

GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 7-8 (376-377) Июль-Август 2026

ТБИЛИСИ - NEW YORK



ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press.
Published since 1994. Distributed in NIS, EU and USA.

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.

Nana Shavlakadze, Irine Phkhakadze, Ana Silagadze, Dali Kobuladze, Alina Pakhuridze. CHRONIC URTICARIA AND LEAD EXPOSURE: EVALUATION OF IMMUNOLOGICAL MARKERS.....	6-16
Jangirashvili T, Kikoria G, Tevdorashvili N, Kapanadze L, Odikadze N. PSYCHOLOGICAL WELL-BEING AMONG MEDICAL STUDENTS AT FIVE UNIVERSITIES IN TBILISI, GEORGIA: A CROSS-SECTIONAL STUDY OF PERCEIVED STRESS, ANXIETY, AND SLEEP QUALITY.....	17-23
Yueyue Lu, Yigao Wu. ADVANCES IN RESEARCH OF PSYCHOTHERAPY FOR SOCIAL ANXIETY DISORDER.....	24-31
Saburov Alisher, Kemelbekov Kanatzhan, Arybzhanov Dauranbek, Abdurakhmanov Babur, Huseinov Zafar, Saburova Saidakhon, Tuktibayeva Saule, Yernazarov Adlet, Alipbekova Sandugash. ROLE OF NEOADJUVANT THERAPY FOR PATIENTS WITH GASTRIC CANCER: MULTIDISCIPLINARY HOSPITAL WITH ONCOLOGY CENTER.....	32-37
David Tchkonია, Nino Gabashvili, Teona Mskhaladze, Tamari Kevlishvili, Mikolay Chkonia. EFFICACY OF ENDOBRONCHIAL VALVE PLACEMENT IN THE MANAGEMENT OF PULMONARY HEMORRHAGE: A COMPARATIVE STUDY.....	38-42
Baglan Kemelbekov, Ainur Amanzholykyz, Samat Saparbayev, Manarbek Askarov, Edgaras Stankevicius. IMPACT OF STEM CELL THERAPY ADDED TO GUIDELINE-DIRECTED MEDICAL THERAPY ON QUALITY OF LIFE IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY.....	43-50
Abramishvili T, Papava K, Mamisashvili M, Tkeshelashvili M, Tsinamdzgvrishvili B. CARDIAC STRAIN IN WOMEN WITH A DOCUMENTED HISTORY OF OVERT OR SUBCLINICAL HYPOTHYROIDISM: AN EXPLORATORY SPECKLE-TRACKING ECHOCARDIOGRAPHY STUDY.....	51-56
TEREZA Y. AZATYAN. FORMATION AND DISTRIBUTION PATTERNS OF FUNCTIONAL INTERHEMISPHERIC BRAIN ASYMMETRY IN CHILDREN WITH INTELLECTUAL DISABILITIES.....	57-63
Fai Twrki Althoini, Ebtehal Solaiman Almogbel. CARDIOMETABOLIC RISK PROFILES IN ADULTS WITH DIABETES: ASSOCIATIONS WITH GLYCEMIC CONTROL, DIABETES TYPE, AND DEMOGRAPHIC CHARACTERISTICS.....	64-77
Datunyan G.S, Shaboyan K.R, Muradyan A.A, Shaboyan E.K, Galstyan A.S, Badalyan A, Sargsyan M.V. IMPACT OF THE COVID-19 PANDEMIC ON THE SEVERITY AND OUTCOMES OF GUNSHOT INJURIES.....	78-84
Zhanar Kozhakhmetova, Nazym Yelemessova, Syzdykova Dinara, Abdullina Sayagul, Nagima Issatayeva, Assiya Turgambayeva, Gulnara Kamalbekova, Diana Zhumagaleyeva, Akmaral Mussakhanova. CRITICAL VALUES OF HEMOSTASIS PARAMETERS IN AN ONCOLOGY CENTER: A RETROSPECTIVE REGISTRY-BASED STUDY.....	85-92
Gradil G.I, Torianyk I.I, Yurko K.V, Shiyan D.M, Merkulova N.F, Mohylenets O.I, Tkachenko V.G, Karmazina I.S, Lantukh A.P, Hryhorov Y.B, Gargin V.V. ASSOCIATION OF PULMONARY AND CUTANEOUS CHANGES IN COVID-19-RELATED CONDITIONS.....	93-98
Alaa MA. Albayaty, Alaa M. Sadiq, Ali SJ. Al Qaissi. ASSOCIATION BETWEEN INFLAMMATORY MARKERS, LIVER ENZYMES, LIPID PROFILE, AND VITAMIN D STATUS IN ADULTS WITH OBESITY: A CROSS-SECTIONAL STUDY.....	99-104
Kenzhebaeva B, Baimuratova M, Kalmakhanov S, Budakoğlu I.I, Laktionova M, Abdulkalikova D. IMPACT OF CLINICAL, ORGANIZATIONAL, AND PSYCHOSOCIAL FACTORS ON THE QUALITY OF LIFE OF PATIENTS WITH DERMATOVENEREOLGICAL DISEASES.....	105-114
Obidov F. Kh, Shamsiev E. A, Samatov F. F, Naimov Dilshod Kayim ugli, Khalimova F. T, Marwan Ismail. BIOMARKER-ORIENTED REHABILITATION IN CHRONIC CEREBRAL ISCHEMIA.....	115-122
Raghad Alkhalify, Lina Almutairi, Fatimah Alghofaili, Wasan Alhawaish, Thekra Alhumidi. COMPARATIVE IN-VITRO QUALITY EVALUATION OF COMMERCIALLY AVAILABLE DICLOFENAC SODIUM TABLETS.....	123-131
Ali S. Jumaah, Ali A. Younis, Shamil H. Othman. EFFECTS OF CURCUMIN ON CLINICAL OUTCOMES AND INFLAMMATORY BIOMARKERS IN KNEE OSTEOARTHRITIS: A RANDOMIZED TRIAL.....	132-138
Ashot Markosyan, Diana Alaverdieva, Mark Danghyan, Ani Mkrtchyan, Lusine Balayan, Khachik Hakobyan, Arpine Geolchanyan, Tigran Soghomonyan, Volodya Mirzoyan. SYNTHESIS AND SOME BIOLOGICAL PROPERTIES OF DERIVATIVES OF 2,3-DISUBSTITUTED 5,5-DIMETHYL-BENZO[h]QUINAZOLIN-4(1H)-ONES.....	139-143

J. Gobadze, M. Nagervadze, T. Gogitidze, N. Bejanidze, N. Zarnadze, K. Dolidze. IMPACT OF GESTATIONAL DIABETES MELLITUS ON NEONATAL BIRTH WEIGHT, LENGTH, AND GESTATIONAL AGE: A RETROSPECTIVE CASE-CONTROL STUDY	144-151
Liudmyla Bashkirova, Iryna Romanova, Vitalii Yatsynovych, Oleksandr Zlobin, Artem Lanskoi. EVIDENCE-BASED PHARMACOTHERAPY FOR ANXIETY DISORDERS COMORBID WITH PTSD: A SYSTEMATIC REVIEW	152-163
Madina Makhmudova, Tolegen Kerimbekov, Zhaina Berikbayeva, Dinara Turebekova, Lyudmila Akhmaltdinova, Yefim Alisseiko, Olga Avdienko, Madina Rashova. IN VITRO INVESTIGATION OF THE POTENTIAL OF C60 FULLERENES AS ADJUVANTS OF NONSPECIFIC IMMUNITY	164-168
Tchernev G, Tchernev KG Jr, Kordeva S. DERMATOLOGIC SURGERY ROUNDS: THE LIMBERG FLAP AND V-TO-T CLOSURE FOR CUTANEOUS/ MUCOCUTANEOUS DEFECTS FOLLOWING SKIN CANCER EXCISION IN HIGH-RISK FACIAL REGIONS	169-174
Nino Nadiradze, Zurab Ckhaidze. SELF-RATED HEALTH IN THE POPULATION OF MEDICAL WORKERS IN GEORGIA	175-180
Argjend Shala, Nexhmedin Shala, Fisnik Jashari, Blert Jashari, Rushit Jashari. SPORADIC CREUTZFELDT-JAKOB DISEASE: CLINICAL FEATURES, DIAGNOSIS AND THERAPEUTIC HORIZONS	181-189
Omar S. Salman, Adeeb A. Al-Zubaidy. ACEBROPHYLLINE REPROGRAMS INFLAMMATORY AND REDOX SIGNALLING IN EXPERIMENTAL ULCERATIVE COLITIS: A DOSE-DEPENDENT STUDY	190-199
Eib K. Eibov, Solikhabonu Khavaskhonova, Kamshat S. Taubay, Karlygash Zh. Sadykova. CALCULATED WHOLE BLOOD VISCOSITY IS SPECIFICALLY ASSOCIATED WITH ABDOMINAL OBESITY, BUT NOT WITH OTHER COMPONENTS OF METABOLIC SYNDROME: A CROSS-SECTIONAL STUDY IN A CENTRAL ASIAN ADULT COHORT	200-208
Shqiponje Gashi, Erza Voca Mulaj, Naser Rugova, Suzana Dvojakovska, Filip Koneski. MANAGEMENT OF PERIOPERATIVE BLEEDING IN PATIENTS WITH PLATELET HYPOAGGREGABILITY DURING DENTOALVEOLAR SURGERY: CLINICAL OUTCOMES AND THERAPEUTIC APPROACHES	209-214
Alina Articulo, Rigor Rey Cuevas, Hani Al-Najjar, Rahaf Alkhuraif, Rasha Aburmeishan, Abdulaziz Almatrody. EXPLORING THE SATISFACTION OF NEWLY HIRED NURSES USING AN EVIDENCE-BASED, PERSONALIZED ONBOARDING PROGRAM: A CROSS-SECTIONAL ANALYSIS	215-222
Nagima Issatayeva, Samal Duisekova, Meruert Saberbekova, Roza Tumanova, Larisa Guruleva, Sholpan Mukanova. APPLICATION OF THE FAILURE MODE AND EFFECTS ANALYSIS METHOD IN HEALTHCARE: A CASE STUDY OF A UNIVERSITY MEDICAL CENTER IN KAZAKHSTAN	223-237
Hisham R. Ezzat, Ibrahim M. Faisal. CARDIOPROTECTIVE EFFECTS OF SILYMARIN AND VITAMIN E AGAINST DOXORUBICIN-INDUCED CARDIOTOXICITY IN RATS: EVIDENCE FROM OXIDATIVE STRESS MARKERS AND HISTOPATHOLOGICAL ANALYSIS	238-245
Shishniashvili D.S, Bedinashvili Z.J, Tsomaia K.B, Svanadze L.M, Chkhikvishvili N.M, Durglishvili G.A. FIRST-VOID URINE VERSUS URETHRAL SWAB FOR MOLECULAR DETECTION OF SEXUALLY TRANSMITTED INFECTIONS IN MEN WITH MULTIPLE SEXUAL PARTNERS	246-252
Chekhovska G.S, Pustova N.O, Syzon O.O, Chaplyk-Chyzho I.O, Dashko M.O, Vozniak I.Ya, Volbyn S.V, Ivaniushko-Nazarko N.V, Zhemela O.D, Gargin V.V. NAIL PLATE DAMAGE INDEX IN DERMATOSCOPIC EXAMINATION OF PATIENTS WITH ONYCHOMYCOSIS	253-258
Meng-Yun Zhou, Shi-qi Yu, Shao-jie Zhu, Xiang Kong, Xin-Ming Yao. A NOVEL KCNJ5 GENE MUTATION ASSOCIATED WITH FAMILIAL ALDOSTERONISM TYPE III WITHOUT HYPERTENSION	259-265
Koba Kamashidze, Tina Beruchashvili, Irina Nakashidze, Sarfraz Ahmad, Tamar Peshkova. BRIDGING THE COVERAGE-PARTICIPATION GAP: BEHAVIORAL DETERMINANTS OF CERVICAL CANCER SCREENING AMONG WOMEN IN ADJARA, GEORGIA	266-273
T.N. Kosayeva, A.T. Amiraslanov, H.K. Muradov, A.Y. Gaziyeu, B.E. Abbasov. PD-L1 EXPRESSION AND SERUM CA125: CLINICOPATHOLOGICAL CORRELATIONS IN HIGH-GRADE SEROUS OVARIAN CARCINOMA	274-280
Ruziyeva Amira Asrorovna, Khamidov Obid Abdurakhmanovich, Murodqosimov Saidolim, Doniyorov Bakhridin Baxrom ugli, Khalimova F.T, Marwan Ismail. ACE I/D AND NOS3 G894T POLYMORPHISMS AND CARDIOVASCULAR ADAPTATION PROFILES IN ADOLESCENT FOOTBALL PLAYERS	281-288

Mukhriddin Umbarov Ochilovich, Shamsutdinova Maksuda Ilyasovna, Abdullayev Ravshanbek Babajonovich, Rokhila Bakhriiddinovna Mengliyeva. ASSOCIATIONS OF CYTOKINE PROFILE AND EXOCRINE PANCREATIC FUNCTION WITH A SYMPTOM-BASED DEHYDRATION CATEGORY AND SEASON OF PRESENTATION IN CHRONIC PANCREATITIS: A RETROSPECTIVE STUDY.....	289-297
Saeed H. Hussein, Hiba M. Ahmed, Ahmed A. Ahmed. DETECTION OF HEPATITIS B AND C VIRAL INFECTION AMONG CHILDREN WITH ACUTE LEUKAEMIA.....	298-302
Davit Kobuladze, Ahishtan Febrian Nishanthan, Nino Kedelidze, Rusudan Vadatchkoria, Magda Davitashvili, Lamara Zuroshvili, Darejan Margalitashvili, Nani Gvarishvili, Nazi Turmanidze, Tamar Peshkova, Naman Chauhan, Teona Gogitidze, Nameera Parveen Shaikh, Aleena Parveen Shaikh, Abeshana Febrian Nishanthan, Irina Nakashidze. SELECTED LABORATORY PARAMETERS IN PEDIATRIC PATIENTS WITH COVID-19 STRATIFIED BY WHITE BLOOD CELL AND PLATELET PROFILES.....	303-309
Rawan Waleed, Abrar Fadlalla, Jana Abdullah, Marwan Ismail, Mohammed Ibrahim Saeed, Ahmad Luay Osman Hashim, Abdelgadir Elamin Eltom. IMPACT OF HELICOBACTER PYLORI INFECTION ON VITAMIN B12 DEFICIENCY LEVELS: A RETROSPECTIVE STUDY.....	310-315
T.A. Asgarova, K.M. Rahimli, G.A. Valiyeva, Sh.I. Hasanova, F.E. Guliyeva, Kh.R. Mammadova. SOME HEREDITARY DISEASES PREVALENT IN THE REPUBLIC OF AZERBAIJAN.....	316-319
Sahadete Shala, Ferdita Haxhiu Derguti. PSOAS MUSCLE ABSCESS FOLLOWING CESAREAN SECTION: A CASE REPORT.....	320-322
N. Kajaia, L. Gabunia, M. Mantskava, S. Kalmakhelidze, G. Ormotsadze, S. Turabelidze-Robaqidze, T. Sanikidze. PRO-INFLAMMATORY INTERLEUKINS AND OXIDATIVE IMBALANCE IN L-NAME-INDUCED HYPERTENSION: COMPARATIVE EFFECTS OF β -BLOCKERS.....	323-330
Hussein Fadhil Abdulameer, Raed Aziz Badeia. COMPARATIVE EVALUATION OF TWO HERBAL MOUTHWASHES AND CHLORHEXIDINE ON CALPROTECTIN IN GINGIVITIS PATIENTS: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL.....	331-340
J. Gobadze, M. Nagervadze, T. Gogitidze, N. Bejanidze, T. Koiava. SOME BIOLOGICAL CHARACTERISTICS ASSOCIATED WITH GESTATIONAL DIABETES.....	341-348
Yurevych N. O, Sazonova O. N, Kachailo I.A, Hnidyk Yu. V, Pokotylo P. B, Podolyuk M.V, Blyshak N. B, Mykhalevych M. M, Zherebkin V. V, Kosynskyi O. V, Aliksieieva V. V. THREE-DIMENSIONAL CT-BASED MORPHOMETRIC ASSESSMENT OF THE MAXILLARY SINUS.....	349-355
Simbarashe Magaisa. PERCEPTIONS AND PRACTICES OF HEALTHCARE PROVIDERS IN MATERNAL MORTALITY AND STILLBIRTH PREVENTION AND MANAGEMENT: INSIGHTS FROM LEJWELEPUTSWA DISTRICT.....	356-363
Akezhan Rustemuly Astrakhanov, Ainur Amanzholkyzy, Samat Sagatovich Saparbayev, Meirambek Sagnaevich Kurmangazin, Aigerim Iskakova, Gulzhanat Nurlanova. THE ROLE OF CELL THERAPY IN THE COMPREHENSIVE TREATMENT OF CHRONIC HEPATITIS C-RELATED LIVER CIRRHOSIS.....	364-370
Miranda Shervashidze, Khatia Dolidze, Tamar Bakhtadze, Tamar Shervashidze. PREVENTING EXERCISE-RELATED SUDDEN CARDIAC DEATH THROUGH SYSTEMATIC PREPARTICIPATION CARDIOVASCULAR SCREENING: A TWO-YEAR REGIONAL COHORT STUDY OF PEDIATRIC ATHLETES IN ADJARA, GEORGIA.....	371-380
Waseem Hashim Alkhaffaf, Muhammad A. Alkataan. COMPARATIVE EFFICACY OF 200 UNITS VERSUS 155 UNITS OF ONABOTULINUMTOXIN A FOR CHRONIC MIGRAINE.....	381-388
K. Tovar Calderón, J. Orozco Pilco, C. Calderón Cabezas, K. Caiza Cuello. ETHNIC DISPARITIES IN BIRTH WEIGHT AND PRENATAL CARE UTILIZATION IN ECUADOR, 2024.....	389-394
Gaukhar Issakova, Suriya Yessentayeva, Daniyar Amangaliyev, Askhat Bralov, Assiya M. Issayeva, Yestay Abzalbek, Marat Akhetov. INDICATIONS FOR REMOVAL OF A PORT SYSTEM IN A PATIENT WITH SUSPECTED SEPTICEMIA IN THE ABSENCE OF OTHER LOCAL SOURCES OF INFECTION.....	395-398
Mohammed A. Hayawi, Duaa M. Al-Nafoly. PREDOMINANCE OF FOLLICULAR ADENOMA AND PAPILLARY CARCINOMA IN THYROID NEOPLASMS.....	399-403
Nino Buadze, Nata Kazakhashvili. POPULATION KNOWLEDGE, RISK PERCEPTION, GOVERNANCE AND PUBLIC HEALTH DETERMINANTS OF COVID-19 IN GEORGIA: A NATIONAL CROSS-SECTIONAL STUDY.....	404-422

Alaa H. Alfarhan, Bahir S. Allawi, Mohammed A. Aljodah, Ahmed Jawad. MINIMALLY INVASIVE FAT TRANSPOSITION IN LOWER BLEPHAROPLASTY	423-427
Ospanova Meruyert, Ospanova Saniya, Yernazarov Adilet, Amanbaev Rauan, Rakhmankulov Umarali. LOW-FREQUENCY ULTRASOUND AND OZONE/NO TECHNOLOGIES IN THE COMBINED TREATMENT OF EXUDATIVE HEMISINUSITIS USING THE YAMIK-3 SINUS CATHETER.....	428-432
Sodikjon Mashraf Ugli Makhmatkulov, Ibragimova Malika Shavkatovna, Khasanov Alisher Yurevich, Mavlyanova Zilola Farkhadovna, Khalimova F.T, Marwan Ismail. COMBINED BOTULINUM TOXIN THERAPY AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN THE REHABILITATION OF WOMEN WITH URGENCY URINARY INCONTINENCE ASSOCIATED WITH DIABETES MELLITUS.....	433-444
Nellia Veretova, Alfiya Samigullina, Aigul Baialieva, Ruslan Abdyldaev, Begimai Muratbekova. PSYCHONEUROLOGICAL THERAPY FOR POST-COVID SYNDROME: A COMPREHENSIVE REVIEW OF METHODS AND CLINICAL EFFECTIVENESS.....	445-451
Azhar Giniyat, Natalya Slivkina, Viktor Tkachev, Gulbana Khussainova, Ayan Baigaliyev, Sara Kubekova, Aizat Seidakhmetova, Zilola Mavlyanova, Mirbanu Aikhodzheyeva, Raikhan Burumbaeva, Larissa Pavlovets, Raikhan Tleulinova, Raushan Baigenzheyeva, Mereke Alaidarova, Joseph Almazan, Aizhan Altynbekova, Bakyt Zhangabulova, Zinugul Baissova, Manzura Kankina, Parida Pirmanova, Magira Shaizadinova, Aliya Utenova, Zhansaya Raiymkul. DEVELOPMENT AND EVALUATION OF A NURSE-LED SELF-DIRECTED PEDIATRIC REHABILITATION MODEL: COMPARATIVE ANALYSIS OF INTERNATIONAL PRACTICES.....	452-465
Florina Sahiti, Argjira Veseli, Marija Peeva Petreska, Shera Kosumi, Nora Berisha, Enis Veseli, Kaltrina Veseli. BIOMARKERS OF BONE REMODELING AND INFLAMMATION IN CHRONIC PERIAPICAL LESIONS: A NARRATIVE REVIEW	466-473

A NOVEL KCNJ5 GENE MUTATION ASSOCIATED WITH FAMILIAL ALDOSTERONISM TYPE III WITHOUT HYPERTENSION

Meng-Yun Zhou¹, Shi-qi Yu¹, Shao-jie Zhu¹, Xiang Kong^{2*}, Xin-Ming Yao^{1*}.

¹Department of Metabolism & Endocrinology, The First Affiliated Hospital of Wannan Medical University (Yijishan Hospital of Wannan Medical University), Wuhu 241001, China.

²Department of Geriatrics, The First Affiliated Hospital of Wannan Medical University (Yijishan Hospital of Wannan Medical University), Wuhu 241001, China.

Address for correspondence: Xin-Ming Yao, Email: yxm6965@wnmc.edu.cn

Xiang Kong, Email: kongxiang@yjsy.com.

*During the submission process, Xin-Ming Yao and Xiang Kong served as the first and the second corresponding author, respectively.

Abstract.

Background: Primary aldosteronism (PA) involves excessive autonomous aldosterone (ALD) secretion by the adrenal cortex, leading to water and sodium retention and renin–angiotensin system inhibition, causing hypertension and K⁺ imbalance. Familial hyperaldosteronism type III (FH-III) is a rare subtype, characterized by hypokalemia with hypertension and adrenal hyperplasia. Eight associated pathogenic potassium inward rectifying channel protein subfamily J member 5 (KCNJ5) mutations have been reported. This study reports a Chinese family with FH-III associated with a rare KCNJ5 variant (c.536A>G, p.Asn179Ser), which has been previously reported in cardiac genetics databases (rs147070381). Our study expands its phenotypic spectrum to include familial aldosteronism.

Methods: A middle-aged female presented with recurrent hypokalemia unresponsive to oral potassium supplementation. She and her family underwent comprehensive clinical examination, biochemical testing, imaging studies, and whole-exome sequencing.

Results: She exhibited recurrent hypokalemia without hypertension, with fluctuating ALD, which were controlled with spironolactone. The proband, along with her sister and mother, were found to carry a heterozygous KCNJ5 variant (exon 2: c.536A>G, p.Asn179Ser).

Conclusion: FH-III symptoms vary widely, making diagnosis challenging in patients who solely present with recurrent hypokalemia. Early gene sequencing facilitates accurate diagnosis to guide appropriate treatment.

Key words. Hypokalemia, primary aldosteronism, KCNJ5, familial hyperaldosteronism issue section: clinical research article.

Introduction.

Primary aldosteronism (PA) is a prevalent etiology of hypokalemia, characterized by hypokalemia and hypertension [1]. It exhibits a higher prevalence in females compared with males and is associated with more pronounced cardiac and renal damage compared with essential hypertension. Familial aldosteronism (FH), an autosomal dominant trait involving germline mutations, accounts for <10% of PA cases. FH often presents at a young age with severe hypertension and hypokalemia, frequently with a positive family history [2]. According to the known pathogenic genes, FH can be classified into four types: FH-I, FH-II, FH-III, and FH-IV [3]. FH-I was

first identified in a father–son family and is characterized by early onset hypertension. Low-dose glucocorticoid therapy can effectively reverse aldosterone secretion and thereby control the disease. FH-I results from a gene crossover event between the mitochondrial enzymes 11 β hydroxylase (CYP11B1) and aldosterone synthase (CYP11B2), which share 93% sequence homology. Biochemically, patients exhibit markedly elevated levels of 18-oxocortisol and 18-hydroxycortisol. Exogenous administration of dexamethasone suppresses adrenocorticotrophic hormone (ACTH) release, thereby reducing aldosterone production [4]. FH-II was first reported by Gordon et al. in 1991. Its diagnosis requires the exclusion of FH-I and the presence of at least two relatives with PA within a family. FH-II has recently been associated with activating variants in CLCN2 on chromosome 1q31, which encodes the chloride channel CIC-2. The clinical phenotype of FH-II resembles that of sporadic PA, and it does not respond to glucocorticoid therapy. FH-III arises from germline mutations in potassium inward rectifying channel protein subfamily J member 5 (KCNJ5), resulting in severe PA and treatment resistance; symptom control often necessitates adrenalectomy [5-6]. Consensus recommendations suggest KCNJ5 testing to identify FH-III in younger patients with PA [7]. FH-IV typically presents in childhood. It is caused by mutations in the CACNA1H gene, located on chromosome 16p13, which encodes the T-type voltage-gated calcium channel. Clinically, calcium channel blockers are helpful in controlling blood pressure in these patients. This study conducted a pathogenic gene analysis on a family with FH-III with mild clinical manifestations. Whole-exome sequencing analysis revealed a heterozygous KCNJ5 variant (c.536A>G, p.Asn179Ser), which has been documented as rs147070381 in cardiac genetics studies, but its association with an aldosteronism-related phenotype has not been previously reported. The results enrich the knowledge base on the FH-III gene mutation spectrum and elucidate the phenotypic relationship between symptoms and FH-III genotype.

Materials and Methods.

Participants:

The patient and her sister were admitted to our hospital due to hypokalemia. Their mother declined further inpatient evaluation and only consented to genetic testing. Comprehensive data were collected, including medical history, physical examination, laboratory tests, imaging studies, and genetic testing; not all subjects were eligible for every analysis. All participants provided written informed consent before inclusion.

Genetic Analyses:

This study was approved by the Medical Ethics Committee of our hospital. Peripheral blood samples were collected from the participants, and high-throughput sequencing (next-generation sequencing) combining whole-exome sequencing with mitochondrial genome sequencing was performed. Sequencing was carried out on the Illumina NovaSeq sequencing platform (Illumina, Inc., San Diego, CA, USA). Libraries were prepared using Exome Research Panel v2.0 capture probes (for whole-exome capture) and the Human mtDNA Research Panel (for mitochondrial genome capture), following standard operating procedures. Raw fastq data were filtered using fastp software (quality filtering, adapter removal, and read trimming). Clean reads were aligned to the human reference genome (GRCh38) using BWA-MEM (version 0.7.12-r1039). Sambamba was used for duplicate removal after sorting. SNP and INDEL detection were performed using GATK HaplotypeCaller. CNV analysis was performed using XHMM and CNVkit. For the mitochondrial genome analysis, mitochondrial DNA reads were extracted from the whole-exome sequencing data, enabling coverage of the complete mitochondrial genome (16,569 bp). The mean depth of the exome sequencing data was 117.38×, and the target regions achieved >20×coverage with an accuracy of 99.72%. Variants were filtered by quality (read depth≥10×, genotype quality≥30), allele frequency (MAF < 0.01 in gnomAD, ExAC, and 1000 Genomes), and functional impact (non-synonymous, splicing, or frameshift variants in genes associated with PA or hypokalemia). Candidate variants were prioritized under an autosomal dominant inheritance model and further filtered by phenotype-based prioritization. No other candidate variants in genes known to cause familial aldosteronism or hereditary hypokalemia were identified. CNV analysis revealed no clinically significant copy-number variations. Structural variants were not analyzed, as WES is not designed for SV detection, and the CYP11B1/CYP11B2 chimeric gene was not investigated due to technical limitations of WES for fusion gene detection.

Potentially pathogenic variants were classified according to the American College of Medical Genetics and Genomics (ACMG) guidelines for variant classification. The ACMG/AMP classification for the identified variant was Uncertain significance, supported by the following evidence codes: PM1 (located in a functional domain), PM2_Supporting (low frequency in population databases), and PP3_Supporting (multiple in silico tools predict deleterious). Variant annotation was performed using ANNOVAR, with validation and cross-referencing against updated databases including gnomAD v4.0, ExAC, TOPMed, and ClinVar (accessed July 2026) to ensure current allele frequency and clinical interpretation. The variant was reported consistently according to HGVS recommendations as *KCNJ5* NM_000890.5:c.536A>G, p.(Asn179Ser), with the following parameters: genomic coordinate chr11:128911809 (GRCh38), exon 2, heterozygous, sequencing depth 112×, and alternate allele fraction 41.67%. Putative pathogenic sequences were amplified by PCR and further validated by Sanger sequencing using the ABI3730 Genetic Analyzer. The sequencing results were analyzed using the SeqMan module of the DNASTAR software. Gene sequencing was completed by Beijing Hongwei Te Biotechnology Co., Ltd.

Ethical considerations:

This retrospective study was performed in accordance with the principles of the

Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Yijishan Hospital, Wannan Medical University, with the approval number (2026) IRB Research No. 198. Written informed consent was obtained from all participants for the use of clinical data and genetic testing.

Biochemical Analyses:

All biochemical analyses were performed following established clinical standards. Plasma renin and aldosterone (ALD) levels were measured using the LIAISON fully automated chemiluminescence immunoassay analyzer.

Results.

Clinical Phenotype:

Kindred A:

A 40-year-old female patient visited our hospital on January 14, 2022 for an outpatient examination because of limb muscle weakness. Blood tests showed K⁺ levels of 2.65 mmol/L, Na⁺ levels of 143.5 mmol/L, Cl⁻ levels of 102.9 mmol/L, and a CO₂ binding capacity of 30.7 mmol/L. Synchronized ALD was 9.24 ng/dL (reference for standing position: 3.0–23.2 ng/dL), while renin was 8.76 μIU/mL (reference for standing position: 4.4–46.1 μIU/mL). No muscle soreness, numbness, vomiting, or diarrhea was reported. Oral KCl sustained-release tablets (1.0 g three times daily) were prescribed.

After 6 days, blood test results showed improved K⁺ (3.12 mmol/L), Na⁺ (137.7 mmol/L), Cl⁻ (103.4 mmol/L), and CO₂ binding capacity (26.3 mmol/L). The patient continued taking KCl. On February 7, 2022, she was admitted to hospital to determine the underlying cause of hypokalemia. The patient had no history of hypertension, chronic diarrhea, or kidney disease but had previously been diagnosed with hypothyroidism and was undergoing treatment with oral sodium levothyroxine tablets once daily. Her mother and sister had similar medical histories.

Physical examination upon admission revealed a body temperature of 36.3 °C, a pulse rate of 116 bpm, a respiratory rate of 18 breaths/min, and a blood pressure of 133/81 mm Hg. The patient was conscious and exhibited normal development. No skin rash or mucous membrane abnormalities were observed. There was no eye protrusion or palpable thyroid enlargement or nodules. Auscultation of the heart and lungs revealed no abnormalities. The liver and spleen were not palpable below the rib cage, and there was no edema in the lower limbs. Limb muscle strength was assessed as level V.

Laboratory tests showed K⁺ levels of 3.35 mmol/L, Na⁺ levels of 144.6 mmol/L, Cl⁻ levels of 108.5 mmol/L, Mg²⁺ levels of 0.73 mmol/L, Ca²⁺ levels of 2.18 mmol/L, and simultaneous 24-hour urine K⁺ levels of 38.88 mmol/L. Urine routine analysis indicated a specific gravity of 1.032 (normal: 1.003–1.03) and a pH of 6.0, with no glucose or protein. Arterial blood gas analysis revealed a pH of 7.403, partial pressure of CO₂ of 39.8 mmHg, residual base in extracellular fluid of 0.1 mmol/L, and bicarbonate ions of 24.5 mmol/L. Electrocardiogram findings showed sinus rhythm with a heart rate of 72 bpm. Thyroid

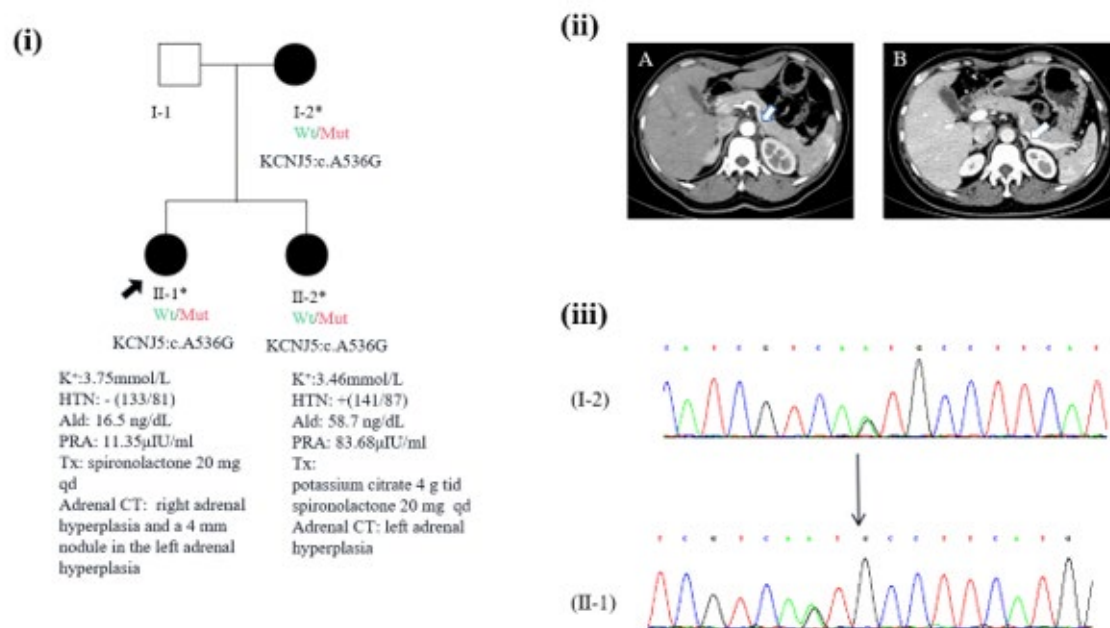


Figure 1. Pedigree, adrenal computed tomography (CT) image and Sanger sequencing chromatograms of the family with a pathogenic *KCNJ5* variant. (i) Pedigree of the family. Squares represent male family members, circles represent female family members. Filled circles indicate affected individuals. The black arrow denotes the proband. Asterisks mark subjects who underwent genetic testing. Genotypes, serum potassium (K^+), hypertension status (HTN, blood pressure values in parentheses), plasma aldosterone concentration (Ald), plasma renin activity (PRA), treatment regimen (Tx), and adrenal CT findings are listed below each available participant. Wt, wild-type allele; Mut, mutant allele. (ii) Representative adrenal CT image of the proband. (iii) Sanger sequencing results showing the heterozygous *KCNJ5*c.A536G variant (p.N179S) in affected family members.

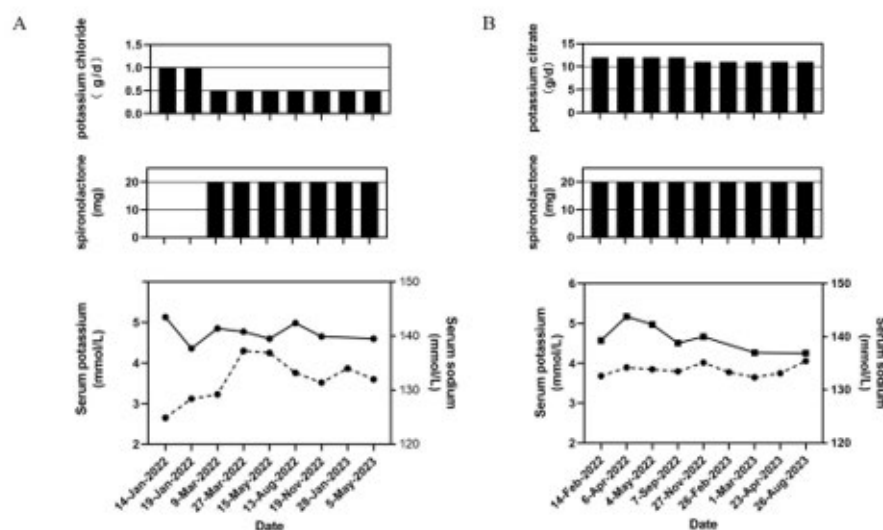


Figure 2. Electrolytes in previous outpatient follow-ups. The dashed line represents the serum K^+ level; the solid line represents the serum Na^+ level. Doses of spironolactone and potassium are also presented.

function parameters were normal, including thyroid-stimulating hormone at 3.906 mIU/L (normal: 0.55–4.78 mIU/L), free triiodothyronine at 4.52 pmol/L (normal: 3.5–6.5 pmol/L), and free thyroxine ft_4 at 18.81 pmol/L (normal: 11.5–22.7 pmol/L). ALD levels were 16.50 ng/dL, while renin levels were 11.35 μ IU/mL.

An adrenal contrast-enhanced computed tomography (CE-CT) scan revealed right adrenal hyperplasia and a 4 mm

nodule in the left adrenal hyperplasia (Figure 1A). The patient was administered supplementary KCl (3.0 g/day) without spironolactone. Follow-up blood tests showed K^+ levels of 3.75 mmol/L, Cl^- levels of 144.6 mmol/L, and Na^+ levels of 141.5 mmol/L. Consequently, the dosage of KCl sustained-release tablets was adjusted to 2.0 g/day. During follow-up 1 month later, K^+ level was measured at 3.23 mmol/L, Cl^- level at 104.5 mmol/L, and Na^+ level at 141.4 mmol/L. KCl was

further adjusted to 1.5 g, and spironolactone was introduced (20 mg/day). After the patient self-discontinued spironolactone in January 2025, follow-up tests revealed a decrease in serum K⁺, accompanied by a renin level of 7.85 μ IU/mL (reference for standing position: 4.4–46.1 μ IU/mL) and a synchronized ALD level of 15 ng/dL (reference for standing position: 3.0–23.2 ng/dL). Following spironolactone resumption (20 mg/day), serum K⁺ returned to normal, with no hypokalemia during subsequent blood tests (Figure 2A).

Kindred B:

The proband's 41-year-old sister experienced muscle weakness starting at the age of 33. Laboratory tests conducted at another hospital revealed hypokalemia with blood K⁺ levels at 3.12 mmol/L. ALD and renin were not measured. She was prescribed potassium citrate granules (4 g twice daily) and spironolactone tablets (20 mg/day). Despite treatment, her symptoms persisted. At the age of 39, she sought medical attention at our hospital.

Upon admission, her blood pressure was normal. Blood tests showed K⁺ levels at 3.46 mmol/L and simultaneous 24-hour urine K⁺ levels at 49.2 mmol/L. ALD was elevated (58.70 ng/dL), and the renin level was significantly increased (83.68 μ IU/mL). Cortisol levels (measured from 7–9 am) were normal (447.00 nmol/L; normal: 138–690 nmol/L), as were adrenocorticotrophic hormone levels (29.80 pg/mL; normal: 0–46 pg/mL). Adrenal CE-CT scan revealed left adrenal hyperplasia (Figure 1B). The patient was prescribed 4 g of potassium citrate three times daily and 20 mg of spironolactone once daily. Subsequent K⁺ and ALD test results returned to normal, and blood pressure remained within the normal range. Potassium citrate was adjusted to 4 g in the morning, 3 g at noon, and 3 g in the evening for maintenance. Since the patient discontinued spironolactone in October 2024, hypokalemia has not recurred (Figure 2B).

Genetic Analyses:

To investigate possible genetic causes, both patients and their mother underwent high-throughput whole-exome and mitochondrial genome sequencing, revealing that all had heterozygous KCNJ5 mutations (NM_000890.5). The mutation identified was a missense mutation (c.A536G, p.N179S) in exon 2 of chromosome 11 (Figure 1). This variant is listed as rs147070381 in dbSNP, with a global minor allele frequency of 0.00002 in gnomAD v4.0 (exomes), and has previously been documented in cardiac genetics cohorts. Population allele frequencies across databases are as follows: ExAC 0.00004, TOPMed 0.00006, and ESP 0.00023. ClinVar status shows conflicting classifications: Uncertain significance (2 submissions) and Likely benign (1 submission). To the best of our knowledge, this variant has not been reported in HGMD in association with an aldosteronism-related phenotype.

In silico prediction tools yielded concordant results: PolyPhen-2 (score 0.997, probably damaging), SIFT (score 0.03, deleterious), and REVEL (score 0.737, likely pathogenic). However, these computational predictions should be interpreted as supportive evidence only and do not independently establish pathogenicity. According to the ACMG/AMP guidelines, the variant was classified as Uncertain significance, supported by evidence codes PM1, PM2_Supporting, and PP3_Supporting (see Methods for details). The Sanger sequencing

chromatograms for all tested relatives are presented in Figure 1, with the heterozygous position clearly marked.

Discussion.

This article reports a family carrying a rare KCNJ5 variant associated with FH-III. A 40-year-old female patient presented with asymptomatic hypokalemia and increased 24-hour urinary potassium excretion. Oral potassium supplementation showed poor therapeutic efficacy, raising clinical suspicion of primary aldosteronism (PA). The proband's initial screening revealed normal plasma renin activity, aldosterone levels within the upper limit of normal, and an aldosterone-to-renin ratio (ARR) of 1.88. Notably, at the initial presentation, the patient had not received any antihypertensive agents or potassium-sparing diuretics; however, the presence of profound hypokalemia (K⁺ 2.65 mmol/L) may have induced hyperpolarization of the adrenocortical cell membrane, partially counteracting the depolarizing effect conferred by the KCNJ5 variant and reducing calcium influx, thereby transiently suppressing aldosterone secretion. The subsequent aldosterone measurement after potassium repletion (16.50 ng/dL) was higher than the initial level, supporting this dynamic interpretation. This case illustrates that a single low aldosterone measurement in a patient with hypokalemia does not exclude the diagnosis of PA, particularly in young or familial cases. ARR can be influenced by various factors such as age, sex, diet, blood potassium levels, medications, and blood sampling methods; since this patient had hypokalemia, false-negative results for ARR were possible.

For patient B (the proband's sister), she had self-discontinued spironolactone prior to admission and was maintained on oral potassium citrate only. Thus, the elevated renin and aldosterone levels at admission were not attributable to spironolactone exposure. The diagnosis of PA in patient B was supported by elevated aldosterone (58.70 ng/dL), elevated 24-hour urinary potassium excretion (49.2 mmol/L) in the setting of hypokalemia, and radiological evidence of adrenal hyperplasia. However, we acknowledge that FH-III is not conclusively established in every variant-positive relative, as the mother lacked complete endocrine phenotyping (genotype only) and the father was not available for testing (parents were divorced and lost to follow-up). In this study, we define “affected” status as meeting the biochemical criteria for PA (plasma aldosterone >15 ng/dL with inappropriately normal renin, or ARR >20, confirmed by elevated 24-hour urinary potassium excretion) in the presence of a KCNJ5 variant.

Genetic testing was conducted after obtaining informed consent to confirm the diagnosis, identifying a KCNJ5 variation (Figure 1); the patient's mother and sister were also found to carry this mutation. According to the ACMG guidelines, combined with the patient's clinical manifestations and auxiliary examination findings, the *KCNJ5* variant in the family was classified as Uncertain significance (PM1 + PM2_Supporting + PP3_Supporting), and the diagnosis of FH-III was made based on clinical and genetic correlation rather than definitive pathogenicity classification alone [8]. Previous case reports suggest that FH-III accounts for approximately 0.3% of patients with PA. Clinical presentations can be complex, and symptoms severe. Multiple mutations in the KCNJ5 gene have been reported, with significant heterogeneity in clinical

phenotypes, disease severity, drug response, and prognosis. Patients carrying the p.Gly151Glu or p.Tyr152Cys mutations typically exhibit mild clinical manifestations, which may or may not be accompanied by hypertension and adrenal abnormalities [9]. In contrast, those harboring the p.Gly151Arg, p.Thr158Ala, p.Ile157Ser, or p.Glu145Gln mutations often present with early disease onset and a poor response to antihypertensive therapy [10]. The absence of typical clinical symptoms and hypertension in the proband in this case was misleading, highlighting peripheral blood genetic testing as the sole dependable method for diagnosing atypical FH-III.

Excessive ALD secretion in PA is an independent risk factor for cardiovascular disease and can lead to endothelial dysfunction, atherosclerosis, renal impairment, and metabolic disorders [11-13]. Hypertension and hypokalemia are the main clinical manifestations of PA, although some patients may only present with low blood K⁺, which can result in misdiagnosis. PA can be classified into six types based on underlying causes, with FH being one; FH can further be divided into four subtypes. Originally, FH-III referred to patients with refractory adrenal hyperplasia who did not respond well to dexamethasone treatment. However, because of the wide range of phenotypic variations observed, FH-III now specifically denotes patients with PA caused by KCNJ5 mutations. The first report of FH-III in a family was presented by Geller et al. in 2008 [10,14,15]. In 2011, Choi et al. discovered that germline KCNJ5 mutations represent the genetic basis for FH-III. Early case reports often highlighted the prevalence of the G151R mutation [16]. However, FH-III exhibits genetic heterogeneity, with eight associated KCNJ5 mutations identified to date (p.Glu145Gln, p.Thr149del, p.Gly151Glu, p.Gly151Arg, p.Tyr152Cys, p.Ile157Ser, p.Thr158Ala, and p.Leu169Ser). The c.536A>G (p.Asn179Ser) variant identified in this study has been previously documented in cardiac genetics studies (rs147070381). However, its association with familial aldosteronism has not been previously described, and our findings therefore expand the phenotypic spectrum of this previously reported KCNJ5 variant. The absence of a prior link to adrenal phenotypes may be attributable to the relatively mild functional impairment conferred by this variant, which may require specific genetic or environmental contexts to manifest clinically.

PA pathogenesis is multifaceted and has been linked to ion channel abnormalities. Various channels have been implicated, including TWIK-related acid-sensitive K⁺ ion channel, G-protein activated inward rectifying potassium channel 4 (GIRK4), the Na⁺/K⁺-α1 subunit of ATPase and plasma membrane Ca²⁺-ATPase 3, and the α1D subunit of L-type voltage-gated calcium channel. KCNJ5, located on 11q24.3, [17] consists of five exons and encodes GIRK4, a channel protein expressed in the heart and central and peripheral neurons [14,18-20] as well as in normal fetal and adult adrenal tissues. Its expression levels are higher in the adrenal gland than in the atrium [21]. Under normal conditions, GIRK4 maintains a hyperpolarized state by allowing K⁺ outflow. However, we hypothesize that, with the *KCNJ5* variant, the channel may lose its selectivity for K⁺ ions, resulting in increased Na⁺ influx, continuous membrane depolarization, and subsequent activation of aldosterone synthase (CYP11B2), leading to autonomous aldosterone synthesis. The relatively

mild clinical phenotype observed in our patients may reflect partial rather than complete loss of channel function, which is consistent with the hypothesis of a mild functional impairment. However, this mechanistic interpretation remains a hypothesis in the absence of functional electrophysiological validation.

McCoy et al. [22] demonstrated that the delI157 mutation disrupts the salt bridge surrounding the GIRK4 channel domain, which is crucial for determining ion selectivity, suggesting that this may be the mechanism underlying pathogenesis. Monticone et al. [23] also found a significant increase in the expression of CYP11B2 and its transcription factor NR4A2 in KCNJ5-mutated adrenocortical cells, promoting ALD production. Boulkroun et al. [24,25] found that the frequency of KCNJ5 mutations is higher in women than in men. In comparison with levels in wild-type littermates, female homozygous KCNJ5 knockout mice showed a more pronounced decrease in circulating aldosterone levels than did their male counterparts. Transcriptomic analysis of adrenal glands using RNA sequencing identified substantially more differentially expressed genes in female knockout mice than in males (396 vs. 7). These findings suggest that PPARα serves as a critical regulator of aldosterone synthesis [26]. Female mice with Task1 knockout exhibit a higher susceptibility to PA than male mice do. In males, TASK-3 expression compensates for the loss of its normal heterodimerization partner, TASK-1. This finding supports a mechanism by which females carrying KCNJ5 mutations may be more susceptible to membrane depolarization and subsequently to the development and progression of aldosterone-producing adenomas. The reason why FH-III is more prevalent in females remains unclear, but may be attributed to the inability of female patients to compensate for GIRK4 dysfunction through other ion channels.

Previous case reports suggest that FH-III is more commonly observed in children, with early onset typically occurring before age 7. It often presents with severe aldosteronism and exhibits resistance to drug treatments, including spironolactone and oral potassium supplementation; adrenalectomy is necessary in such cases to control symptoms. Severe phenotypes have been associated with p.Gly151Arg, p.Thr158Ala, p.Ile157Ser, and p.Tyr152Cys mutations; however, there are also reports of well-controlled hypertension and hypokalemia through drug treatments such as spironolactone and amiloride. In this case, the initial patient presented with hypokalemia without hypertension, and blood K⁺ levels were effectively controlled within the normal range through medication. Laboratory findings in patient A revealed an increase in aldosterone levels following treatment. This phenomenon may be attributed to several mechanisms. Severe hypokalemia at admission likely induced hyperpolarization of the mutant cell membrane, which partially counteracted the depolarizing effect conferred by the mutation and reduced calcium influx, thereby temporarily suppressing aldosterone synthesis. Although aldosterone levels remained within the low-normal range, they were higher than expected for a healthy individual under similar degrees of severe hypokalemia. Potassium repletion partially alleviated this hyperpolarized state, resulting in the restoration of depolarization-driven calcium influx and increased aldosterone secretion in mutant cells. This case demonstrates that a single low aldosterone measurement in a patient with hypokalemia does not

exclude the diagnosis of primary aldosteronism, particularly in young or familial cases. Dynamic assessment of the potassium–aldosterone relationship combined with genetic testing is essential to avoid misdiagnosis. In patient B, plasma renin and aldosterone levels at admission were elevated compared with baseline, with a more pronounced increase in renin. This may be attributed to the pharmacological action of spironolactone as a mineralocorticoid receptor antagonist, which competitively binds to aldosterone receptors in the distal renal tubules, thereby blocking the sodium-retaining and potassium-excreting effects of aldosterone. Following spironolactone therapy, the enhanced excretion of sodium and water leads to normalization or even a mild reduction in plasma volume, thereby relieving the chronic suppression of the renin–angiotensin system. Consequently, renin secretion, which had been maintained at low levels, begins to recover, manifesting as an increase in plasma renin activity. The subsequent elevation in renin accelerates the conversion of angiotensinogen to angiotensin II. As the primary physiological stimulator of aldosterone secretion, angiotensin II contributes to the observed post-treatment rise in aldosterone levels relative to baseline. Adrenal hyperplasia was observed in both sisters, but their conditions were mild. Although both patients had previously received oral potassium supplementation, the therapeutic response was suboptimal. Following admission, the dosage of potassium replacement was increased based on their prior regimens, and subsequent adjustments were made according to serial serum biochemical measurements. These individualized modifications ultimately enabled the patients to maintain their serum potassium levels within the normal range. This finding suggests that effective management of this condition requires dynamic optimization of the treatment regimen guided by laboratory parameters, rather than adherence to fixed standard doses of potassium supplementation alone. The p.Asn179Ser variant seen in this family is associated with mild clinical symptoms, possibly because of partial rather than complete functional impairment of the channel protein. However, further research is necessary to better understand the pathogenesis of KCNJ5 variants, providing a basis for diagnosis and the development of targeted therapies.

Study Limitations.

Several limitations of this study should be acknowledged. First, functional experiments, including patch-clamp electrophysiology to assess ion selectivity and calcium imaging to evaluate downstream signalling, were not performed. Consequently, the proposed causal relationship between the p.Asn179Ser variant and GIRK4 functional impairment remains a hypothesis requiring further validation through heterologous expression systems and electrophysiological assays. Second, the family pedigree is limited: the mother lacked complete endocrine phenotyping (genotype only), the father was not tested (lost to follow-up), and no clearly unaffected relatives were available for analysis. This restricts the statistical power of the co-segregation analysis and FH-III is therefore not definitively established in every variant-positive relative. Third, the sample size is small, and the findings may not be generalizable to broader populations with FH-III. Fourth, structural variants and the CYP11B1/CYP11B2 chimeric gene were not assessed due to technical limitations of WES. Future

studies incorporating functional assays and larger family cohorts are needed to confirm the pathogenicity of this variant and its role in aldosterone dysregulation.

Conclusion.

In conclusion, a rare KCNJ5 missense variant (c.536A>G, p.Asn179Ser), previously reported as rs147070381 in cardiac genetics cohorts, was identified in a Chinese family with FH-III and exhibited a strong relationship with the clinical phenotype. This study expands the phenotypic spectrum of this previously reported variant to include familial aldosteronism, providing a scientific foundation for precise clinical diagnosis and treatment. However, due to the absence of functional experiments and the limited family pedigree, these findings should be interpreted with caution, and the causal role of p.Asn179Ser in FH-III pathogenesis requires further validation.

Acknowledgments.

Disclosure Summary: The authors have nothing to disclose.

We thank Lisa Oberding, MSc, from Liwen Bianji (Edanz) (www.liwenbianji.cn) for editing the English text of a draft of this manuscript.

Conflict of Interest.

None

Funding Statement.

This research is funded by the Anhui Provincial Natural Science Foundation (2308085MH252) and Wuhu Science and Technology Project (2023jc27).

Data Availability.

All data generated or analyzed during this study are included in this published article.

REFERENCES

1. RAGNARSSON O, JUHLIN C C, ÅKERSTRÖM T, et al. Emerging methods for subtype differentiation in primary aldosteronism. *J Intern Med.* 2026;299:178-195.
2. Wang TJ, Xie LD. Interpretation of the updated key points of the Expert Consensus on the Diagnosis and Treatment of Primary Aldosteronism (2020 Edition). *Chin J Hypertens.* 2021;29:3.
3. Sutherland DJ, Ruse JL, Laidlaw JC. Hypertension, increased aldosterone secretion and low plasma renin activity relieved by dexamethasone. *Can Med Assoc J.* 1966;95:1109-1119.
4. Gordon RD, Stowasser M, Tunny TJ, et al. Clinical and pathological diversity of primary aldosteronism, including a new familial variety. *Clin Exp Pharmacol Physiol.* 1991;18:283-286.
5. ARAUJO-CASTRO M, PARRA P, MARTÍN ROJAS-MARCOS P, et al. Differences in the clinical and hormonal presentation of patients with familial and sporadic primary aldosteronism. *Front Endocrinol (Lausanne).* 2024;15:1336306.
6. MIR-BASHIRI S, TETTI M, FRÖBEL D, et al. Primary Aldosteronism: Small Molecule Antagonists of Mutant KCNJ5 Potassium Channels. *Hypertension.* 2025.
7. Scholl UI, Stoltzing G, Nelson-Williams C, et al. Recurrent gain of function mutation in calcium channel CACNA1H causes early onset hypertension with primary aldosteronism. *Elife.* 2015;4:e06315.

8. Mulatero P, Tauber P, Zennaro MC, et al. KCNJ5 mutations in European families with nonglucocorticoid remediable familial hyperaldosteronism. *Hypertension*. 2012;59:235-240.
9. Perez-Rivas LG, Williams TA, Reincke M. Inherited Forms of Primary Hyperaldosteronism: New Genes, New Phenotypes and Proposition of a New Classification. *Exp Clin Endocrinol Diabetes*. 2019;127:93-99.
10. Scholl U I, Nelson-Williams C, Yue P, et al. Hypertension with or without adrenal hyperplasia due to different inherited mutations in the potassium channel KCNJ5. *Proc Natl Acad Sci U S A*. 2012;109:2533-2538.
11. Monticone S, Sconfienza E, D'ascenzo F, et al. Renal damage in primary aldosteronism: a systematic review and meta-analysis. *J Hypertens*. 2020;38:3-12.
12. Monticone S, D'ascenzo F, Moretti C, et al. Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2018;6:41-50.
13. Chang YY, Liao CW, Tsai CH, et al. Left Ventricular Dysfunction in Patients with Primary Aldosteronism: A Propensity Score-Matching Follow-Up Study with Tissue Doppler Imaging. *J Am Heart Assoc*. 2019;8:e013263.
14. Choi M, Scholl U I, Yue P, et al. K⁺ channel mutations in adrenal aldosterone-producing adenomas and hereditary hypertension. *Science*. 2011;331:768-772.
15. Geller D S, Zhang J, Wisgerhof M V, et al. A novel form of human mendelian hypertension featuring nonglucocorticoid-remediable aldosteronism. *J Clin Endocrinol Metab*. 2008;93:3117-3123.
16. Korah HE, Scholl UI. An Update on Familial Hyperaldosteronism. *Horm Metab Res*. 2015;47:941-946.
17. Monticone S, Tetti M, Burrello J, et al. Familial hyperaldosteronism type III. *J Hum Hypertens*. 2017;31:776-781.
18. Marionneau C, Couette B, Liu J, et al. Specific pattern of ionic channel gene expression associated with pacemaker activity in the mouse heart. *J Physiol*. 2005;562:223-234.
19. Mintert E, Börsche L I, Rinne A, et al. Generation of a constitutive Na⁺-dependent inward-rectifier current in rat adult atrial myocytes by overexpression of Kir3.4. *J Physiol*. 2007;585:3-13.
20. Monticone S, Hattangady NG, Nishimoto K, et al. Effect of KCNJ5 mutations on gene expression in aldosterone-producing adenomas and adrenocortical cells. *J Clin Endocrinol Metab*. 2012;97:E1567-1572.
21. Monticone S, Bandulik S, Stindl J, et al. A case of severe hyperaldosteronism caused by a de novo mutation affecting a critical salt bridge Kir3.4 residue. *J Clin Endocrinol Metab*. 2015;100:E114-118.
22. Murthy M, Azizan EA, Brown MJ, et al. Characterization of a novel somatic KCNJ5 mutation delI157 in an aldosterone-producing adenoma. *J Hypertens*. 2012;30:1827-1833.
23. Monticone S, Hattangady NG, Penton D, et al. a Novel Y152C KCNJ5 mutation responsible for familial hyperaldosteronism type III. *J Clin Endocrinol Metab*. 2013;98:E1861-1865.
24. Monticone S, Hattangady NG, Nishimoto K, et al. Effect of KCNJ5 mutations on gene expression in aldosterone-producing adenomas and adrenocortical cells. *J Clin Endocrinol Metab*. 2012;97:E1567-1572.
25. Chang YY, Lee BC, Chen ZW, et al. Cardiovascular and metabolic characters of KCNJ5 somatic mutations in primary aldosteronism. *Front Endocrinol (Lausanne)*. 2023;14:1061704.
26. Hardege I, Long L, Al Maskari R, et al. Targeted disruption of the Kcnj5 gene in the female mouse lowers aldosterone levels. *Clin Sci (Lond)*. 2018;132:145-156.
27. Marrano N, Biondi G, Borrelli A, et al. Irisin and incretin hormones: Similarities, differences, and implications in type 2 diabetes and obesity. *Biomolecules*. 2021;11:286.