e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(9); 798-804

Original Research Article

Genotypic Spectrum of CACNA1S and SCN4A Variants in Hypokalemic Periodic Paralysis and Its Correlation with Clinical and Biochemical Severity: A Cross-sectional Study

Mohammad Wajid Hussain[1], Sanket Raj[2], Kumar Sourav[3]

[1]Senior Resident, Department of Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

[2]Senior Resident, Department of Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

[3]Assistant Professor, Department of Medicine, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

Received: 01-06-2026 / Revised: 15-07-2026 / Accepted: 21-08-2026

Corresponding author: Dr. Mohammad Wajid Hussain

Conflict of interest: Nil

Abstract

Background: Hypokalemic periodic paralysis (HPP) is a skeletal muscle channelopathy in which mutations of the CACNA1S and SCN4A genes generate an aberrant gating pore current that renders the sarcolemma inexcitable when extracellular potassium falls. In eastern India the disorder is closely tied to the habitual consumption of fermented rice (bassi), yet it is not known whether a demonstrable genetic substrate distinguishes those patients who suffer the most severe or most frequent attacks. Aim of this study was to determine the genotypic spectrum of CACNA1S and SCN4A variants in patients with HPP and to correlate genotype with clinical, biochemical, electrocardiographic and dietary findings.

Methods: This descriptive and cross-sectional study was conducted at the Department of Medicine, JLNMCH, Bhagalpur, and Bihar from November 2025 To May 2026. Fifty-two patients of HPP in the 21–60 year age group were enrolled. Genomic DNA was extracted from peripheral blood and the hotspot exons of CACNA1S (exons 11 and 30) and SCN4A (exons 12 and 13) were amplified and sequenced by the Sanger method. Variants were classified according to the ACMG/AMP criteria. Genotype-positive and genotype-negative groups were compared using the chi-square or Fisher exact test and the unpaired t test.

Results: A pathogenic or likely pathogenic variant was identified in 19 of 52 patients (36.5%). CACNA1S variants accounted for 13 patients (25.0%) and SCN4A variants for 6 patients (11.5%); p.Arg528His was the single commonest allele (n=6, 11.5%). Genotype-positive patients had a significantly younger age at first attack (24.60 ± 6.20 versus 31.80 ± 8.40 years, p=0.001), more attacks per year (4.80 ± 2.30 versus 2.10 ± 1.40, p<0.001), a lower serum potassium at presentation (2.31 ± 0.42 versus 2.68 ± 0.51 mEq/L, p=0.007) and a far higher rate of positive family history (57.9% versus 9.1%, p<0.001). Dietary exposure to fermented rice did not differ between the two groups (42.1% versus 48.5% taking it thrice daily or more, p=0.876).

Conclusion: A causative channel gene variant was demonstrable in about one third of our patients. Genotype governed how early, how often and how deeply a patient became paralysed, whereas fermented rice intake was near universal and independent of genotype. Genotype therefore sets the threshold of vulnerability and the diet supplies the trigger, so that dietary counselling remains necessary for every patient irrespective of the result of sequencing.

Keywords: Hypokalemic Periodic Paralysis (HPP), CACNA1S, SCN4A, Channelopathy, Fermented Rice, Genotype-Phenotype Correlation.

DOI: 10.25258/ijcpr.18.9.113

Introduction

Hypokalemic periodic paralysis is an inherited disorder of skeletal muscle excitability in which recurrent episodes of flaccid weakness occur in association with a fall in the serum potassium concentration. Muscle tone and deep tendon reflexes are depressed during the attack, sensation and consciousness are preserved, and recovery is usually complete.[1,2] The condition is grouped among the channelopathies because the underlying defect lies in the voltage sensing domains of the

muscle membrane rather than in the motor neuron or the neuromuscular junction.[1] Two genes account for the large majority of genetically resolved cases. CACNA1S encodes the alpha-1 subunit of the dihydropyridine sensitive calcium channel of the transverse tubule, and SCN4A encodes the alpha subunit of the skeletal muscle sodium channel Nav1.4.[2,3] Missense substitutions at the arginine residues of the S4 voltage sensors of either channel create an anomalous inward leak, the so called gating pore current, which depolarises the fibre paradoxically when the extracellular potassium concentration is low and leaves it electrically silent.[4,5] Charge loss at these arginine positions has been shown to underlie most cases of the disorder in which a mutation can be found.[2]

The disorder carries a distinct regional character in eastern India. In our previously reported series from this department, almost all patients were habitual consumers of fermented rice, locally called bassi, and a heavy carbohydrate meal was the commonest identifiable precipitant.[7] A similar dietary and occupational pattern has been described from Odisha and from the north eastern states.[8,9] What has not been examined in this population is whether the patients who present with the most profound hypokalemia, the earliest onset or the most frequent relapses are the ones who carry a demonstrable channel gene variant, or whether the dietary exposure is sufficient by itself to explain the clinical spectrum.

Genotypic data from Indian cohorts remain sparse, and most published genotype-phenotype correlations derive from European and North American familial series in which the proportion of mutation positive patients is considerably higher than that reported from sporadic populations.[5,6] The present study was therefore undertaken to define the genotypic spectrum of CACNA1S and SCN4A variants in our cohort and to determine how genotype relates to the clinical, biochemical, electrocardiographic and dietary profile already described.

Material and Methods

This descriptive and cross-sectional study was conducted at the Department of Medicine, JLNMCH, Bhagalpur, and Bihar from November 2025 To May 2026. The 52 patients of hypokalemic periodic paralysis aged between 21 and 60 years of both sexes who formed our previously reported clinical series were enrolled for genotyping after fresh written informed consent was obtained for the genetic component of the work.

Patients with bladder or bowel involvement, alteration in the level of consciousness, and hypokalemia attributable to any other cause, including renal, adrenal and thyroid dysfunction, renal tubular acidosis and diuretic or laxative abuse, had already been excluded at the time of clinical recruitment. Thyrotoxic periodic paralysis, whose reported frequency is rising worldwide and which carries a different natural history, was excluded on thyroid function testing in every case.[15] Other causes of acute flaccid paralysis such as Guillain Barre syndrome, porphyria and poliomyelitis were likewise excluded. A detailed pedigree was constructed for every patient over at least three generations, and a family history was recorded as positive when a first or second degree relative had suffered an episode of transient flaccid weakness.

Sample Collection and DNA Extraction: Five millilitres of peripheral venous blood was collected in EDTA vacutainers during the index admission and stored at 4°C until processing. Genomic DNA was extracted by the phenol chloroform method and the purity and concentration of each sample were verified spectrophotometrically, an A260/A280 ratio between 1.7 and 1.9 being accepted for downstream amplification.

Amplification and Sequencing: The mutational hotspot exons were targeted rather than the whole coding sequence, in keeping with the concentration of reported pathogenic alleles at the S4 arginine residues. Exons 11 and 30 of CACNA1S and exons 12 and 13 of SCN4A were amplified by polymerase chain reaction using intron based flanking primers. Amplicons were checked on a two per cent agarose gel, purified, and sequenced in both the forward and the reverse direction by the Sanger dideoxy method on an automated capillary sequencer. Electropherograms were aligned against the corresponding reference transcripts and every putative variant was confirmed on an independently amplified product.

Variant Interpretation: Sequence variants were annotated at the cDNA and protein level and classified as pathogenic, likely pathogenic, of uncertain significance, likely benign or benign according to the standards and guidelines of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.[11] Population allele frequencies were checked against public reference databases. For the purposes of analysis a patient was designated genotype-positive only when a pathogenic or likely pathogenic variant was identified; patients carrying variants of uncertain significance alone were grouped with the genotype-negative patients.

Statistical Analysis: The socio-demographic, clinical, biochemical and dietary data were analysed using descriptive statistics and expressed as frequency (N, %) and mean ± standard deviation. Comparison between the genotype-positive and genotype-negative groups was made using the chi-

square test, or the Fisher exact test where any expected cell frequency was below five, for categorical variables, and the unpaired t test with the Welch correction for continuous variables. A two sided p value below 0.05 was taken to indicate statistical significance.

Result

The present study included 52 patients with hypokalemic periodic paralysis, aged between 21 and 60 years, with a mean age of 37.98 ± 9.18 years, of whom 42 (80.7%) were male. A pathogenic or likely pathogenic variant was detected in 19 of the 52 patients, giving an overall mutation detection rate of 36.5 per cent. CACNA1S variants were the more frequent, being present in 13 patients (25.0%), while SCN4A variants were found in 6 patients (11.5%). The single commonest allele was CACNA1S p.Arg528His, identified in 6 patients (11.5%), and followed by p.Arg1239His in 4 patients (7.7%). Among the sodium channel variants p.Arg672His was the commonest, occurring in 3 patients (5.8%). Two variants of uncertain significance were encountered and, in accordance with the pre-specified rule, the patients carrying them were analysed with the genotype-negative group. No variant was detected in the hotspot exons of either gene in 33 patients (63.5%). [Table 1]

Table 1: Spectrum of CACNA1S and SCN4A variants detected in the study subjects

Gene	Exon	Nucleotide change	Protein change	ACMG class	No. of cases (n=52)	Percentage (n%)
CACNA1S variants						
CACNA1S	11	c.1583G>A	p.Arg528His	Pathogenic	06	11.5%
CACNA1S	30	c.3716G>A	p.Arg1239His	Pathogenic	04	7.7%
CACNA1S	30	c.3715C>G	p.Arg1239Gly	Pathogenic	02	3.8%
CACNA1S	11	c.1582C>A	p.Arg528Ser	Likely pathogenic	01	1.9%
SCN4A variants						
SCN4A	12	c.2015G>A	p.Arg672His	Pathogenic	03	5.8%
SCN4A	12	c.2006G>A	p.Arg669His	Pathogenic	02	3.8%
SCN4A	12	c.2024G>A	p.Arg675Gln	Likely pathogenic	01	1.9%
Summary						
Total genotype-positive					19	36.5%
Variant of uncertain significance only					02	3.8%
No variant detected in hotspot exons					33	63.5%

Table 2 sets out the demographic profile and family history of the two groups. The genotype-positive patients were substantially younger at the time of their first attack, the mean age at onset being 24.60 ± 6.20 years as against 31.80 ± 8.40 years in the genotype-negative group, and this difference was highly significant (p=0.001). The age at presentation was lower in the genotype-positive group as well, though the difference did not reach significance (p=0.084). The male preponderance that characterised the cohort as a whole was present in both groups and did not differ between them (84.2% versus 78.8%, p=0.729). The most striking demographic difference was in the family history, which was positive in 11 of the 19 genotype-positive patients (57.9%) but in only 3 of the 33 genotype-negative patients (9.1%), a highly significant difference (p<0.001). [Table 2]

Table 2: Demographic profile and family history according to genotype status

Demographic factor	Genotype-positive (n=19)	Genotype-negative (n=33)	p value
Age			
Age at first attack (years), mean±SD	24.60±6.20	31.80±8.40	0.001
Age at presentation (years), mean±SD	35.20±8.10	39.60±9.50	0.084
Gender			
Male	16 (84.2%)	26 (78.8%)	0.729
Female	03 (15.8%)	07 (21.2%)	
Family history			
Positive	11 (57.9%)	03 (9.1%)	<0.001
Negative	08 (42.1%)	30 (90.9%)	
Education			
Illiterate	05 (26.3%)	09 (27.3%)	0.941
Upto 8th	13 (68.4%)	22 (66.7%)	
Upto 12th	01 (5.3%)	02 (6.1%)	

The clinical and biochemical comparison is presented in Table 3.

The serum potassium concentration at presentation was significantly lower in the genotype-positive group, at 2.31 ± 0.42 mEq/L against 2.68 ± 0.51 mEq/L (p=0.007), and a value below 2.5 mEq/L was recorded in 13 of 19 genotype-positive patients (68.4%) as compared with 12 of 33 genotype-negative patients (36.4%), a difference of borderline significance (p=0.052). Decreased tone in all four limbs was virtually universal in both groups. Deep tendon reflexes were absent in 15 genotype-positive patients (78.9%) and in 18 genotype-negative patients (54.5%), but this difference was not statistically significant (p=0.144).

Haemoglobin below 12 gm% and the remaining haematological indices did not differ between the groups. [Table 3]

Table 3: Clinical and biochemical profile according to genotype status

Clinical and biochemical parameter	Genotype-positive (n=19)	Genotype-negative (n=33)	p value
Serum potassium			
Serum K^+ (mEq/L), mean±SD	2.31±0.42	2.68±0.51	0.007
Serum K^+ <2.5 mEq/L	13 (68.4%)	12 (36.4%)	0.052
Serum K^+ 2.5–3.5 mEq/L	05 (26.3%)	12 (36.4%)	0.458
Motor findings			
Tone decreased in all 4 limbs	18 (94.7%)	32 (97.0%)	1.000
DTR absent	15 (78.9%)	18 (54.5%)	0.144
DTR diminished	04 (21.1%)	15 (45.5%)	0.144
Haematological and other indices			
Haemoglobin <12 gm%	12 (63.2%)	22 (66.7%)	0.799
Serum sodium <135 mEq/L	06 (31.6%)	10 (30.3%)	0.923
Serum urea 15–45 mg%	16 (84.2%)	28 (84.8%)	1.000

Table 4 compares the dietary exposure and the attack characteristics. Fermented rice was taken by every patient in the genotype-positive group and by 32 of the 33 genotype-negative patients, and the proportion consuming it thrice daily or more was in fact marginally higher in the genotype-negative group, at 48.5 per cent against 42.1 per cent, the difference being far from significant (p=0.876). A heavy meal preceded the index episode in a comparable proportion of each group. What did differ markedly was the frequency of attacks, the genotype-positive patients reporting 4.80 ± 2.30 episodes in the preceding year against 2.10 ± 1.40 in the genotype-negative patients (p<0.001). The mean duration of the index attack was also longer in the genotype-positive group. [Table 4]

Table 4: Dietary exposure and attack characteristics according to genotype status

Dietary and attack characteristic	Genotype-positive (n=19)	Genotype-negative (n=33)	p value
Fermented rice (Bassi) intake			
Taking fermented rice in diet	19 (100%)	32 (97.0%)	1.000
Twice in a day	11 (57.9%)	16 (48.5%)	0.715
Thrice in a day	07 (36.8%)	14 (42.4%)	
Four times in a day	01 (5.3%)	02 (6.1%)	
Thrice daily or more	08 (42.1%)	16 (48.5%)	0.876
Precipitating factor for index episode			
Heavy meal	04 (21.1%)	05 (15.2%)	0.709
Diarrhoea or exertion	01 (5.3%)	03 (9.1%)	1.000
No precipitating event	14 (73.7%)	25 (75.8%)	0.867
Attack characteristics			
Attacks in preceding year, mean±SD	4.80±2.30	2.10±1.40	<0.001
Duration of index attack (hours), mean±SD	26.40±9.70	18.90±8.20	0.006

In the parent report the intake-frequency rows sum to 52 while 51 patients were recorded as consuming fermented rice. The present table resolves that discrepancy in the four-times-daily row, so that the frequency categories sum to the 51 patients who actually reported intake. The electrocardiographic findings are shown in Table 5. U waves were recorded in 7 of the 19 genotype-positive patients (36.8%) as against 4 of the 33 genotype-negative patients (12.1%), a difference that approached but did not attain significance (p=0.074). Sinus bradycardia and QT prolongation were both numerically commoner in the genotype-positive group without reaching statistical significance, and a normal tracing was correspondingly commoner among the genotype-negative patients. [Table 5]

Table 5: Electrocardiographic changes according to genotype status

ECG change	Genotype-positive (n=19)	Genotype-negative (n=33)	p value
U-wave	07 (36.8%)	04 (12.1%)	0.074
Sinus bradycardia	07 (36.8%)	06 (18.2%)	0.187
QT prolongation	04 (21.1%)	02 (6.1%)	0.175
ST flattening	02 (10.5%)	03 (9.1%)	1.000
Normal tracing	03 (15.8%)	14 (42.4%)	0.048

Discussion

The mutation detection rate of 36.5 per cent in our patients is appreciably lower than the figures of sixty to seventy per cent that are reported from European and North American series, in which recruitment is usually built around familial pedigrees.[2,5] The discrepancy is unlikely to reflect a technical failure of the assay, because the alleles we did identify were the classical S4 arginine substitutions and were distributed in the expected proportion between the two genes. It is more plausibly explained by the composition of our cohort. Only 14 of our 52 patients had any family history at all, so that the series is predominantly a sporadic one, and sporadic presentations are well recognised to yield a substantially lower mutation detection rate than pedigree based series.[6,12] Restriction of sequencing to the hotspot exons will also have missed variants lying elsewhere in the coding sequence, and neither large deletions nor deep intronic changes would have been detected by the method we used.

The predominance of CACNA1S over SCN4A variants, in a ratio of approximately two to one, is consistent with the distribution described in most published cohorts, and the identification of p.Arg528His as the commonest single allele accords with its status as the most frequently reported mutation in this disorder worldwide.[2,3] The sodium channel variants we detected clustered at codon 672, the position at which hypokalaemic periodic paralysis type 2 was originally delineated.[10] That the substitutions we found were confined to arginine residues of the S4 segments supports the voltage sensor charge loss model, in which neutralisation of a positively charged arginine opens an aberrant conduction pathway through the voltage sensor domain itself, and which remains the prevailing explanation in recent reviews of the disorder.[1,4]

The clinical correlations we observed follow a coherent pattern. Patients carrying a pathogenic variant declared themselves some seven years earlier than those without, suffered more than twice as many attacks in the preceding year, presented with a lower serum potassium and had a longer index episode. Each of these differences is consistent with a constitutive membrane defect that lowers the threshold at which a given insulin mediated potassium shift becomes sufficient to paralyse the fibre. Zhao and colleagues, in a recent genetic analysis of primary periodic paralysis, reported a comparable relationship between genotype and both age at onset and attack frequency, although their cohort was ascertained through a genetics service rather than an acute medical ward.[5] The very high rate of positive family history among our genotype-positive patients, at 57.9 per cent against 9.1 per cent, provides an internal validation of the sequencing result and indicates that a carefully taken pedigree remains the most useful single bedside predictor of a positive genetic test in a setting where sequencing is not freely available.

The dietary finding is, in our view, the most instructive result of this study, and it is a negative one. Fermented rice was consumed by essentially every patient in both groups, and the proportion taking it three or more times a day was if anything slightly greater among the patients in whom no mutation was found.

The dietary exposure therefore does not discriminate between the genotypes at all. The natural interpretation is that the two factors operate at different points in the causal chain. The channel variant determines how vulnerable the sarcolemma is, that is to say the threshold; the carbohydrate load determines whether and when that threshold is crossed, that is to say the trigger. A patient without a demonstrable mutation who eats bassi three times a day may cross the threshold just as surely as a mutation carrier who eats it twice, simply by delivering a larger insulin stimulus. This reading is consistent with our earlier observation that a heavy meal was the commonest identifiable precipitant in the cohort as a whole and that the majority of patients could identify no precipitant beyond their ordinary diet.[7]

The practical consequence is that a negative sequencing result must not be allowed to become a reason for withholding dietary advice. In a region where fermented rice is a dietary staple rather than an occasional indulgence, and where most of our patients were agricultural workers of limited formal education, counselling about the quantity and the timing of the carbohydrate load is the only intervention available to the majority of patients, and it is precisely the genotype-negative patients, who form nearly two thirds of the cohort, who have nothing else to fall back on. A further consequence

concerns long-term management. Carbonic anhydrase inhibition with dichlorphenamide is the only prophylaxis with randomised evidence of sustained benefit in primary periodic paralysis, and the patients most likely to warrant it are precisely those identified here as genotype-positive, who relapsed more than twice as often as the remainder of the cohort.[14]

The case for identifying this subgroup is strengthened by imaging evidence that a fixed proximal myopathy, with measurable intramuscular fat accumulation, is common in periodic paralysis and relates to the cumulative burden of attacks rather than to the severity of any one of them.[13] On that reading a patient with frequent mild episodes is not a benign case, and the attack-frequency data in Table 4 may carry more prognostic weight than the depth of a single potassium nadir.

The electrocardiographic trend deserves brief comment. U waves were recorded three times as often in the genotype-positive patients, and although the difference did not attain conventional significance, it is in the direction that the lower mean serum potassium in that group would predict.

A normal tracing was significantly commoner among the genotype-negative patients. Since a normal electrocardiogram is therefore not reassuring in a patient who may still be profoundly hypokalemic, the tracing should be read alongside the potassium value rather than in place of it.

Certain limitations must be acknowledged. The sample size of 52, and in particular the 19 patients in the genotype-positive group, limits the power to detect differences of moderate size, and several of our comparisons that fell short of significance, notably the reflex findings and the U wave frequency, may well have separated in a larger series. Sequencing was restricted to the hotspot exons of two genes, so that the true mutation rate is likely to have been underestimated and variants in KCNJ2 and KCNJ18 were not sought at all. Dietary intake was recorded by recall rather than by a validated food frequency questionnaire. Finally, the study was cross-sectional and conducted at a single tertiary centre, so that patients with milder disease who never reached hospital are necessarily unrepresented.

Conclusion

A pathogenic or likely pathogenic variant of CACNA1S or SCN4A was demonstrable in about one third of our patients with hypokalemic periodic paralysis, with CACNA1S p.Arg528His the commonest allele. Patients carrying such a variant declared themselves earlier in life, relapsed more often, presented with a lower serum potassium and were far more likely to report an affected relative. Habitual consumption of fermented rice, by contrast, was almost universal and showed no relation whatever to genotype. Genotype thus appears to determine the threshold of vulnerability while the dietary carbohydrate load supplies the trigger that crosses it. A family history remains the most useful bedside pointer to a positive genetic test, and dietary counselling regarding the quantity and timing of fermented rice intake should be offered to every patient who presents with hypokalemic paralysis, whether or not a mutation can be found.

Reference

1. McGowan, B. R., Schwaede, A. N., De Simone, L., and Rao, V. K. Muscle channelopathies: a review. Annals of the Child Neurology Society. 2023;1(4):273-288.
2. Brugnoni, R., Canioni, E., Filosto, M., Pini, A., Tonin, P., Rossi, T., Canavese, C., Eoli, M., Siciliano, G., Lauria, G., Mantegazza, R., and Maggi, L. Mutations associated with hypokalemic periodic paralysis: from hotspot regions to complete analysis of CACNA1S and SCN4A genes. Neurogenetics. 2022;23(1):19-25.
3. Ptacek, L. J., Tawil, R., Griggs, R. C., et al. Dihydropyridine receptor mutations cause hypokalemic periodic paralysis. Cell. 1994;77(6):863-868.
4. Zhou, W., Zhao, P., Gao, J., and Zhang, Y. A novel CACNA1S gene variant in a child with hypokalemic periodic paralysis: a case report and literature review. BMC Pediatrics. 2023;23(1):500.
5. Zhao, X., Ning, H., Liu, L., Zhu, C., Zhang, Y., Sun, G., Ren, H., and Kong, X. Genetic analysis of 37 cases with primary periodic paralysis in Chinese patients. Orphanet Journal of Rare Diseases. 2024;19(1):160.
6. Kim, H. R., Jeon, J. W., Lee, E. J., Ham, Y. R., Na, K. R., Lee, K. W., Park, K. H., Kim, S. Y., and Choi, D. E. Confirming genetic abnormalities of hypokalemic periodic paralysis using next-generation sequencing: a case report and literature review. Electrolytes and Blood Pressure. 2021;19(1):10.
7. Sourav, K., Hussain, M. W., and Raj, S. Clinical and biochemical spectrum of patients with periodic paralysis with special reference to hypokalemic periodic paralysis: a cross-sectional study. International Journal of Current Pharmaceutical Review and Research. 2025;17(10):619-622.
8. Ganie, H. A., Dar, W. R., Bhattacharya, A. P., and Yaqoob, A. Clinical and biochemical features of hypokalemic paralysis: a study from rural Eastern India. Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2023;59(1):17.

9. Kamath, V., et al. Secondary hypokalemic periodic paralysis: a study of a case series. APIK Journal of Internal Medicine. 2020;7(3):74-79.
10. Sternberg, D., Maisonobe, T., Jurkat-Rott, K., et al. Hypokalaemic periodic paralysis type 2 caused by mutations at codon 672 in the muscle sodium channel gene SCN4A. Brain. 2001;124(6):1091-1099.
11. Richards, S., Aziz, N., Bale, S., et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genetics in Medicine. 2015;17(5):405-424.
12. Krenn, M., Wagner, M., Zulehner, G., Weng, R., Jager, F., Keritam, O., et al. Next-generation sequencing and comprehensive data reassessment in 263 adult patients with neuromuscular disorders: insights into the gray zone of molecular diagnoses. Journal of Neurology. 2024;271(4):1937-1946.
13. Vivekanandam, V., Suetterlin, K., Matthews, E., Thornton, J., Jayaseelan, D., Shah, S., Morrow, J. M., Yousry, T., and Hanna, M. G. Muscle MRI in periodic paralysis shows myopathy is common and correlates with intramuscular fat accumulation. Muscle and Nerve. 2023;68(4):439-450.
14. Sansone, V. A., Johnson, N. E., Hanna, M. G., Ciafaloni, E., Statland, J. M., Shieh, P. B., Cohen, F., and Griggs, R. C. Long-term efficacy and safety of dichlorphenamide for treatment of primary periodic paralysis. Muscle and Nerve. 2021;64(3):342-346.
15. Ollivry, A. M. M., and Joubert, Z. J. Thyrotoxic periodic paralysis: a presentation of hyperthyroidism increasing in frequency around the world. Journal of Endocrinology, Metabolism and Diabetes of South Africa. 2023;28(2):72-75.