time interval from symptom onset to confirmed AS diagnosis). Full details of candidate variables are presented in Table 3.

A parsimonious and clinically interpretable model was successfully constructed using only three predictor variables. The probability of developing lumbar ankylosis was estimated using the logistic function:

$p = 1 / (1 + e^{(-z)})$, where $z = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3$

(Equation 1)

Performance of the model was evaluated using receiver operating characteristic (ROC) curve analysis of the predicted probabilities. The area under the curve (AUC) was 0.917 ($p < 0.0001$, 95% CI 0.856–0.978), indicating excellent discriminatory ability. In the predicted subgroup, AUC reached 0.816 ($p < 0.0001$, 95% CI 0.711–0.921), with sensitivity of 80%, specificity of 87%, positive predictive value of 37%, negative predictive value of 98%, and overall diagnostic accuracy of 87%.

Multivariable analysis of factors influencing cervical spine involvement:

In the subsequent stage of the analysis, more advanced statistical methods were applied to investigate factors potentially contributing to the development and severity of cervical spine ankylosis in patients with AS. Cervical spine ankylosis was selected as the primary outcome variable. Multivariable analysis of variance (MANOVA) was employed, with occiput-to-wall distance (measured in centimeters) serving as the continuous dependent variable. This parameter reflects the degree of forward stoop and restriction of cervical extension due to progressive ankylosis.

The independent variables were dichotomous and included: sex, HLA-B27 status, smoking history, family history of ankylosing spondylitis, psoriasis, inflammatory bowel disease (IBD), presence of occupational hazards, history of trauma,

Table 2. *Comparative analysis of clinical characteristics of the studied subgroups according to the HLA-B27 gene.*

Characteristic		HLAB27+ (N=57)		HLAB27- (N=13)		The probability level, p
		Me, n/%	Q1-Q3 95% CI	Me, n/%	Q1-Q3 95% CI	
Clinical stages of disease	Early	0	-	3/23.1	8.2-50.3	$\chi2$=13.743 df=1 p=0.005
	Progressive	7/12.3	6.1-23.2	2/15.4	4.3-42.2	0.763
	Late	50/87.7	76.8-93.9	8/61.5	35.5-82.3	$\chi2$=5.108 df=1 p=0.039
Peripheral manifestations		29/50.9	38.3-63.4	7/53.8	29.1-76.8	0.847
	Peripheral arthritis	23/40.4	28.6-53.3	3/23.1	8.2-50.3	0.345
	Enthesitis	20/35.1	24-48.1	6/46.2	23.2-70.9	0.531
	Dactylitis	7/12.3	6.1-23.2	2/15.4	4.3-42.2	0.670
Extra-articular manifestations		17/29.8	19.5-42.7	3/23.1	8.2-50.3	0.744
	Uveitis	10/17.5	9.8-29.4	1/7.7	1.4-33.3	0.676
	IBD	1/1.8	0.3-9.3	1/7.7	1.4-33.3	0.339
	Psoriasis	7/12.3	6.1-23.2	1/7.7	1.4-33.3	1.0
BASDAI		3.85	1.65-6.0	3.5	2.36-6.68	0.757
BASFI		2.1	0.3-5.2	1	0.35-3.15	0.183
ASDAS CRP		2.5	1.6-3.2	2.35	1.7-3.72	0.883
ESR		21	8-37	17.5	15.25-30	0.935
CRP		4.2	1.4-17.4	2.75	0.8-6	0.339
Brucellosis Ig G		0.25	0.2-0.36	0.26	0.2-2.17	0.535
Brucellosis Ig M		0.11	0.1-0.13	0.12	0.09-0.54	0.263
Hepatitis B		0.37	0.31-0.41	0.34	0.28-0.35	0.058
Hepatitis C		0.09	0.08-0.11	0.09	0.07-0.12	0.808

IBD — Inflammatory Bowel Disease, BASDAI — Bath Ankylosing Spondylitis Disease Activity Index, BASFI — Bath Ankylosing Spondylitis Functional Index, ASDAS-CRP — Ankylosing Spondylitis Disease Activity Score with C-reactive protein, ESR — Erythrocyte Sedimentation Rate, CRP — C-reactive protein.

Table 3. *Covariates included in the logistic equation.*

Covariates		Regression coefficient, B	P value	EXP B	95% CI
X1	Occupational hazard	1,478	0,045	4,382	1,030 - 18,638
X2	Duration of disease	0,278	0,000	1,321	1,130 - 1,544
X3	Contusions	2,050	0,020	7,765	1,390 - 43,375
B	Constant	-4,915	0,000	0,007	

Table 4. *Evaluation of statistically significant interaction effects on occiput-to-wall distance (MANOVA results).*

№	Interacting factors	Assessment of the effect on occiput-to-wall distance		Level of significance of factor interaction
		η^2, %	p	
1	Peripheral arthritis	1,2	0,378	0,025
	Smoking	7,2	0,027	
2	Family history of ankylosing AS	0,6	0,527	0,05
	Psoriasis	0,8	0,476	

peripheral arthritis, enthesitis, dactylitis, uveitis, IBD, psoriasis, diagnostic delay exceeding 2 years, and disease onset in childhood. Results of the MANOVA are detailed in Table 4, with significant interaction effects summarized in Table 5.

Isolated peripheral arthritis did not demonstrate a significant association with increased risk or severity of cervical ankylosis. However, the combination of peripheral arthritis and a positive smoking history showed a statistically significant interaction ($p = 0.025$). Smoking contributed substantially more to the variance in occiput-to-wall distance (partial $\eta^2 = 7.2\%$) than peripheral arthritis alone ($\eta^2 = 1.2\%$), while their combined effect accounted for $\eta^2 = 7.4\%$.

An additional significant interaction was observed between family history of AS and the presence of psoriasis in the patient ($p = 0.05$). Neither factor alone reached statistical significance, but their interaction was associated with greater cervical involvement ($\eta^2 = 0.6\%$ for family history of AS, $\eta^2 = 0.8\%$ for psoriasis, and $\eta^2 = 5.5\%$ for the interaction term).

Although occupational hazard exposure did not achieve statistical significance when combined with other factors, its isolated main effect demonstrated a notable tendency toward association with increased severity of cervical involvement (partial $\eta^2 = 10\%$). This finding suggests that occupational hazards, particularly prolonged exposure to physical stress and low temperatures, may represent an under-recognized environmental contributor to axial ankylosis progression in AS and merit further prospective investigation.

Discussion.

Undoubtedly, developing reliable predictive tools for lumbar ankylosis in patients with ankylosing spondylitis (AS) remains a major challenge in disease management, as does the

Table 5. *Pairwise p-values for interactions between dichotomous factors (upper triangle matrix).*

Factor	Sex	HLA-B27	Smoking	Fam. hist. AS	Fam. hist. Ps	Fam. hist. IBD	Occ. hazards	Trauma	Periph. arthr.	Enthesitis	Dactylitis	Uveitis	IBD	Psoriasis	Diag. delay	Childh. onset
Sex	—	0.654	0.288	0.773	0.964	1.000	0.816	0.814	0.610	0.497	0.486	0.704	0.630	0.784	0.694	0.661
HLA-B27		—	0.117	0.711	0.635	0.886	0.348	0.656	0.468	0.434	0.682	0.805	0.892	0.920	0.402	0.698
Smoking			—	0.451	0.692	0.774	0.960	0.066	**0.025***	0.225	0.384	0.736	1.000	0.296	0.698	1.000
Family history of AS				—	0.135	1.000	0.075	0.872	0.489	0.239	0.845	0.409	1.000	**0.05***	0.088	1.000
Family history of psoriasis					—	1.000	0.459	0.177	0.291	0.761	0.347	1.000	0.867	0.133	0.203	1.000
Family history of IBD						—	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Occupational hazards							—	0.523	0.990	0.223	0.333	0.480	0.503	0.503	0.964	0.716
History of trauma								—	0.491	0.444	0.786	0.959	1.000	0.661	0.700	0.851
Peripheral arthritis									—	0.572	0.845	0.787	0.684	0.083	0.059	1.000
Enthesitis										—	0.403	0.734	0.794	0.919	0.687	1.000
Dactylitis											—	0.136	0.796	0.370	0.711	1.000
Uveitis												—	1.000	1.000	1.000	1.000
IBD													—	1.000	0.056	1.000
Psoriasis														—	0.966	1.000
Diagnostic delay															—	1.000
Childhood onset																—

identification of factors that may contribute to its development.

In our study, we applied the block method for modelling. Given the well-recognized association of male gender with a more severe disease course, it was excluded from the model at the outset and not evaluated as a potential factor associated with ankylosis. Although HLA-B27 positivity was present in 54 of 70 participants, it was not incorporated into the model and did not meaningfully influence the adjusted R^2 value.

Several studies have explored potential laboratory indicators of ankylosis progression. Various biomarkers, such as calprotectin, vascular endothelial growth factor, C2M, C3M, and citrullinated metalloproteinase-degraded fragments of vimentin, have been linked to disease activity in prior research [12,13,25,15,16]. However, the search for reliable and specific laboratory markers to predict disease progression has not yet yielded a biomarker with strong clinical utility, and many of these markers have limited practicality in routine clinical settings. C-reactive protein (CRP) has been associated with spinal ankylosis in some reports [26], although it remains a non-specific marker of inflammation.

Due to important limitations of the present cross-sectional design — including a relatively short observation period in some patients and the fact that many already had lumbar ankylosis at the time of inclusion — we were unable to incorporate laboratory markers into the multivariable associations. Current values of these markers did not appear to function as objective predictors in this snapshot assessment.

Our analysis therefore focused on aspects of disease onset and medical history. Disease duration appeared to play a notable role in the observed outcomes among our patients, although findings on this association vary across the literature [16,26,27]. Ethnic differences in disease course and limited access to biologic therapies in our setting may partly explain this observation.

Our findings are consistent with previous reports suggesting that smoking may contribute to more pronounced spinal ankylosis, as several studies have indicated an association between smoking and accelerated disease progression or poorer outcomes [27-30].

One of the principal findings of this study is that occupational hazard exposure, specifically intensive physical labor in low-temperature conditions, was significantly more prevalent in the HLA-B27-positive cohort and demonstrated a strong association with lumbar ankylosis in the multivariable model. This observation is of considerable clinical importance.

Although the precise mechanisms linking chronic cold exposure to spinal ossification are not yet fully understood, occupational cold stress has been independently associated with an increased risk of musculoskeletal disorders, including low back pain and radiculopathy [31]. When combined with repetitive mechanical loading, cold-induced tissue changes — such as vasoconstriction, differential thermal contraction, and microtrauma — are likely to exacerbate enthesitis, the hallmark lesion of AS. Foundational biomechanical studies have shown that sustained mechanical strain at entheseal sites promotes both local inflammation and pathological new bone formation via mechanotransduction pathways, including stromal cell activation and Erk1/2 signalling, ultimately contributing to ossification and ankylosis [32,33]. In HLA-B27-positive individuals, who already display heightened innate immune responses at entheses, these combined environmental stressors appear to accelerate progression toward structural damage.

Factors such as a history of spinal contusions and occupational hazards also emerged as relevant in our model. For instance, one

study found that 44% of AS patients in the UK recalled physical trauma as a potential trigger for disease onset, although its long-term effect on progression was not specifically examined [34,35]. This aligns with our findings regarding occupational hazards.

These characteristics are infrequently emphasized in routine assessments. We suggest that clinicians consider including a detailed inquiry into them when taking the medical history to better understand individual disease trajectories and guide patient management.

Limitations. The cross-sectional nature of this study precludes conclusions about causality or temporal prediction. In addition, the relatively small sample size (n=70) in relation to the number of variables included in the multivariable model increases the risk of overfitting, which is reflected in wide confidence intervals for some estimates. All associations identified should therefore be interpreted with caution and viewed as exploratory. The relatively advanced disease stage in many participants at inclusion further limited the ability to evaluate laboratory markers as potential predictors. Confirmation in larger prospective longitudinal studies with longer follow-up is required.

Conclusion.

This single-center cross-sectional study highlights distinct clinical and anamnestic profiles in ankylosing spondylitis (AS) patients stratified by HLA-B27 status, with earlier onset and longer disease duration observed in HLA-B27-positive individuals. Occupational hazard exposure emerged as a notable differentiator between subgroups.

These findings underscore the potential relevance of non-genetic, modifiable, and environmental exposures—such as smoking and occupational conditions—in AS progression, beyond traditional genetic markers like HLA-B27. However, given the cross-sectional design and the statistical limitations of the multivariable model (including the risk of overfitting), these results represent associations only and cannot be interpreted as prognostic factors. Incorporating a detailed assessment of these elements into routine clinical history-taking may nevertheless support more individualized risk stratification and management strategies. Further prospective studies with larger sample sizes, longer follow-up, and repeated measures are warranted to validate these associations, clarify their temporal relationships, and explore potential mechanistic links.

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Факторы, определяющие анкилоз позвоночника у казахстанских пациентов с анкилозирующим спондилитом: перекрестное исследование

Абстракт.

Актуальность: Прогрессирующий анкилоз позвоночника является основной причиной инвалидизации при анкилозирующем спондилите (АС), приводящей к серьезному ограничению и возможной потере подвижности позвоночника.

Цель: Разработать и оценить прогностические модели анкилоза поясничного отдела позвоночника у казахстанских пациентов с АС.

Методы: В это обсервационное перекрестное исследование были включены 70 пациентов с подтвержденным АС. Клиническая оценка включала сбор анамнеза заболевания и стандартизированные показатели (BASDAI, BASFI, BASMI, ASDAS). Лабораторные исследования включали полный анализ крови, биохимию, определение СРБ и генотипирование по HLA-B27. Прогностическое моделирование проводилось с использованием многомерной бинарной логистической регрессии и метода MANOVA.

Результаты: Анкилоз поясничного отдела позвоночника наблюдался у 51,4% пациентов. Многофакторная логистическая регрессия выявила три независимых предиктора: воздействие профессиональных факторов риска, более длительная продолжительность заболевания и травма позвоночника в анамнезе. Модель показала отличные прогностические характеристики (AUC = 0,917, 95% ДИ 0,856–0,978; чувствительность 80%, специфичность 87%). Были обнаружены значимые взаимосвязи в развитии поражения шейки матки между курением и периферическим артритом, а также между семейным анамнезом АС и псориазом.

Вывод: Профессиональные вредности, длительность заболевания и травма позвоночника являются ключевыми независимыми предикторами развития поясничного анкилоза у казахстанских пациентов с АС. Разработанная модель демонстрирует высокую точность прогнозирования и подтверждает важность модифицируемых факторов окружающей среды в структурном прогрессировании АС.

Ключевые слова: анкилозирующий спондилоартрит, анкилоз позвоночника, предикторы, профессиональные вредности, логистическая регрессия.

ზურგის ანკილოზის დეტერმინანტები ყაზახურ პაციენტებში ანკილოზური სპონდილიტით: განივი კვლევა

რეზიუმე

ფონს. პროგრესირებადი ხერხემლის ანკილოზი არის ანკილოზური სპონდილიტის (AS) ინვალიდობის მთავარი მიზეზი, რაც იწვევს ხერხემლის მობილობის მძიმე შეზღუდვას და საბოლოოდ დაკარგვას.

მიზანი. წელის ხერხემლის ანკილოზის პროგნოზირების მოდელების შემუშავება და შეფასება ყაზახურ პაციენტებში AS.

მეთოდები: ეს სადამკვირვებლო კვეთის კვლევა მოიცავდა 70 პაციენტს, რომლებსაც დადასტურებული ჰქონდათ როგორც. კლინიკური შეფასება მოიცავდა დაავადების ისტორიას და სტანდარტიზებულ ინდექსებს (BASDAI, BASFI, BASMI, ASDAS). ლაბორატორიული ტესტები მოიცავდა სისხლის სრულ რაოდენობას, ბიოქიმიას, CRP-ს და HLA-b27 გენოტიპებს. პროგნოზირებადი მოდელირება განხორციელდა მრავალმხრივი ბინარული ლოგისტიკური რეგრესიისა და მანოვას გამოყენებით.

შედეგები: წელის ხერხემლის ანკილოზი იყო პაციენტების 51.4% - ში. მრავალმხრივი ლოგისტიკური რეგრესიის შედეგად გამოვლინდა სამი დამოუკიდებელი პროგნოზირებელი: პროფესიული საფრთხის ექსპოზიცია, დაავადების ხანგრძლივი ხანგრძლივობა და ხერხემლის ტრავმის ისტორია. მოდელმა აჩვენა შესანიშნავი პროგნოზირებადი შესრულება (AUC = 0.917, 95% CI 0.856–0.978; მგრძნობელობა 80%, სპეციფიკა 87%). საშვილოსნოს ყელის ჩართულობის მნიშვნელოვანი ურთიერთქმედება გამოვლინდა მოწევასა და პერიფერიულ ართრიტს შორის, ასევე AS-ს ოჯახურ ისტორიასა და ფსორიაზს შორის.

დასკვნა: პროფესიული საფრთხეები, დაავადებების ხანგრძლივობა და ხერხემლის ტრავმა ყაზახურ პაციენტებში ლუმბალური ანკილოზის ძირითადი დამოუკიდებელი პროგნოზირებელია. შემუშავებული მოდელი აჩვენებს მაღალი პროგნოზირების სიზუსტეს და მხარს უჭერს მოდიფიცირებადი გარემო ფაქტორების მნიშვნელობას as-ის სტრუქტურულ პროგრესირებაში.

საკვანძო სიტყვები: ანკილოზური სპონდილიტი, ხერხემლის ანკილოზი, პრედიქტორები, პროფესიული საფრთხეები, ლოგისტიკური რეგრესია.