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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 ВИНТИ 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 ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

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. Корректур авторам не высылаются, 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 computer-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 საყურადღებო!

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, შემავსებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების 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 ფხიხლებში 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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ASSOCIATIONS OF CYTOKINE PROFILE AND EXOCRINE PANCREATIC FUNCTION WITH A SYMPTOM-BASED DEHYDRATION CATEGORY AND SEASON OF PRESENTATION IN CHRONIC PANCREATITIS: A RETROSPECTIVE STUDY

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Abstract.

Aim: To evaluate the associations of C-reactive protein (CRP), fecal elastase-1 (FE-1), interleukin-2 receptor (IL-2R), interleukin-6 (IL-6), and transforming growth factor-beta 1 (TGF- β 1) with the symptom-based dehydration category and season of presentation in chronic pancreatitis; clinical-group comparisons were secondary.

Materials and methods: Of 132 consecutive inpatient records screened in 2023–2025, 80 with complete results for the five laboratory outcomes were analyzed and 52 incomplete records were excluded; each patient contributed one observation. Unadjusted Kruskal–Wallis, Mann–Whitney U, and Spearman analyses used Holm correction. Five linear models with HC3 robust standard errors simultaneously adjusted for dehydration category, summer presentation, clinical group, age, sex, and disease duration.

Results: Unadjusted analyses associated higher dehydration category with higher CRP and IL-6 and lower FE-1. After mutual adjustment, only IL-6 remained associated with each one-category increase in dehydration (+36.94 pg/mL; 95% CI, 17.98–55.90; Holm-adjusted $p=0.0011$). Summer presentation was independently associated with higher CRP (+8.46 mg/L) and IL-6 (+44.23 pg/mL), lower FE-1 (–22.89 μ g/g), and lower TGF- β 1 (–61.12 pg/mL) (all Holm-adjusted $p<0.05$), but not IL-2R. The five outcomes did not differ across clinical groups.

Conclusion: After adjustment, dehydration category remained independently associated only with IL-6, whereas summer presentation retained associations with CRP, IL-6, FE-1, and TGF- β 1. The retrospective observational design precludes causal attribution to heat or dehydration.

Key words. Chronic pancreatitis, C-reactive protein, interleukin-6, fecal elastase-1, dehydration, season of presentation, retrospective study.

Introduction.

Chronic pancreatitis (CP) is a fibroinflammatory syndrome that develops as a pathological, sustained response to injury of the pancreatic parenchyma in individuals with genetic, metabolic, toxic, autoimmune, obstructive, or other risk factors. As the disease progresses, parenchymal atrophy, fibrosis, ductal-system deformity, pain, and exocrine and endocrine dysfunction may develop [1–17].

Activation of pancreatic stellate cells plays a central role in pancreatic fibrogenesis. Upon activation, these cells acquire a myofibroblast-like phenotype and produce excessive extracellular matrix proteins; inflammatory mediators and autocrine–paracrine signaling help maintain this process [1,3].

Interleukin-6 (IL-6) is a major mediator of the inflammatory response, whereas transforming growth factor-beta 1 (TGF- β 1) is regarded as a profibrogenic signal associated with pancreatic stellate-cell activation and collagen synthesis [18–20].

In a prospective biomarker analysis based on the PROCEED cohort, circulating IL-6 and IL-8 concentrations were higher in patients with CP than in healthy controls and increased with the addition of metabolic complications, including exocrine pancreatic dysfunction and diabetes [7]. These findings suggest that circulating cytokines may help characterize the clinical heterogeneity of CP; however, no single biomarker independently establishes disease activity or fibrosis.

Exocrine pancreatic insufficiency may manifest as steatorrhea, diarrhea, bloating, weight loss, and nutrient malabsorption [4,18]. Endocrine dysfunction and the risk of pancreatogenic diabetes are also clinically important in CP; a small retrospective Central Asian study reported a clinical association between CP and impaired glucose metabolism [12].

When idiopathic disease is considered, recurrent acute pancreatitis, hypertriglyceridemia, hypercalcemia, medication-related causes, anatomical abnormalities, and genetic factors should be evaluated systematically [9,19]. Pancreatic disease occurring with ulcerative colitis is also etiologically heterogeneous. In a large multicenter cohort, most cases of autoimmune pancreatitis associated with inflammatory bowel disease were type 2 disease [5]. Therefore, autoimmune and medication-related pancreatic injury should be considered in the differential diagnosis of patients with ulcerative colitis.

Studies of acute biliary pancreatitis have shown that systemic inflammatory markers, C-reactive protein (CRP), and oxidative-stress indicators vary with disease severity [13,14]. These observations support the biological importance of systemic and oxidative mechanisms in pancreatic inflammation, but evidence from acute pancreatitis cannot be directly extrapolated to CP or to the effects of a hot climate.

Aim of the study.

The primary aim of this study is to evaluate the associations of CRP, fecal elastase-1, interleukin-2 receptor (IL-2R), IL-6, and TGF- β 1 with the retrospectively assigned symptom-based dehydration category and season of presentation in patients with chronic pancreatitis. The secondary aims are to compare these laboratory outcomes across the three clinical groups and to examine correlations among the outcomes.

Materials and Methods.

Medical records of 80 patients with chronic pancreatitis (CP) treated in the Department of Gastroenterology of the

Surkhandarya Regional Multidisciplinary Medical Center between 2023 and 2025 were retrospectively reviewed. Before data extraction and analysis, all patient information was de-identified.

Patient selection.

Inpatient records were screened consecutively until 80 eligible cases were identified. Eligibility required documented chronic pancreatitis in one of the three study groups and complete results for all five laboratory outcomes. Of 132 records screened, 52 were excluded for incomplete laboratory data; no imputation was used. Screening then stopped although other patients with chronic pancreatitis were treated during the study period. One hospitalization per patient was included, and the 80 analyzed records had no missing laboratory outcomes.

Diagnostic definition and supporting evidence.

Chronic pancreatitis was the treating gastroenterologist's routine-care diagnosis supported by compatible symptoms and structural and/or functional findings; no uniform imaging score was retrospectively applied. Structural evidence included pancreatic-duct dilatation or narrowing and calcifications or calculi. Ultrasonography was available in all 80 patients, CT in 5, and conventional MRI in 4; MRCP and endoscopic ultrasonography were not performed. Fecal elastase-1 assessed exocrine function: <100 µg/g indicated strong evidence of insufficiency, whereas 100–200 µg/g was indeterminate [18].

Clinical-group classification.

Patients were classified as chronic pancreatitis without a documented specific etiology (n=20), chronic pancreatitis with documented cholecystitis (n=40), or chronic pancreatitis with ulcerative colitis (n=20). These routine-record clinical associations were not definitively adjudicated etiologic categories.

Etiologic assessment.

Records were reviewed for alcohol exposure, medication use, family history, triglycerides, calcium, autoimmune-pancreatitis work-up, prior acute pancreatitis, and structural causes. These routine-care assessments were incomplete and nonuniform; no standardized etiologic protocol was used.

Extracted variables were age, sex, disease duration, presentation month and season, dehydration-classification symptoms, six major clinical manifestations, chronic anemia, hypertension, treatment, and the five outcomes (CRP, fecal elastase-1, IL-2R, IL-6, and TGF-β1). Table 1 variables had no missing data.

Laboratory measurements.

All specimens were collected at index admission before any treatment or infusion. Serum CRP was measured on a Mindray BS-200E analyzer (reference <8 mg/L). Stool fecal elastase-1 was assayed by ELISA (ScheBo Biotech AG, Germany) on a Bio-Rad Model 680 reader; >200 µg/g was normal, 100–200 µg/g indeterminate, and <100 µg/g markedly reduced. No patient received pancreatic enzyme replacement therapy at collection. Serum IL-6 was measured by chemiluminescence on a Mindray CL-1000i analyzer (reference <7 pg/mL). Serum soluble IL-2R and TGF-β1 were assayed by ELISA using kits from the State Research Institute of Highly Pure Biopreparations (Saint Petersburg, Russia) and DRG Diagnostica (Germany),

respectively, with Bio-Rad Model 680 reading. Archived records lacked the CRP and IL-6 reagent manufacturers, assay-specific detection limits, exact storage conditions, internal/external quality-control details, IL-2R and TGF-β1 reference intervals, and detailed stool handling.

Treatment documentation.

After collection, all patients received indicated standard inpatient treatment, including infusion, analgesic/antispasmodic therapy, and proton-pump inhibitors; all 20 patients with ulcerative colitis received mesalazine or sulfasalazine.

Assessment of dehydration.

Physician-authors retrospectively applied one study-specific rule to admission symptoms recorded before treatment; no validated scale was used. Mild meant thirst or dry mouth without marked systemic symptoms; moderate meant either with at least one of weakness, sweating, dark urine, or reduced oral intake; severe meant several pronounced findings, including marked thirst or weakness, dizziness, dark urine, or general deterioration. Laboratory outcomes were not used for classification.

Seasonal classification.

Season was assigned from the index hospitalization month: summer was June–August, and September–May was the comparison group. Month and year were retained descriptively. This calendar proxy did not measure ambient temperature, humidity, fluid intake, or individual heat exposure.

Analytical priorities.

No preregistration existed. Primary unadjusted analyses assessed each outcome against dehydration category and season; mutually adjusted models addressed confounding. Clinical-group comparisons and biomarker correlations were secondary. This reporting hierarchy was not prespecified.

Statistical analysis. Continuous variables are median [Q1–Q3] and categorical variables n (%). Clinical groups and dehydration categories were compared with Kruskal–Wallis tests; pairwise Mann–Whitney U tests used within-outcome Holm adjustment. Categorical variables used the Fisher–Freeman–Halton Monte Carlo test (50,000 resamples) and Cramér's V. Spearman correlations had 95% bootstrap confidence intervals (5,000 resamples), with Holm correction across 10 biomarker pairs. Seasonal comparisons used Mann–Whitney U tests with Holm correction across five outcomes. Each outcome was modeled by ordinary least squares with HC3 robust standard errors; Holm correction was applied separately to the five dehydration and five summer coefficients. All tests were two-sided ($\alpha=0.05$). Python 3.12.13, pandas 2.2.3, NumPy 2.3.5, and SciPy 1.17.0 were used.

Regression specification and diagnostics. Each model used 80 complete observations and eight parameters (intercept plus seven predictor degrees of freedom; residual df=72). Dehydration was ordinal (mild=1, moderate=2, severe=3), so β is the adjusted mean change per category and has no reference category. Summer=1 versus September–May=0; male=1 versus female=0. Clinical-group indicators used chronic pancreatitis without documented specific etiology as reference. Age and disease duration were continuous per year; component symptoms were excluded because they defined dehydration. For every

term, Table 5 reports unstandardized β , HC3 95% confidence intervals, and exact raw two-sided p values; Table 3 adds Holm-adjusted p values for the primary exposures. Diagnostics were variance inflation factors, R^2 , adjusted R^2 , leave-one-out PRESS R^2 , Breusch–Pagan, Shapiro–Wilk, leverage, and Cook’s distance. Models were exploratory association analyses, not prediction models.

Ethical considerations. Patient data were de-identified before analysis. The Local Ethics Committee of the Termez Branch of Tashkent State Medical University approved the study and waived the requirement for written informed consent (Protocol No. 18, 13 March 2023). Only anonymized, aggregate data were analyzed.

Results.

Of 132 consecutive inpatient records screened, 80 met the eligibility criteria and were included; 52 were excluded because the required laboratory data were incomplete. Each included patient contributed one hospitalization and one observation.

All 80 patients underwent abdominal ultrasonography; CT and conventional MRI were available in 5 (6.3%) and 4 (5.0%) patients, respectively. No patient underwent MRCP or endoscopic ultrasonography. Pancreatic-duct abnormalities (dilatation, narrowing, or both) were documented in 72 patients (90.0%). Pancreatic calcifications or calculi were documented in 33 unique patients (41.3%): by ultrasonography in 24, CT in 5, and MRI in 4. Fecal elastase-1 was <100 $\mu\text{g/g}$ in 28 patients (35.0%), 100–200 $\mu\text{g/g}$ in 52 (65.0%), and >200 $\mu\text{g/g}$ in 0 patients (0%).

Regarding etiologic assessment, all patients denied current alcohol use; some reported remote use that had ceased at least 4–5 years earlier, but lifetime amount and duration were not documented consistently. Mesalazine or sulfasalazine use was documented in all 20 patients with ulcerative colitis, but its temporal relationship to pancreatitis and drug causality could not be determined from the records. No specific autoimmune-pancreatitis assessment was documented. Serum triglyceride results were not available uniformly; elevated values were recorded in three patients. Serum calcium was not measured. No genetic testing was performed, and no family history suggestive of hereditary pancreatitis was documented. Available imaging did not identify a clear primary obstructive cause; however, the absence of MRCP and endoscopic ultrasonography limited comprehensive assessment. The number of patients with prior recurrent acute pancreatitis could not be established reliably from the records.

Baseline characteristics by clinical group are summarized in Table 1. The cohort comprised 47 women (58.8%) and 33 men (41.3%); sex distribution differed across groups (Monte Carlo $p=0.039$; Cramér’s $V=0.291$). Median age did not show a statistically significant between-group difference ($p=0.054$), whereas disease duration differed ($p<0.001$). Between-group comparisons of dehydration category and season yielded $p=0.630$ and $p=1.000$, respectively. These nonsignificant comparisons should not be interpreted as evidence that the clinical groups were equivalent.

Pain (92.5%), dyspepsia (86.3%), and bloating (78.8%) were the most frequent clinical manifestations. Chronic anemia was documented in 15 patients (18.8%) and differed across groups

($p=0.030$); hypertension was present in 19 (23.8%; $p=0.184$). All 80 patients received standard inpatient treatment after specimen collection; mesalazine or sulfasalazine use was documented in all 20 patients with ulcerative colitis, and no patient was receiving pancreatic enzyme replacement therapy at stool sampling. There were no missing data for the variables shown in Table 1.

Primary analyses: symptom-based dehydration category and season of presentation:

In unadjusted analyses, the retrospectively assigned symptom-based categories were mild ($n=22$), moderate ($n=38$), and severe ($n=20$). With increasing symptom-based category, median CRP increased from 13.5 [12.2–20.6] to 22.1 [18.6–26.2] and 24.1 [21.5–27.2] mg/L ($H=19.62$; Holm-adjusted $p<0.001$; $\varepsilon^2=0.229$). IL-6 increased from 281.9 [234.4–305.1] to 317.8 [255.2–344.7] and 366.6 [334.4–396.0] pg/mL ($H=23.19$; Holm-adjusted $p<0.001$; $\varepsilon^2=0.275$), whereas fecal elastase-1 decreased from 132.7 [115.9–142.5] to 104.7 [93.0–116.6] and 92.6 [68.3–107.9] $\mu\text{g/g}$ ($H=14.65$; Holm-adjusted $p=0.0020$; $\varepsilon^2=0.164$). IL-2R and TGF- $\beta 1$ did not differ across dehydration categories. Pairwise comparisons showed that, for CRP and fecal elastase-1, the mild category differed from both the moderate and severe categories; for IL-6, all three pairwise comparisons were significant (Holm-adjusted $p<0.05$ within each outcome).

Across all 80 index hospitalizations, monthly presentation counts were January 1, February 3, March 6, April 7, May 7, June 15, July 23, August 6, September 5, October 5, November 0, and December 2. Calendar-year counts were 29 in 2023, 21 in 2024, and 30 in 2025. Forty-four presentations occurred in summer (June 15, July 23, and August 6), including 14 in 2023, 13 in 2024, and 17 in 2025; 36 presentations occurred outside summer. In summer versus other seasons, median CRP was 24.6 [21.9–28.2] versus 15.2 [12.4–19.0] mg/L (Holm-adjusted $p<0.001$), and IL-6 was 340.1 [312.3–391.4] versus 285.2 [228.3–315.7] pg/mL (Holm-adjusted $p<0.001$); fecal elastase-1 was lower, at 95.5 [69.1–115.1] versus 127.3 [108.2–139.3] $\mu\text{g/g}$ (Holm-adjusted $p<0.001$). Although the unadjusted p value for TGF- $\beta 1$ was 0.038, the difference was not significant after adjustment across the five laboratory outcomes (Holm-adjusted $p=0.076$); IL-2R also did not differ (Holm-adjusted $p=0.828$). The distribution of dehydration categories differed between summer and other-season presentations (Monte Carlo $p<0.001$; Cramér’s $V=0.456$). Summer accounted for 5 of 22 mild, 22 of 38 moderate, and 17 of 20 severe presentations.

Because summer presentation and the ordinal symptom-based dehydration category were correlated ($r_s=0.455$; $p=0.00002235$), both were entered simultaneously in the multivariable models. After adjustment for season, clinical group, age, sex, and disease duration, each one-category increase in dehydration remained associated with IL-6 (+36.94 pg/mL ; 95% confidence interval, 17.98–55.90; raw $p=0.0002260$; Holm-adjusted $p=0.001130$). The dehydration coefficients for CRP, fecal elastase-1, IL-2R, and TGF- $\beta 1$ did not remain significant after Holm adjustment. Independently, summer presentation was associated with higher CRP (+8.46 mg/L ; 6.43–10.48; raw $p=3.788\text{E-}12$; Holm-adjusted $p=1.894\text{E-}11$), higher IL-6 (+44.23 pg/mL ; 8.74–79.73; raw $p=0.01531$; Holm-adjusted $p=0.04357$), lower fecal elastase-1 (–22.89 $\mu\text{g/g}$; –36.11 to –9.67; raw $p=0.0009379$;

Table 1. Baseline characteristics, comorbidities, and treatment by clinical group.

Characteristic	Overall (n=80)	Group I (n=20)	Group II (n=40)	Group III (n=20)	Missing, n	p value
Demographic characteristics						
Age, years	52.4 [47.5–56.4]	48.7 [47.2–52.6]	53.3 [47.5–59.5]	52.3 [49.4–55.8]	0	0.054
Female sex	47 (58.8)	12 (60.0)	28 (70.0)	7 (35.0)	0	0.039
Male sex	33 (41.3)	8 (40.0)	12 (30.0)	13 (65.0)	0	—
Disease history						
Disease duration, years	9.2 [7.4–11.2]	10.5 [9.4–11.9]	9.5 [8.1–11.5]	7.0 [5.7–8.3]	0	<0.001
Symptom-based dehydration category						
Mild	22 (27.5)	6 (30.0)	10 (25.0)	6 (30.0)	0	0.630
Moderate	38 (47.5)	9 (45.0)	22 (55.0)	7 (35.0)	0	—
Severe	20 (25.0)	5 (25.0)	8 (20.0)	7 (35.0)	0	—
Season of presentation						
Winter	7 (8.8)	2 (10.0)	3 (7.5)	2 (10.0)	0	1.000
Spring	16 (20.0)	4 (20.0)	8 (20.0)	4 (20.0)	0	—
Summer	44 (55.0)	11 (55.0)	22 (55.0)	11 (55.0)	0	—
Autumn	13 (16.3)	3 (15.0)	7 (17.5)	3 (15.0)	0	—
Clinical symptoms at presentation						
Pain syndrome	74 (92.5)	19 (95.0)	35 (87.5)	20 (100.0)	0	0.303
Dyspepsia	69 (86.3)	19 (95.0)	34 (85.0)	16 (80.0)	0	0.396
Bloating	63 (78.8)	17 (85.0)	31 (77.5)	15 (75.0)	0	0.823
Diarrhea/steatorrhea	51 (63.8)	10 (50.0)	25 (62.5)	16 (80.0)	0	0.148
Asthenia/general weakness	58 (72.5)	14 (70.0)	30 (75.0)	14 (70.0)	0	0.847
Weight loss	43 (53.8)	10 (50.0)	21 (52.5)	12 (60.0)	0	0.876
Dry mouth/thirst	55 (68.8)	12 (60.0)	29 (72.5)	14 (70.0)	0	0.664
Increased sweating	50 (62.5)	12 (60.0)	26 (65.0)	12 (60.0)	0	0.865
Dark urine	40 (50.0)	10 (50.0)	20 (50.0)	10 (50.0)	0	1.000
Dizziness	30 (37.5)	6 (30.0)	15 (37.5)	9 (45.0)	0	0.630
Documented comorbidities						
Chronic anemia	15 (18.8)	3 (15.0)	4 (10.0)	8 (40.0)	0	0.030
Hypertension	19 (23.8)	7 (35.0)	6 (15.0)	6 (30.0)	0	0.184
Treatment						
Standard inpatient treatment after specimen collection	80 (100.0)	20 (100.0)	40 (100.0)	20 (100.0)	0	—
Mesalazine or sulfasalazine	20 (25.0)	0 (0.0)	0 (0.0)	20 (100.0)	0	—
Pancreatic enzyme replacement at stool sampling	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0	—

Values are median [Q1–Q3] or n (%). Groups: I, chronic pancreatitis without a documented specific etiology; II, chronic pancreatitis with documented cholecystitis; III, chronic pancreatitis in patients with ulcerative colitis. Symptom rows show the presence of the listed symptom. Missing, n is the number of patients with unavailable data for each variable. Continuous variables were compared with the Kruskal–Wallis test and categorical variables with the Fisher–Freeman–Halton Monte Carlo test (50,000 resamples). Treatment rows were not tested because standard care was uniform, mesalazine/sulfasalazine use was specific to ulcerative colitis, and pancreatic enzyme replacement use was uniformly absent. Between-group p values are unadjusted descriptive comparisons; a nonsignificant p value does not establish equivalence.

Table 2. Comparison of laboratory outcomes by symptom-based dehydration category. Values are median [Q1–Q3]; Holm-adjusted p, adjustment across five laboratory outcomes; r_s , ordinal Spearman coefficient.

Marker	Mild (n=22)	Moderate (n=38)	Severe (n=20)	H	Holm-adjusted p	r_s
CRP, mg/L	13.5 [12.2–20.6]	22.1 [18.6–26.2]	24.1 [21.5–27.2]	19.62	<0.001	0.480
Fecal elastase-1, μ g/g	132.7 [115.9–142.5]	104.7 [93.0–116.6]	92.6 [68.3–107.9]	14.65	0.0020	–0.420
IL-2R, pg/mL	772.0 [760.1–800.1]	786.5 [766.5–814.9]	797.5 [774.0–810.3]	1.85	0.795	0.153
TGF- β 1, pg/mL	844.4 [727.1–891.5]	834.4 [725.1–917.6]	772.2 [738.1–833.3]	0.73	0.795	–0.081
IL-6, pg/mL	281.9 [234.4–305.1]	317.8 [255.2–344.7]	366.6 [334.4–396.0]	23.19	<0.001	0.540

Table 3. Mutually adjusted associations of symptom-based dehydration category and summer presentation with laboratory outcomes. Values are unstandardized β coefficients (95% confidence intervals); *p* columns show exact raw and Holm-adjusted *p* values.

Marker	Dehydration β (95% CI)	<i>p</i> (raw; Holm)	Summer β (95% CI)	<i>p</i> (raw; Holm)
CRP, mg/L	+1.58 (0.04 to 3.12)	0.04456; 0.1782	+8.46 (6.43 to 10.48)	3.788E-12; 1.894E-11
Fecal elastase-1, $\mu\text{g/g}$	-8.69 (-18.42 to 1.03)	0.07898; 0.2369	-22.89 (-36.11 to -9.67)	0.0009379; 0.003752
IL-2R, pg/mL	+7.04 (-2.64 to 16.72)	0.1514; 0.3029	-3.17 (-17.67 to 11.34)	0.6648; 0.6648
TGF- β 1, pg/mL	+10.00 (-20.43 to 40.43)	0.5146; 0.5146	-61.12 (-109.76 to -12.47)	0.01452; 0.04357
IL-6, pg/mL	+36.94 (17.98 to 55.90)	0.0002260; 0.001130	+44.23 (8.74 to 79.73)	0.01531; 0.04357

Each model used $n=80$ complete observations and simultaneously included dehydration category, summer presentation, clinical group, age, sex, and disease duration. Reference categories were September–May, female sex, and chronic pancreatitis without a documented specific etiology. Dehydration was an ordinal term (1–3), and age and disease duration were entered per year. HC3 robust standard errors were used. Holm adjustment was applied separately across the five dehydration coefficients and the five summer coefficients. The table reports the two exposure coefficients of primary interest; complete coefficient estimates for every model term are provided in Table 5. CI, confidence interval.

Table 4. Regression model diagnostics.

Outcome	<i>n</i>	R^2	Adjusted R^2	PRESS R^2	Breusch–Pagan <i>p</i>	Maximum Cook's <i>D</i>
CRP	80	0.611	0.573	0.514	0.3383	0.0858
Fecal elastase-1	80	0.306	0.239	0.147	0.3496	0.1131
IL-2R	80	0.112	0.026	-0.100	0.6860	0.0752
TGF- β 1	80	0.198	0.120	0.024	0.01450	0.1315
IL-6	80	0.384	0.324	0.237	0.2681	0.1241

All models estimated eight parameters including the intercept (residual $df=72$). PRESS R^2 is the leave-one-out predicted coefficient of determination. Predictor VIFs were 1.11–2.10; no Cook's distance exceeded 1.0. HC3 robust standard errors were used for coefficient inference.

Table 5. Complete coefficient estimates from the mutually adjusted linear regression models.

Outcome / model term	β	95% CI	Exact <i>p</i>
CRP, mg/L			
Intercept	25.84	17.21 to 34.48	8.2740E-08
Symptom-based dehydration category (per one-category increase)	1.58	0.04 to 3.12	0.04456
Summer presentation (vs September–May)	8.46	6.43 to 10.48	3.7880E-12
Age (per year)	-0.15	-0.29 to -0.01	0.03858
Male sex (vs female)	1.56	-0.39 to 3.50	0.11442
Disease duration (per year)	-0.56	-1.03 to -0.08	0.02245
CP with documented cholecystitis (vs CP without documented specific etiology)	0.41	-2.00 to 2.83	0.7335
CP in patients with ulcerative colitis (vs CP without documented specific etiology)	-3.11	-6.10 to -0.13	0.04132
Fecal elastase-1, $\mu\text{g/g}$			
Intercept	153.28	97.70 to 208.87	5.5459E-07
Symptom-based dehydration category (per one-category increase)	-8.69	-18.42 to 1.03	0.07898
Summer presentation (vs September–May)	-22.89	-36.11 to -9.67	0.0009379
Age (per year)	-0.29	-1.14 to 0.56	0.49905
Male sex (vs female)	-2.51	-14.65 to 9.64	0.68197
Disease duration (per year)	-0.22	-2.89 to 2.45	0.86772
CP with documented cholecystitis (vs CP without documented specific etiology)	2.13	-13.15 to 17.41	0.78221
CP in patients with ulcerative colitis (vs CP without documented specific etiology)	2.88	-14.22 to 19.97	0.73827
IL-2R, pg/mL			
Intercept	785.49	724.29 to 846.68	7.0430E-38
Symptom-based dehydration category (per one-category increase)	7.04	-2.64 to 16.72	0.15144
Summer presentation (vs September–May)	-3.17	-17.67 to 11.34	0.6648
Age (per year)	0.37	-0.81 to 1.55	0.53257
Male sex (vs female)	-12.57	-26.75 to 1.62	0.08158
Disease duration (per year)	-1.89	-4.71 to 0.93	0.18559
CP with documented cholecystitis (vs CP without documented specific etiology)	-7.90	-23.93 to 8.14	0.32965
CP in patients with ulcerative colitis (vs CP without documented specific etiology)	-16.45	-38.59 to 5.69	0.14284
TGF-β1, pg/mL			
Intercept	879.92	649.17 to 1110.68	8.4831E-11
Symptom-based dehydration category (per one-category increase)	10.00	-20.43 to 40.43	0.51457

Outcome / model term	β	95% CI	Exact p
Summer presentation (vs September-May)	-61.12	-109.76 to -12.47	0.01452
Age (per year)	-2.92	-6.61 to 0.76	0.11809
Male sex (vs female)	-19.00	-64.57 to 26.58	0.40877
Disease duration (per year)	7.58	-0.72 to 15.88	0.07266
CP with documented cholecystitis (vs CP without documented specific etiology)	58.75	7.80 to 109.70	0.02444
CP in patients with ulcerative colitis (vs CP without documented specific etiology)	32.77	-34.23 to 99.78	0.3328
IL-6, pg/mL			
Intercept	315.67	167.21 to 464.14	6.5712E-05
Symptom-based dehydration category (per one-category increase)	36.94	17.98 to 55.90	0.000226
Summer presentation (vs September-May)	44.23	8.74 to 79.73	0.01531
Age (per year)	-1.31	-3.66 to 1.03	0.26702
Male sex (vs female)	-5.67	-34.22 to 22.88	0.69342
Disease duration (per year)	-2.62	-8.28 to 3.05	0.35984
CP with documented cholecystitis (vs CP without documented specific etiology)	3.13	-31.42 to 37.69	0.85709
CP in patients with ulcerative colitis (vs CP without documented specific etiology)	-22.31	-65.93 to 21.31	0.31136

Values are unstandardized β coefficients with HC3-based 95% confidence intervals. Exact *p* values are two-sided and unadjusted; Holm-adjusted *p* values for the dehydration and summer coefficients are reported in Table 3. Coefficients for the other terms are shown for adjustment transparency; their nominal *p* values were not multiplicity-adjusted and should not be interpreted as confirmatory tests. Each model included all listed terms simultaneously and used *n*=80 complete observations. Dehydration was coded 1–3; summer was compared with September–May; male sex with female sex; and both clinical group indicators with chronic pancreatitis without a documented specific etiology. Age and disease duration were entered per year. CI, confidence interval; CP, chronic pancreatitis.

Table 6. Comparison of laboratory markers across clinical groups. Values are median [Q1–Q3]; *p*, Kruskal–Wallis test; Holm-adjusted *p*, adjustment across five laboratory outcomes.

Marker	CP without documented etiology (n=20)	CP with documented cholecystitis (n=40)	CP in patients with UC (n=20)	H	p	Holm-adjusted p
CRP, mg/L	21.6 [17.9–24.4]	21.5 [16.4–26.1]	20.5 [14.6–26.7]	0.22	0.895	1.000
Fecal elastase-1, $\mu\text{g/g}$	107.7 [83.9–129.0]	109.8 [92.9–130.7]	108.2 [93.0–120.1]	0.05	0.975	1.000
IL-2R, pg/mL	790.0 [769.4–812.3]	790.0 [763.8–814.7]	776.1 [754.6–803.0]	1.50	0.473	1.000
TGF- β 1, pg/mL	786.2 [725.1–869.4]	862.5 [733.1–924.6]	780.3 [726.1–850.4]	4.07	0.130	0.652
IL-6, pg/mL	321.1 [274.8–361.3]	323.6 [261.7–386.8]	312.2 [284.6–340.6]	0.47	0.790	1.000

Holm-adjusted *p*=0.003752), and lower TGF- β 1 (–61.12 pg/mL; –109.76 to –12.47; raw *p*=0.01452; Holm-adjusted *p*=0.04357), but not with IL-2R (–3.17 pg/mL; –17.67 to 11.34; raw and Holm-adjusted *p*=0.6648) (Table 3). These findings represent mutually adjusted associations and do not establish a causal effect of heat or dehydration.

All five models included 80 observations and eight estimated parameters (10.0 observations per parameter). Variance inflation factors ranged from 1.11 to 2.10. *R*² ranged from 0.112 to 0.611, adjusted *R*² from 0.026 to 0.573, and PRESS-based predicted *R*² from –0.100 to 0.514 (Table 4). The Breusch–Pagan test indicated heteroscedasticity for the TGF- β 1 model (*p*=0.01450) but not for the other models (*p*=0.2681–0.6860), supporting use of HC3 inference. Maximum Cook’s distance ranged from 0.0752 to 0.1315, and no observation exceeded 1.0. Residual Shapiro–Wilk *p* values exceeded 0.20 for four models; the IL-2R model showed a departure from normality (*p*=0.02881). The negative predicted *R*² for IL-2R indicated no useful leave-one-out predictive performance.

Complete coefficient estimates for all terms in the five mutually adjusted models are presented in Table 5.

Secondary analyses: clinical-group comparisons and biomarker correlations:

None of the five laboratory outcomes differed across clinical groups: CRP, *H*=0.22, *p*=0.895; fecal elastase-1, *H*=0.05,

p=0.975; IL-2R, *H*=1.50, *p*=0.473; TGF- β 1, *H*=4.07, *p*=0.130; and IL-6, *H*=0.47, *p*=0.790. Holm-adjusted *p* values for the five laboratory outcomes ranged from 0.652 to 1.000. No evidence was found that cytokine or CRP levels differed among the three clinical groups (Table 6).

In correlation analyses, IL-6 showed a moderate positive association with CRP (*r*_s=0.460; 95% bootstrap confidence interval, 0.262–0.634; Holm-adjusted *p*<0.001). CRP was negatively associated with fecal elastase-1 (*r*_s=–0.403; 95% confidence interval, –0.570 to –0.202; Holm-adjusted *p*=0.0019), and fecal elastase-1 was also negatively correlated with IL-6 (*r*_s=–0.402; 95% confidence interval, –0.576 to –0.204; Holm-adjusted *p*=0.0019). The remaining correlations involving IL-2R and TGF- β 1 were not significant after adjustment for multiple comparisons.

Discussion.

The unadjusted pattern—higher CRP and IL-6 and lower fecal elastase-1 with increasing symptom-based dehydration category and during summer—changed after mutual adjustment. Only IL-6 remained associated with dehydration category, whereas summer retained associations with higher CRP and IL-6 and lower fecal elastase-1 and TGF- β 1. Confounding by season may therefore partly explain the unadjusted dehydration associations with CRP and fecal elastase-1. The five outcomes did not differ across clinical groups.

The positive correlation of IL-6 with CRP and its negative correlation with fecal elastase-1 suggest that systemic inflammatory activity and exocrine dysfunction may occur concurrently. In the PROCEED cohort, IL-6 and IL-8 were also higher in patients with CP than in healthy controls and increased with the presence of exocrine dysfunction and diabetes [7]. However, correlation does not establish directionality or a causal mechanism, and the present study did not include a healthy control group.

TGF- β 1 did not differ across clinical groups or dehydration categories and was not significantly correlated with IL-6. In human pancreatic stellate cells and tissue from alcohol-related CP, IL-6 has been shown to enhance stellate-cell activation and type I collagen synthesis through the TGF- β 1/Smad2/3 pathway [20]. This mechanistic evidence provides biological context, but our serum findings do not directly confirm an IL-6/TGF- β 1 relationship or pancreatic fibrosis.

Fecal elastase-1 results require particular caution. The American Gastroenterological Association recommends performing the test on a semi-solid or solid stool specimen; <100 $\mu\text{g/g}$ provides strong evidence of exocrine pancreatic insufficiency, whereas 100–200 $\mu\text{g/g}$ is considered indeterminate [18]. In a study of watery stool specimens, 29 of 41 initially low results (71%) at ≤ 199 $\mu\text{g/g}$ were ≥ 200 $\mu\text{g/g}$ when retested on formed stool [8]. Because diarrhea or steatorrhea was documented in 63.8% of the cohort and stool consistency could not be retrospectively determined, dilution-related underestimation and misclassification between fecal elastase-1 categories cannot be excluded. Accordingly, these categories should be interpreted as descriptive laboratory strata rather than definitive diagnostic classifications.

The ulcerative colitis group requires careful etiologic interpretation. In the multicenter study by Eder et al., 72% of autoimmune pancreatitis cases associated with inflammatory bowel disease were type 2 autoimmune pancreatitis, and 79% were associated with ulcerative colitis [5]. In the present cohort, mesalazine or sulfasalazine exposure was documented in all 20 patients with ulcerative colitis, but a temporal relationship and drug causality could not be established, and no specific autoimmune-pancreatitis assessment was available. Accordingly, this group should be interpreted as a clinical association rather than a uniform pancreatic etiology.

The group with documented cholecystitis likewise represents a clinical association and does not by itself establish a single biliary mechanism. Incomplete metabolic and autoimmune testing, the absence of genetic testing, and limited advanced pancreatic imaging prevented exhaustive etiologic adjudication.

Mutual adjustment helped distinguish overlapping seasonal and symptom-based dehydration associations but could not establish a mechanism or causality. Acute biliary pancreatitis studies report inflammatory and oxidative-stress changes with severity [13,14], although acute and chronic processes are not directly comparable. Recurrent acute pancreatitis, occult hypertriglyceridemia, and structural factors also require systematic evaluation in idiopathic disease [9, 19]. Because ambient temperature, humidity, individual heat exposure, and fluid intake were not measured, season cannot be interpreted as a direct effect of heat or dehydration.

Study Limitations.

The retrospective single-center design, relatively small and unequal groups totalling 80 patients, absence of a healthy control group, and stopping of record screening once 80 eligible cases had been identified limit generalizability. Because not all chronic-pancreatitis admissions during the study period were screened, selection bias cannot be excluded. Diagnostic imaging was not standardized: although abdominal ultrasonography was available for all patients, only 5 had CT and 4 had MRI, and neither MRCP nor endoscopic ultrasonography was performed. The chronic-pancreatitis diagnoses were not retrospectively re-adjudicated using a uniform imaging score. Because etiologic investigations were based on information available in routine medical records and were not standardized across all patients, some etiologic uncertainty remains. The clinical groups should therefore be interpreted as pragmatic categories for comparison rather than definitive etiologic phenotypes. Dehydration categories were assigned retrospectively by the physician-authors using a study-specific symptom-based rule applied to admission complaints. This rule was not an externally validated dehydration scale, and objective physiologic measures were not incorporated into category assignment. Accordingly, the categories should be interpreted as symptom-based ordinal classifications rather than direct measurements of volume depletion. Stool consistency could not be retrospectively determined. Given that diarrhea or steatorrhea was documented in 63.8% of the cohort, dilution-related underestimation and category misclassification of fecal elastase-1 cannot be excluded. In addition, the absence of patients with fecal elastase-1 >200 $\mu\text{g/g}$ precluded comparison with a group having preserved exocrine function. TGF- β 1 was not a direct imaging or histological measure of fibrosis. Season does not substitute for measured ambient conditions or individual heat exposure. Although variance inflation factors did not indicate problematic multicollinearity, the sample size limited the number of covariates that could be included. Adjustment was confined to available variables; body mass index, nutritional status, diabetes status, measured ambient conditions, and individual fluid intake were unavailable. HC3 regression cannot eliminate residual confounding. Although multiple comparisons were controlled using the Holm method, the seasonal and regression findings should be interpreted cautiously.

Regression-related limitations. Each model estimated eight parameters from only 80 observations, equivalent to 10 observations per parameter. This is a limited ratio for a multivariable model and leaves a material risk of overfitting and coefficient instability despite restricting the covariates to clinically relevant variables available in the records. PRESS-based predicted R^2 values were lower than the apparent R^2 values and were negative for IL-2R, indicating limited internal predictive performance for some outcomes. No external validation, penalized regression, or shrinkage method was performed. Consequently, the regression results should be interpreted as exploratory adjusted associations rather than a validated prediction model; the diagnostics do not eliminate residual confounding or model misspecification.

The incomplete archival reporting of assay-specific detection limits, specimen-storage conditions, quality-control procedures,

selected reagent manufacturers, and reference intervals limits full methodological reproducibility; these details could not be reconstructed retrospectively.

Conclusion.

Higher symptom-based dehydration category was unadjustedly associated with higher CRP and IL-6 and lower fecal elastase-1. After adjustment for season, clinical group, age, sex, and disease duration, only IL-6 remained associated with dehydration after Holm correction; summer remained associated with higher CRP and IL-6 and lower fecal elastase-1 and TGF- β 1. No outcome differed across clinical groups. The retrospective design, symptom-based classification, and unmeasured heat exposure preclude causal interpretation.

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Competing Interests.

The authors declare that they have no competing interests.

Author Contributions.

M.U.O. contributed to study conception, data collection, data curation, statistical analysis, and drafting of the manuscript. S.M.I. contributed to study design, methodology, supervision, and critical revision of the manuscript. R.B.A. contributed to interpretation of the results, supervision, and critical revision of the manuscript. All authors reviewed and approved the final manuscript.

Availability of Data and Materials.

The de-identified dataset is not publicly available because of ethical and patient-privacy restrictions. It may be made available by the corresponding author upon reasonable request and subject to approval by the relevant ethics committee.

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СВЯЗЬ ЦИТОКИНОВОГО ПРОФИЛЯ И ЭКЗОКРИННОЙ ФУНКЦИИ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ С КАТЕГОРИЕЙ ОБЕЗВОЖИВАНИЯ, ОПРЕДЕЛЁННОЙ ПО СИМПТОМАМ ПРИ ПОСТУПЛЕНИИ, И СЕЗОНОМ ОБРАЩЕНИЯ ПРИ ХРОНИЧЕСКОМ ПАНКРЕАТИТЕ: РЕТРОСПЕКТИВНОЕ ИССЛЕДОВАНИЕ

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РЕЗЮМЕ.

Цель: оценить связь С-реактивного белка (CRP), фекальной эластазы-1 (FE-1), рецептора интерлейкина-2

(IL-2R), интерлейкина-6 (IL-6) и трансформирующего фактора роста бета-1 (TGF- β 1) с симптоматической категорией обезвоживания и сезоном обращения при хроническом панкреатите; сравнение клинических групп было вторичной задачей.

Материалы и методы: из 132 последовательно просмотренных стационарных историй болезни за 2023–2025 гг. проанализированы 80 с полными результатами пяти лабораторных показателей; 52 неполные истории исключены. Каждый пациент представил одно наблюдение. Нескорректированные критерии Краскела–Уоллиса, Манна–Уитни U и корреляция Спирмена применялись с поправкой Холма. Пять линейных моделей с робастными стандартными ошибками HC3 одновременно учитывали категорию обезвоживания, обращение летом, клиническую группу, возраст, пол и длительность заболевания.

Результаты: в нескорректированных анализах более высокая категория обезвоживания была связана с более высокими CRP и IL-6 и более низкой FE-1. После взаимной корректировки только IL-6 сохранял связь с повышением категории обезвоживания на одну ступень (+36,94 пг/мл; 95% ДИ 17,98–55,90; p Холма=0,0011). Обращение летом независимо было связано с более высокими CRP (+8,46 мг/л) и IL-6 (+44,23 пг/мл), более низкими FE-1 (–22,89 мкг/г) и TGF- β 1 (–61,12 пг/мл) (все p Холма<0,05), но не с IL-2R. Пять показателей не различались между клиническими группами.

Заключение: после корректировки категория обезвоживания сохраняла независимую связь только с IL-6, тогда как обращение летом — с CRP, IL-6, FE-1 и TGF- β 1. Ретроспективный наблюдательный дизайн не позволяет установить причинную роль жары или обезвоживания.

Ключевые слова: хронический панкреатит, C-реактивный белок, интерлейкин-6, фекальная эластаза-1, обезвоживание, сезон обращения, ретроспективное исследование.

ციტოკინური პროფილისა და პანკრეასის ეგზოკრინული ფუნქციის კავშირი დეჰიდრატაციის სიმპტომებზე დაფუძნებულ კატეგორიასა და მიმართვის სეზონთან ქრონიკული პანკრეატიტის დროს: რეტროსპექტული კვლევა

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მიზანი: ქრონიკული პანკრეატიტის დროს C-რეაქტიული ცილის (CRP), ფეკალური ელასტაზა-1-ის (FE-1), ინტერლეიკინ-2-ის რეცეპტორის (IL-2R), ინტერლეიკინ-6-ის (IL-6) და ტრანსფორმირებელი ზრდის ფაქტორი ბეტა-1-ის (TGF- β 1) კავშირის შეფასება დეჰიდრატაციის სიმპტომებზე დაფუძნებულ კატეგორიასა და მიმართვის სეზონთან; კლინიკური ჯგუფების შედარება იყო მეორეული ამოცანა.

მასალა და მეთოდები: 2023–2025 წლებში თანმიმდევრულად გადახედილი 132 სტაციონარული ჩანაწერიდან გაანალიზდა ხუთივე ლაბორატორიული შედეგის მქონე 80; 52 არასრული ჩანაწერი გამოირიცხა. თითოეულმა პაციენტმა ერთი დაკვირვება შეიტანა. დაურეგულირებელ ანალიზებში გამოყენებული იყო Kruskal–Wallis, Mann–Whitney U და Spearman-ის ტესტები Holm-ის შესწორებით. ხუთმა HC3-რობასტულმა ხაზოვანმა მოდელმა ერთდროულად გაითვალისწინა დეჰიდრატაციის კატეგორია, ზაფხულში მიმართვა, კლინიკური ჯგუფი, ასაკი, სქესი და დაავადების ხანგრძლივობა.

შედეგები: დაურეგულირებლად დეჰიდრატაციის უფრო მაღალი კატეგორია დაკავშირებული იყო უფრო მაღალ CRP-სა და IL-6-თან და უფრო დაბალ FE-1-თან. ურთიერთ კორექციის შემდეგ დეჰიდრატაციის ერთი კატეგორიით მატებასთან კავშირი მხოლოდ IL-6-მა შეინარჩუნა (+36.94 pg/mL; 95% CI 17.98–55.90; Holm-ის p =0.0011). ზაფხულში მიმართვა დამოუკიდებლად უკავშირდებოდა უფრო მაღალ CRP-ს (+8.46 mg/L) და IL-6-ს (+44.23 pg/mL), უფრო დაბალ FE-1-ს (–22.89 μ g/g) და TGF- β 1-ს (–61.12 pg/mL) (ყველა Holm-ის p <0.05), მაგრამ არა IL-2R-ს. ხუთი მაჩვენებელი კლინიკურ ჯგუფებს შორის არ განსხვავდებოდა.

დასკვნა: კორექციის შემდეგ დეჰიდრატაციის კატეგორია დამოუკიდებლად მხოლოდ IL-6-თან დარჩა დაკავშირებული, ხოლო ზაფხულში მიმართვა — CRP-სთან, IL-6-თან, FE-1-თან და TGF- β 1-თან. რეტროსპექტული დაკვირვებითი დიზაინი სიცხის ან დეჰიდრატაციის მიზეზობრივ როლს ვერ ადგენს.

საკვანძო სიტყვები: ქრონიკული პანკრეატიტი, C-რეაქტიული ცილა, ინტერლეიკინ-6, ფეკალური ელასტაზა-1, დეჰიდრატაცია, მიმართვის სეზონი, რეტროსპექტული კვლევა.