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Genotyping of Vitamin-D Receptor (VDR) gene polymorphisms rs7975232, rs1544410, rs731236 and analysis of their association with susceptibility to SARS-CoV-2 among the Kazakh ethnic group

This pilot study investigated the single nucleotide polymorphisms rs731236, rs1544410, and rs7975232 of the VDR gene using real-time ARMS-PCR in a cohort of 119 individuals of Kazakh ethnic group. Participants were stratified into COVID-19-positive (p-COVID-19; n = 88) and COVID-19-negative (no-COVID-19; n = 31) groups based on the detection of SARS-CoV-2-specific IgM and IgG antibodies by ELISA. The allelic and genotypic distributions of all three SNPs conformed to Hardy–Weinberg equilibrium. No statistically significant differences in allele or genotype frequencies were observed between the groups for rs731236, rs7975232, or rs1544410 ($p > 0.05$), indicating that these polymorphisms do not influence susceptibility to SARS-CoV-2 infection in the studied population. A borderline association was noted for the heterozygous CT genotype of rs1544410 ($p = 0.0548$), suggesting a potential protective effect (OR = 0.426; 95 % Cl: 0.1816 — 0.9563). Despite the limited sample size, this is the first study to examine rs731236, rs1544410, and rs7975232 in relation to SARS-CoV-2 susceptibility within the Kazakh ethnic population, as well as one of the few to simultaneously analyze all four alleles of rs1544410.

Keywords: vitamin D receptor (VDR) gene, single nucleotide polymorphism, rs731236, rs7975232, rs1544410, SARS-CoV-2, COVID-19, susceptibility, Kazakh ethnic group.

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a devastating impact on global health and economic systems. Marked by high transmissibility, substantial mortality, and long-term health consequences, the pandemic has revealed the limitations of current treatment strategies. Although mass vaccination campaigns and public health measures have helped curb the spread of the virus, there remains no universally effective therapy, especially in patients suffering from severe respiratory complications. This highlights the urgent need to identify biological factors that influence susceptibility to the virus. One promising area of investigation is the role of genetic variation, particularly single nucleotide polymorphisms (SNPs), which may influence individual susceptibility to infection. The vitamin D receptor (VDR) gene has emerged as a potential genetic marker of interest in this context [1, 2].

Vitamin D is known for its immunomodulatory and anti-inflammatory properties. Deficient levels of vitamin D have been associated with a higher risk of various chronic and infectious diseases, including cancers, autoimmune conditions, cardiovascular disorders, and respiratory infections [3]. Increasingly, clinical and epidemiological data suggest a strong link between low serum levels of vitamin D and an elevated risk of contracting COVID-19 [4]. This association has also been observed in individuals of Kazakh ethnicity, among whom vitamin D deficiency is relatively prevalent [5].

The biological effects of vitamin D are mediated through its active form, calcitriol, which binds to the VDR—a nuclear receptor encoded by a highly polymorphic gene located on chromosome 12. Among the numerous SNPs identified in the VDR gene, four have been widely studied for their potential role in disease susceptibility: rs228570, rs7975232, rs1544410, and rs731236. Of these, rs7975232, rs1544410, and rs731236 are positioned in the 3′ untranslated region (3′ UTR) and are in strong linkage disequilibrium, often referred to collectively as the 3′ UTR polymorphisms [6, 7].

According to dbSNP data, the rs731236 polymorphism includes three alleles, with A and G being predominant; rs7975232 comprises the A and C alleles; and rs1544410 contains all four possible allelic variants [8–10]. However, both the reported allele composition and the number of alleles analyzed for these SNPs can vary across studies. For example, some researchers investigate rs731236 in terms of the T and C alleles [11, 12], while rs1544410 is commonly analyzed using only two allelic variants at a time—either A

and G [11] or A and T [13]. Therefore, in the present study, the allele composition is considered according to the dbSNP database, and all four alleles of rs1544410 are analyzed simultaneously.

Although numerous studies have examined the association between these three VDR variants and COVID-19 susceptibility, their findings remain inconclusive and vary across different ethnic groups and methodological approaches. Given these discrepancies, the present study aims to explore the relationship between VDR polymorphisms rs731236, rs1544410, rs7975232 and susceptibility to SARS-CoV-2 infection in individuals of Kazakh ethnic group.

Experimental

A total of 119 volunteers participated in the study. Participant selection was based on a preliminary questionnaire, with key inclusion criteria being age over 18 years, no COVID-19 vaccination received within the past 12 to 18 months, and belonging to the Kazakh ethnic group. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Local Bioethics Committee of the Non-commercial Joint-Stock Company "Karaganda Medical University" (Protocol No. 2, dated 11 October 2022). Written informed consent was obtained from all participants.

Venous blood samples were collected into two EDTA tubes. One tube was centrifuged to obtain plasma, which was subsequently analyzed via enzyme-linked immunosorbent assay (ELISA) to detect SARS-CoV-2-specific IgM and IgG antibodies. The following diagnostic kits were employed: SARS-CoV-2-IgG-ELISA-BEST and SARS-CoV-2-IgM-ELISA-BEST (Vector-Best, Novosibirsk, Russia).

Previous studies have shown that IgM and IgG antibody levels typically begin rising simultaneously within the first week of SARS-CoV-2 infection [14]. IgM titers typically decline and become undetectable within approximately three months of symptom onset, whereas IgG antibodies persist, gradually decreasing over a period of 4–7 months [15, 16]. Therefore, IgM and/or IgG titers exceeding the diagnostic threshold (>1 ng/mL) were considered as evidence of an active or recently resolved SARS-CoV-2 infection (within 1 week to 6 months prior to sampling).

Based on ELISA results, participants were stratified into two groups: SARS-CoV-2-positive (p-COVID-19) and SARS-CoV-2-negative (no-COVID-19). Summary demographic and clinical characteristics of the participants by group are provided in Table 1.

Table 1

General characteristics of the study groups

	p-COVID-19	**no-COVID-19**
Total (n)	88	31
Age (years; mean ± SD)	43 ± 14.38	41 ± 15.24
Sex (M / F)	27 / 61	12 / 19
IgM (ng/mL; mean ± SD)	1.691 ± 3.008	0.399 ± 0.181
IgG (ng/mL; mean ± SD)	7.086 ± 3.881	0.3191 ± 0.2282

The second blood sample was used for genotyping the VDR gene SNPs rs731236, rs1544410, and rs7975232. Genomic DNA was isolated from whole blood using the RIBO-prep kit (AmpliSens, Moscow, Russia) following the manufacturer's instructions. DNA concentration and purity were assessed using a DS-11 spectrophotometer (DeNovix Inc., Wilmington, DE, USA). Genotyping was performed using real-time polymerase chain reaction (PCR) with forward and reverse outer and inner primers (Lumiprobe, Russia), based on the amplification-refractory mutation system (ARMS) technique.

Each 25 μL PCR reaction included 50 ng of genomic DNA, 10 pmol of each allele-specific or control primer pair (FIP–ROP, RIP–FOP, or FOP–ROP), Taq polymerase, dNTPs, and PCR buffer (GeneLab, Astana, Kazakhstan). Amplification was carried out in a DTlite real-time PCR system (DNA Technology, Moscow, Russia) using Real-Time_PCR software v.7.9 (DNA Technology). Primer sequences and PCR cycling parameters are provided in Figure.

SNP	Alleles	Primer sequence	PCR protocol
rs731236	A G	FIP 5'-CGGTCCTGGATGGCCGCA-3' RIP 5'-CAGGACGCCGCGCTGCTC-3' FOP 5'-TTGGCATAGAGCAGGTGGCTGCC-3' ROP 5'-CCCAGCTGAGAGCTCCTGTGCCTT-3'	94°C / 3 min (94°C / 15 sec, 62°C / 30 sec) × 40
rs7975232	A C	FIP 5'-CACAGGAGCTCTCAGCTGGACA-3' RIP 5'-TGGTGGGATTGAGCAGTGAAGG-3' FOP 5'-CCTGGATGGCCTCAATCAGC-3' ROP 5'-GTCATAGAGGGGTGGCCTAGGG-3'	94°C / 3 min (94°C / 15 sec, 62°C / 30 sec) × 40
rs1544410	C A	FIP 5'-CAGAGCCTGAGTATTGGGAACGC-3' RIP 5'-GGGGCCACAGACAGGCCTACT-3' FOP 5'-TTTTGTACCCTGCCCGCAAGA-3' ROP 5'-TGTGCAGGCGATTCGTAGGG-3'	
	C G	FIP 5'-AGCAGAGCCTGAGTATTGGGAAAGC-3' RIP 5'-GGCCACAGACAGGCCTCCC-3' FOP 5'-AAGTTTTGTACCCTGCCCGCAAG-3' ROP 5'-GTGCAGGCGATTCGTAGGGG-3'	94°C / 3 min (94°C / 15 sec, 62°C / 30 sec) × 40
	T C	FIP 5'-GCAGAGCCTGAGTATTGGGAAGGT-3' RIP 5'-GGCCACAGACAGGCCTTCG-3' FOP 5'-AAGTTTTGTACCCTGCCCGCAA-3' ROP 5'-TGTGCAGGCGATTCGTAGGG-3'	

Figure. The designed primer sequences and thermal cycling conditions for genotyping rs731236, rs7975232, and rs1544410 using the ARMS-PCR

Following real-time amplification, allele-specific reactions were subjected to melting curve analysis under the following protocol: 15 seconds at 90 °C followed by 100 cycles with 0.5 °C increments.

A complete description of the genotyping methodology for rs731236, rs1544410, and rs7975232 is provided in the methodological guidelines [17].

Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were reported as percentages and compared using the chi-square or Fisher's exact test where appropriate. Hardy–Weinberg equilibrium (HWE) was assessed using chi-square distribution. Odds ratios (ORs) with 95 % confidence intervals (CIs) were calculated. Two-tailed p-values < 0.05 were considered statistically significant. Statistical analyses were performed using GraphPad Prism 8.0 (GraphPad Software, San Diego, CA, USA).

Results and Discussion

To evaluate whether the VDR gene polymorphisms rs731236, rs1544410, and rs7975232 influence susceptibility to SARS-CoV-2 infection, we compared allele and genotype frequencies for each SNP between COVID-19-positive and COVID-19-negative groups. All genotype distributions were in Hardy–Weinberg equilibrium (HWE), with p-values > 0.05: p = 0.0628 for rs731236, p = 0.1125 for rs7975232, and p = 0.5381 for rs1544410. Genotyping results and comparisons for these VDR SNPs are presented in Table 2.

Table 2

Allele and genotype frequencies of rs731236, rs1544410, and rs7975232 within the studied groups

	p-COVID-19 (n)	no-COVID-19 (n)	OR (CI 95 %)	χ^2	p-value[#]
1	2	3	4	5	6
rs731236					
Alleles	n = 176 (Freq.)	n = 62 (Freq.)			
A	115 (65.34 %)	41 (66.13 %)	0.9656 (0.5176 — 1.772)	0.01261	0.9106
G	61 (34.66 %)	21 (33.87 %)	1.036 (0.5643 — 1.932)	0.01261	0.9106

Continuation of Table 2

1	2	3	4	5	6
Genotypes	n = 88 (Freq.)	n = 31(Freq.)			
AA	47 (53.41 %)	18 (58.06 %)	0.8279 (0.3520 — 1.822)	0.2004	0.6807
AG	21 (23.86 %)	5 (16.13 %)	0.63 (0.5898 — 4.282)	0.8032	0.4548
GG	20 (22.73 %)	8 (25.81 %)	0.8456 (0.3198 — 2.179)	0.1208	0.8064
rs7975232					
Alleles	n = 176 (Freq.)	n = 62 (Freq.)			
A	77 (43.75 %)	25 (40.32 %)	1.151 (0.6481 — 2.046)	0.2199	0.6576
C	99 (56.25 %)	37 (59.68 %)	0.8687 (0.4888 — 1.543)	0.2199	0.6576
Genotypes	n = 88 (Freq.)	n = 31(Freq.)			
AA	20 (22.73 %)	6 (19.35 %)	1.225 (0.4706 — 3.401)	0.1527	0.8039
AC	37 (42.05 %)	13 (41.94 %)	1.005 (0.4542 — 2.372)	0.0001138	0.9915
CC	31 (35.63 %)	12 (38.71 %)	0.8765 (0.3878 — 1.954)	0.09346	0.8291
rs1544410					
Alleles	n = 176 (Freq.)	n = 62 (Freq.)			
C	120 (68.18 %)	43 (69.35 %)	0.9468 (0.5175 — 1.779)	0.02923	0.8642
G	14 (7.95 %)	2 (3.23 %)	2.593 (0.6581 — 11.74)	1.635	0.2514
T	42 (23.86 %)	17 (27.42 %)	0.8397 (0.4380 — 1.635)	0.3109	0.6095
Genotypes	n = 88 (Freq.)	n = 31(Freq.)			
CC	40 (45.45 %)	12 (38.71 %)	1.319 (0.5964 — 2.934)	0.4239	0.5363
TT	5 (5.68 %)	NA	NA	1.839	0.3248
GG	1 (1.14 %)	NA	NA	0.3553	0.5512
CT	30 (34.09 %)	17 (54.84 %)	0.426 (0.1816 — 0.9563)	4.13	0.0548
GT	2 (2.27 %)	NA	NA	0.7166	0.3973
CG	10 (11.36 %)	2 (6.45 %)	1.859 (0.4541 — 8.861)	0.61	0.7293

[#]p-values were calculated using Fisher's exact test
$p > 0.05$ = not significant.
Abbreviation: NA, not available

As shown in Table 2, no statistically significant differences were found in allele or genotype frequencies between the p-COVID-19 and no-COVID-19 groups for any of the three 3′ UTR polymorphisms.

In the case of rs731236, allele A was present in 65.34 % of the p-COVID-19 group and 66.13 % of no-COVID-19, while allele G occurred in 34.66 % and 33.87 %, respectively. The odds ratio (OR) for alleles A and G were 0.9656 (95 % CI: 0.5176–1.772; $p = 0.9106$) and 1.036 (95 % CI: 0.5643–1.932; $p = 0.9106$), indicating no significant association with infection risk.

The genotypic analysis showed that genotype AA was present in 53.41 % of COVID-19-positive participants and 58.06 % of COVID-19-negative ones, yielding an OR = 0.8279 (95 % CI: 0.3520–1.822), $p = 0.6807$. Heterozygous genotype AG occurred in 23.86 % of p-COVID-19 versus 16.13 % in no-COVID-19 (OR = 0.63, $p = 0.4548$), while homozygous GG was found in 22.73 % and 25.81 % respectively (OR = 0.8456, $p = 0.8064$). None of these comparisons reached statistical significance, indicating that rs731236 genotypes do not appear to be associated with susceptibility to SARS-CoV-2 infection in this sample.

For rs7975232, the A allele appeared in 43.75 % of COVID-19-positive individuals and 40.32 % of COVID-19-negative ones. The C allele was slightly more prevalent in both groups (56.25 % and 59.68 %, respectively). The OR for allele A was 1.151 (95 % CI: 0.6481–2.046; $p = 0.6576$).

Genotype frequencies were also comparable. The AA genotype was observed in 22.73 % of COVID-19-positive individuals and 19.35 % in no-COVID-19 group (OR = 1.225, $p = 0.8039$). The AC genotype was almost equally represented (42.05 % in cases vs. 41.94 % in controls; OR = 1.005, $p = 0.9915$), and CC occurred in 35.63 % and 38.71 % of the respective groups (OR = 0.8765, $p = 0.8291$).

These findings are consistent with results reported by Jafarpoor et al. in an Iranian cohort, where no association was found between rs731236 or rs7975232 and COVID-19 susceptibility [18]. An ecological study involving data from 26 countries did report a positive correlation between the frequency of the rs731236 TT genotype and COVID-19 prevalence ($r = 0.42$, $p = 0.03$), as well as between the rs7975232 AA genotype and both COVID-19 prevalence ($r = 0.45$, $p = 0.02$) and mortality ($r = 0.42$, $p = 0.03$) [12]. However, methodological differences and population heterogeneity preclude direct comparison with our data.

Analysis of rs1544410 allele frequencies also revealed no significant differences between groups. The C allele was most prevalent across both groups, with 68.18 % in p-COVID-19 and 69.35 % in no-COVID-19 (OR = 0.9468, p = 0.8642). The T allele was present in 23.86 % and 27.42 %, respectively (OR = 0.8397, p = 0.6095), while the G allele occurred in only 7.95 % of COVID-19-positive participants and 3.23 % of COVID-19-negative (OR = 2.593, 95 % CI: 0.6581–11.74, p = 0.2514), indicating a non-significant trend toward higher G allele frequency in p-COVID-19 group.

Importantly, allele A at the rs1544410 locus was absent in all participants, consistent with the known allele distribution in the Kazakh ethnic group, possibly due to regional or ethnic-specific genetic architecture.

Among genotypes, CC was observed in 45.45 % of COVID-19-positive subjects and 38.71 % of COVID-19-negative (OR = 1.319, p = 0.5363). The heterozygous CT genotype was less frequent in p-COVID-19 group (34.09 %) compared to no-COVID-19 group (54.84 %), yielding a result at the threshold of statistical significance (OR = 0.426, 95 % CI: 0.1816–0.9563, p = 0.0548). This may suggest a potential protective effect of this genotype, although it narrowly missed the conventional threshold for statistical significance.

The TT genotype was found in 5.68 % of COVID-19-positive participants and was absent in no-COVID-19 group, precluding calculation of a reliable odds ratio (χ^2 = 1.839, p = 0.3248). Several genotypes—such as GG, GT, and CG—were detected at very low frequencies in our sample. This limited occurrence reduces statistical power and makes it challenging to draw meaningful conclusions about their association with SARS-CoV-2 susceptibility. As a result, any observed trends involving these rare variants should be interpreted with caution and considered exploratory rather than confirmatory.

Thus, despite some numeric variation, rs1544410 did not show a statistically significant association with SARS-CoV-2 susceptibility. Similar findings, despite methodological and population differences, were reported in the ecological study by Karcıoğlu et al. [12].

More data are available regarding the association of 3′ UTR polymorphisms with COVID-19 severity and mortality than with infection risk. However, these studies vary considerably in methodology, populations, and outcomes. For example, a 2024 systematic review encompassing 12 studies found that the rs7975232 AA and rs731236 TT genotypes were associated with increased risk of COVID-19-related death. Additionally, rs1544410 may serve as a predictive biomarker for disease severity, while all three polymorphisms were considered potential markers of mortality risk [19]. In contrast, a study by Tentolouris et al. in a Caucasian Greek cohort found no association between rs7975232, rs731236, and COVID-19 severity [20] and Saba et al. found that in the recessive model, the T/T rs7975232 genotype was statistically associated with a lower risk of the infection severity [7].

We acknowledge that limitations of the current work include a relatively small sample size, which may have reduced the statistical power to detect modest genotype–phenotype associations. This limitation increases the risk of errors, particularly in the analysis of rare genotypes such as GG, GT, and CG, which were underrepresented in our cohort.

Despite these limitations, the study possesses several notable strengths. To our knowledge, this is the first investigation of VDR gene polymorphisms and SARS-CoV-2 susceptibility conducted specifically within the Kazakh ethnic population. Primer combinations were also developed for the ARMS-PCR technique to allow simultaneous analysis of all four allelic variants of the rs1544410 polymorphism.

Although our study in Kazakh individuals did not find a significant association between rs731236, rs1544410, or rs7975232 and COVID-19 susceptibility, inconsistent results across populations and study designs highlight the need for further investigation of the role of VDR gene polymorphisms in SARS-CoV-2 infection, including larger multi-ethnic cohorts to improve generalizability and statistical robustness.

Conclusions

This pilot study was conducted among 119 individuals of Kazakh ethnic origin, who were stratified into COVID-19-positive and COVID-19-negative groups based on ELISA testing for the presence or absence of antibodies against SARS-CoV-2. Genotyping of the VDR gene single nucleotide polymorphisms rs731236, rs1544410, and rs7975232, followed by a comparative analysis of allele and genotype frequencies between the groups, revealed no statistically significant differences.

Based on these findings, it can be generally concluded that the rs731236, rs1544410, and rs7975232 polymorphisms do not appear to influence susceptibility to COVID-19 within the Kazakh population (p > 0.05). However, the observation of borderline statistical significance for the rs1544410 CT genotype,

the relatively small sample size, the limited number of peer-reviewed studies on this topic, and the conflicting results reported in the literature underscore the need for further research in this area.

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript. CRediT: **Protas V.V.** – Conceptualization, Data curation, Investigation, Writing draft; **Pogossyan G.P.** – Supervision, Conceptualization, Data curation, Formal analysis, Writing – review and editing; **Li K.G.** – Methodology, Supervision, Conceptualization, Formal analysis; **Zhumina A.G.** – Formal analysis, Writing – review and editing; **Bisseneva A.K.** – Investigation, Data curation, Editing.

References

1 Ren H. Association of genetic polymorphisms with COVID-19 infection and outcomes: An updated meta-analysis based on 62 studies / H. Ren, Y. Lin, L. Huang, W. Xu, D. Luo, C. Zhang // Heliyon. — 2024. — Vol. 10(1). — e236–262. — DOI: 10.1016/j.heliyon.2023.e23662

2 Gupta K. Systematic review and meta-analysis of human genetic variants contributing to COVID-19 susceptibility and severity / K. Gupta, G. Kaur, T. Pathak, I. Banerjee // Gene. — 2022. — Vol. 844. — P. 1467–1490. — DOI: 10.1016/j.gene.2022.146790

3 Holick M. F. Vitamin D deficiency / M. F. Holick // New England Journal of Medicine. — 2007. — Vol. 357 (3). — P. 266–281. — DOI: 10.1056/NEJMra070553

4 Kazemi A. Association of vitamin D status with SARS-CoV-2 infection or COVID-19 severity: A systematic review and meta-analysis / A. Kazemi, V. Mohammadi, S. K. Aghababaee, M. Golzarand, C. C. T. Clark, S. Babajafari // Advances in Nutrition. — 2021. — Vol. 12 (5). — P. 1636–1658. — DOI: 10.1093/advances/nmab012

5 Protas V. V. Plasma 25-Hydroxyvitamin D level and VDR gene single nucleotide polymorphism rs2228570 influence on COVID-19 susceptibility among the Kazakh ethnic group—A pilot study / V. V. Protas, G. P. Pogossyan, K. G. Li, A. G. Zhumina, A. K. Bisseneva, D. N. Shaikina // Nutrients. — 2023. — Vol. 15(7). — P. 1781. — DOI: 10.3390/nu15071781

6 Uitterlinden A. G. Genetics and biology of vitamin D receptor polymorphisms / A. G. Uitterlinden, Y. Fang, J. B. J. van Meurs, H. A. P. Pols, J. P. T. M. van Leeuwen // Gene. — 2004. — Vol. 338 (2). — P. 143–156. — DOI: 10.1016/j.gene.2004.05.014

7 Saba A. A. Single nucleotide variants rs7975232 and rs2228570 within vitamin D receptor gene confers protection against severity of COVID-19 infection in Bangladeshi population / A. A. Saba, Z. Mahmud, F. Ansari, R. Ahmed, J. Nur, M. S. Alam, S. Chakraborty, A. H. M. N. Nabi, L. N. Islam, Md. Z. H. Howlader // Gene Reports. — 2024. — Vol. 36. — P. 101981. — DOI: 10.1016/j.genrep.2024.101981

8 National Center for Biotechnology Information (dbSNP). — [Electronic resource]. — Access mode: https://www.ncbi.nlm.nih.gov/snp/rs731236#frequency_tab (дата обращения: [18.4.2025])

9 National Center for Biotechnology Information (dbSNP). — [Electronic resource]. — Access mode: https://www.ncbi.nlm.nih.gov/snp/rs7975232#frequency_tab (дата обращения: [18.4.2025])

10 National Center for Biotechnology Information (dbSNP). — [Electronic resource]. — Access mode: https://www.ncbi.nlm.nih.gov/snp/rs1544410#frequency_tab (дата обращения: [18.4.2025])

11 Alagarasu K. Association of vitamin D receptor gene polymorphisms with clinical outcomes of dengue virus infection / K. Alagarasu, T. Honap, A. P. Mulay, R. V. Bachal, P. S. Shah, D. Cecilia // Human Immunology. — 2012. — Vol. 73 (11). — P. 1194–1199. — DOI: 10.1016/j.humimm.2012.08.007

12 Karcioğlu L. Correlation of the variations in prevalence of coronavirus disease 2019 and vitamin D receptor gene polymorphisms in cohorts from 26 countries / L. Karcioğlu // Anadolu Kliniği Tıp Bilimleri Dergisi. — 2022. — Vol. 27 (1). — P. 60–70. — DOI: 10.21673/anadoluklin.987578

13 Wang Y. A meta-analysis on associations between vitamin D receptor genetic variants and tuberculosis / Y. Wang, H. Li // Microbial Pathogenesis. — 2019. — Vol. 130. — P. 59–64. — DOI: 10.1016/j.micpath.2019.02.027

14 To K.K. - W. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: An observational cohort study / K. K. -W. To, O. T. -Y. Tsang, W. -S. Leung, A. R. Tam, T. -C. Wu, D. C. Lung, C. C. -Y. Yip, J. -P. Cai, J. M. -C. Chan, … K. -Y. Yuen // The Lancet Infectious Diseases. — 2020. — Vol. 20 (5). — P. 565–574. — DOI: 10.1016/S1473-3099(20)30196-1

15 Luo C. Dynamic changes and prevalence of SARS-CoV-2 IgG/IgM antibodies: Analysis of multiple factors / C. Luo, M. Liu, Q. Li, X. Zheng, W. Ai, F. Gong, J. Fan, S. Liu, X. Wang, J. Luo // International Journal of Infectious Diseases. — 2021. — Vol. 108. — P. 57–62. — DOI: 10.1016/j.ijid.2021.04.078

16 Zhou C. Evaluation of serum IgM and IgG antibodies in COVID-19 patients by enzyme linked immunosorbent assay / C. Zhou, G. Bu, Y. Sun, C. Ren, M. Qu, Y. Gao, Y. Zhu, L. Wang, L. Sun, Y. Liu // Journal of Medical Virology. — 2021. — Vol. 93 (5). — P. 2857–2866. — DOI: 10.1002/jmv.26741

17 Протас В. В. Рекомендации по генотипированию однонуклеотидных полиморфизмов rs731236, rs7975232 и rs1544410 гена VDR / В. В. Протас, Г. П. Погосян, К. Г. Ли, А. К. Бисенева. — Караганда, 2024. — 26 с.

18 Jafarpoor A. VDR gene polymorphisms are associated with the increased susceptibility to COVID-19 among Iranian population: A case-control study / A. Jafarpoor, S.M. Jazayeri, F. Bokharaei-Salim, A. Ataei-Pirkooh, A. Ghaziasadi, S. Soltani, A. Sadeghi, M. Parsania // International Journal of Immunogenetics. — 2022. — Vol. 49 (4). — P. 243–253. — DOI: 10.1111/iji.12585

19 Da Ronda R. D. S. C. Single-nucleotide polymorphisms related to vitamin D metabolism and severity or mortality of COVID-19: A systematic review and meta-analysis / R. D. S. C. Da Ronda, M. Berlofa Visacri, J. Tiemi Siguemoto, C. Motta Neri, M. Crispim Lopo De Abreu, A. De Souza Nicoletti, I. Rotta, C. Dagli-Hernandez, P. Moriel // Gene. — 2024. — Vol. 906. — P. 148236. — DOI: 10.1016/j.gene.2024.148236

20 Tentolouris N. The association of vitamin D receptor polymorphisms with COVID-19 severity / N. Tentolouris, C. Achilla, I.A. Anastasiou, I. Eleftheriadou, A. Tentolouris, D. Basoulis, O. Kosta, A. Lambropoulos, A. Chatzikyriakidou, E. B. Jude // Nutrients. — 2024. — Vol. 16 (5). — P. 727. — DOI: 10.3390/nu16050727

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Қазақ этникалық тобындағы SARS-CoV-2-ге бейімділікпен байланыстағы витамин D рецепторы (VDR) генінің rs7975232, rs1544410 және rs731236 полиморфизмдерін генотиптеу және олардың байланысын талдау

Бұл пилоттық зерттеуде қазақ этникалық тобына жататын 119 адамның үлгісінде VDR генінің rs731236, rs1544410 және rs7975232 бір нуклеотидті полиморфизмдері нақты уақытта ARMS-ПЦР әдісімен зерттелді. Қатысушылар SARS-CoV-2-ге спецификалық IgM және IgG антиденелерінің ИФА арқылы анықталуына байланысты COVID-19-оң (p-COVID-19; n = 88) және COVID-19-теріс (no-COVID-19; n = 31) топтарға бөлінді. Үш SNP бойынша аллельдік және генотиптік таралу Харди–Вайнберг тепе-теңдігіне сәйкес келді. rs731236, rs7975232 және rs1544410 үшін топтар арасында аллельдер мен генотиптер жиіліктерінде статистикалық тұрғыдан маңызды айырмашылықтар анықталған жоқ (p > 0.05), бұл осы полиморфизмдердің зерттеліп отырған популяцияда SARS-CoV-2 инфекциясына бейімділікке әсер етпейтінін көрсетеді. rs1544410-ның гетерозиготалы CT генотипі үшін шекті маңыздылықтағы байланыс байқалды (p = 0.0548), бұл генотиптің мүмкін болатын қорғаныштық әсерін ұсынады (OR = 0.426; 95 % Cl: 0.1816 — 0.9563). Үлгінің көлемі шектеулі болғанына қарамастан, бұл — қазақ этникалық тобында rs731236, rs1544410 және rs7975232 полиморфизмдерінің SARS-CoV-2-ге бейімділікпен байланысын зерттеген алғашқы жұмыс, сондай-ақ rs1544410 полиморфизмінің барлық төрт аллелін бір мезгілде талдаған сирек зерттеулердің бірі.

Кілт сөздер: D дәрумені рецепторы (VDR) гені, бір нуклеотидті полиморфизм, rs731236, rs7975232, rs1544410, SARS-CoV-2, COVID-19, бейімділік, қазақ этникалық тобы.

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Генотипирование полиморфизмов гена рецептора витамина D (VDR) rs7975232, rs1544410, rs731236 и анализ их связи с восприимчивостью к SARS-CoV-2 среди представителей казахской этнической группы

В настоящем пилотном исследовании проведено генотипирование однонуклеотидных полиморфизмов rs731236, rs1544410 и rs7975232 гена рецептора витамина D (VDR) методом ARMS-ПЦР в реальном времени среди 119 представителей казахской этнической группы. Участники были разделены на две группы: COVID-19-положительную (p-COVID-19; n = 88) и COVID-19-отрицательную (no-COVID-19; n = 31) на основании наличия или отсутствия специфических антител IgM и IgG к SARS-CoV-2, выявленных методом иммуноферментного анализа (ИФА). Распределение аллелей и генотипов всех трех полиморфизмов соответствовало закону Харди–Вайнберга. По результатам исследования не было выявлено статистически значимых различий в частотах аллелей и генотипов между группами для rs731236, rs7975232 и rs1544410 (p > 0,05), что позволяет предположить отсутствие их влияния на восприимчивость организма к инфицированию SARS-CoV-2 в исследуемой популяции. При этом для гетерозиготного генотипа CT полиморфизма rs1544410 зафиксирована тенденция к ассоциации с инфицированием на границе статистической значимости (p = 0,0548), что может свидетельствовать о возможном защитном эффекте (OR = 0,426; 95 % Cl: 0.1816–0,9563). Несмотря на ограниченный объем выборки, это первое исследование, посвященное анализу связи rs731236, rs1544410, rs7975232 с

восприимчивостью к SARS-CoV-2 среди представителей казахской этнической группы, а также одно из немногих, в котором проведено одновременное генотипирование всех четырех аллелей rs1544410.

Ключевые слова: ген рецептора витамина D (VDR), однонуклеотидный полиморфизм, rs731236, rs7975232, rs1544410, SARS-CoV-2, COVID-19, восприимчивость, казахская этническая группа.

References

1 Ren, H., Lin, Y., Huang, L., Xu, W., Luo, D., & Zhang, C. (2024). Association of genetic polymorphisms with COVID-19 infection and outcomes: An updated meta-analysis based on 62 studies. *Heliyon*, *10*(1), e236–262. https://doi.org/10.1016/j.heliyon.2023.e23662

2 Gupta, K., Kaur, G., Pathak, T., & Banerjee, I. (2022). Systematic review and meta-analysis of human genetic variants contributing to COVID-19 susceptibility and severity. *Gene*, *844*, 1467–1490. https://doi.org/10.1016/j.gene.2022.146790

3 Holick, M. F. (2007). Vitamin D Deficiency. *New England Journal of Medicine*, *357*(3), 266–281. https://doi.org/10.1056/NEJMra070553

4 Kazemi, A., Mohammadi, V., Aghababaee, S. K., Golzarand, M., Clark, C. C. T., & Babajafari, S. (2021). Association of Vitamin D Status with SARS-CoV-2 Infection or COVID-19 Severity: A Systematic Review and Meta-analysis. *Advances in Nutrition*, *12*(5), 1636–1658. https://doi.org/10.1093/advances/nmab012

5 Protas, V. V., Pogossyan, G. P., Li, K. G., Zhumina, A. G., Bisseneva, A. K., & Shaikina, D. N. (2023). Plasma 25-Hydroxyvitamin D Level and VDR Gene Single Nucleotide Polymorphism rs2228570 Influence on COVID-19 Susceptibility among the Kazakh Ethnic Group—A Pilot Study. *Nutrients*, *15*(7), 1781. https://doi.org/10.3390/nu15071781

6 Uitterlinden, A. G., Fang, Y., van Meurs, J. B. J., Pols, H. A. P., & van Leeuwen, J. P. T. M. (2004). Genetics and biology of vitamin D receptor polymorphisms. *Gene*, *338*(2), 143–156. https://doi.org/10.1016/j.gene.2004.05.014

7 Saba, A. A., Mahmud, Z., Ansari, F., Ahmed, R., Nur, J., Alam, M. S., Chakraborty, S., Nabi, A. H. M. N., Islam, L. N., & Howlader, Md. Z. H. (2024). Single nucleotide variants rs7975232 and rs2228570 within vitamin D receptor gene confers protection against severity of COVID-19 infection in Bangladeshi population. *Gene Reports*, *36*, 101981. https://doi.org/10.1016/j.genrep.2024.101981

8 National Center for Biotechnology Information (dbSNP). Retrieved from https://www.ncbi.nlm.nih.gov/snp/rs731236#frequency_tab

9 National Center for Biotechnology Information (dbSNP). Retrieved from https://www.ncbi.nlm.nih.gov/snp/rs7975232#frequency_tab

10 National Center for Biotechnology Information (dbSNP). Retrieved from https://www.ncbi.nlm.nih.gov/snp/rs1544410#frequency_tab

11 Alagarasu, K., Honap, T., Mulay, A. P., Bachal, R. V., Shah, P. S., & Cecilia, D. (2012). Association of vitamin D receptor gene polymorphisms with clinical outcomes of dengue virus infection. *Human Immunology*, *73*(11), 1194–1199. https://doi.org/10.1016/j.humimm.2012.08.007

12 Karcioğlu, L. (2022). Correlation of the variations in prevalence of coronavirus disease 2019 and vitamin D receptor gene polymorphisms in cohorts from 26 countries. *Anadolu KliniğiTıpBilimleriDergisi*, *27*(1), 60–70. https://doi.org/10.21673/anadoluklin.987578

13 Wang, Y., & Li, H. (2019). A meta-analysis on associations between vitamin D receptor genetic variants and tuberculosis. *Microbial Pathogenesis*, *130*, 59–64. https://doi.org/10.1016/j.micpath.2019.02.027

14 To, K. K. -W., Tsang, O. T. -Y., Leung, W. - S., Tam, A. R., Wu, T. -C., Lung, D. C., Yip, C. C. - Y., Cai, J. -P., Chan, J. M.-C., … Yuen, K. -Y. (2020). Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: An observational cohort study. *The Lancet Infectious Diseases*, *20*(5), 565–574. https://doi.org/10.1016/S1473-3099(20)30196-1

15 Luo, C., Liu, M., Li, Q., Zheng, X., Ai, W., Gong, F., Fan, J., Liu, S., Wang, X., & Luo, J. (2021). Dynamic changes and prevalence of SARS-CoV-2 IgG/IgM antibodies: Analysis of multiple factors. *International Journal of Infectious Diseases*, *108*, 57–62. https://doi.org/10.1016/j.ijid.2021.04.078

16 Zhou, C., Bu, G., Sun, Y., Ren, C., Qu, M., Gao, Y., Zhu, Y., Wang, L., Sun, L., & Liu, Y. (2021). Evaluation of serum IgM and IgG antibodies in COVID-19 patients by enzyme linked immunosorbent assay. *Journal of Medical Virology*, *93*(5), 2857–2866. https://doi.org/10.1002/jmv.26741

17 Protas, V. V., Pogossyan, G. P., Li, K. G., & Bisseneva, A. K. (2024). *Rekomendatsii po genotipirovaniiu odnonukleotidnykh polimorfizmov rs731236, rs7975232 i rs1544410 gena VDR* [Recommendations for Genotyping Single Nucleotide Polymorphisms rs731236, rs7975232, and rs1544410 of the VDR Gene]. Karaganda [in Russian].

18 Jafarpoor, A., Jazayeri, S. M., Bokharaei-Salim, F., Ataei-Pirkooh, A., Ghaziasadi, A., Soltani, S., Sadeghi, A., & Parsania, M. (2022). VDR gene polymorphisms are associated with the increased susceptibility to COVID-19 among iranian population: A case-control study. *International Journal of Immunogenetics*, *49*(4), 243–253. https://doi.org/10.1111/iji.12585

19 Regina Da Silva Correa Da Ronda, C., BerlofaVisacri, M., TiemiSiguemoto, J., Motta Neri, C., CrispimLopo De Abreu, M., De Souza Nicoletti, A., Rotta, I., Dagli-Hernandez, C., &Moriel, P. (2024). Single-nucleotide polymorphisms related to vitamin D

metabolism and severity or mortality of COVID-19: A systematic review and meta-analysis. *Gene*, *906*, 148236. https://doi.org/10.1016/j.gene.2024.148236

20 Tentolouris, N., Achilla, C., Anastasiou, I. A., Eleftheriadou, I., Tentolouris, A., Basoulis, D., Kosta, O., Lambropoulos, A., Chatzikyriakidou, A., & Jude, E. B. (2024). The Association of Vitamin D Receptor Polymorphisms with COVID-19 Severity. *Nutrients*, *16*(5), 727. https://doi.org/10.3390/nu16050727

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