Short Communication

Role of OAS1 Gene Polymorphism in the Severity of Infection in COVID-19 Patients in Babylon Province, Iraq

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Abstract

Background: Immunogenetics can help explain the heterogeneity of susceptibility to the viral disease progression. A candidate gene is associated with severe COVID-19, where the risk alleles are linked with decreased *OAS1* expression. **Objectives:** The aim of this ongoing study is to investigate the polymorphism of *OAS1*gene (rs1131454) with the severity of COVID-19 in local patients in urban and rural of Babylon province. **Materials and Methods:** In total, 140 samples of blood were obtained from urban and rural areas patients (70 samples from each) who had positive results and severe symptoms of (COVID-19) infection were provided by the medical staff of Marjan Teaching Hospital from December/2021 to February/2022. Then, blood DNA was used to amplify a partial sequence of *OAS1*gene. Genotypes and alleles frequencies based on PCR-RFLP assay and gel electrophoresis. **Results:** The AA genotype was most common in patients inhabiting urban areas. There was a high value of odds ratio (OR) (OR = 8.9) for A allele with a significant difference ($P = 0.04$) in genotype AA. The allele frequency of A allele in patients for urban area 49 (35%) was more frequent compared with rural of Babylon Province 39 (27.86%). Based on the value of OR (OR = 8.9). **Conclusions:** This study found that the A allele is considered a risk allele of SNP rs1131454 in *OAS1*, and mutation of Guanine to Adenine (G > A) plays a role in the severity of COVID-19 infection in these populations.

Keywords: COVID-19, *OAS1* gene, PCR-RFLP, polymorphism

Introduction

The variability of susceptibility and protection to viral infection and illness progression can be explained in part by immunogenetics and examining basic gene polymorphism for initiating the immunological reactions connected to a viral infection, particularly with the COVID-19 mechanisms.[1]

In December 2019, SARS-COV-2 was found for the first time in the respiratory tracts of pneumonia patients in Wuhan, Hubei, China. It was identified as a newly discovered b-coronavirus (nCoV).[2] The infection's starting point was not distinguished until January 2020, when an infection from the crown family was identified (COVID-19).[3] COVID-19 showed up two times before the new one over the most recent 20 years, specifically, Serious Intense Respiratory Disorder in 2002 and Center East Respiratory Condition in 2012.[4] The symptoms of the virus differ from one patient to another, with some experiencing no symptoms at all while others needing extensive treatment and possibly even dying.[5]

Numerous genes and single nucleotide polymorphisms (SNPs) have been linked to the susceptibility to infection or certain aspects of sickness severity, such as the requirement for hospitalization, respiratory failure, or fatality.[6]

The SNPs represent genetic variation for an SNP containing only two alleles.[7]

An allele that can only be filled by one of two nitrogenous bases, making it a specific allele. A site of nitrogenous bases where there are probably two mutual

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bases in each allele in the genome is referred to as an SNP. When the second is resolved, it becomes the other allele. Population studies can track this SNP because it is present in at least 1% of the population and because it does not significantly change from generation to generation.[8]

The majority of SNPs are located beyond the coding sequences since only around 3%–5% of the DNA sequence codes for protein synthesis; nevertheless, the SNPs that are inside the coding sequence are of importance to researchers because they typically modify the crucial function of the protein.[9] Two out of three SNPs result from the substitution of the base (cytosine) for the base (thymine).[10]

Genetic differences represented by SNPs are one of the main factors for the existence of differences between individuals, which distinguish them from one another. They serve as signals that aid in determining the genetic sequence, and an SNP takes place when one nucleotide is changed for another, such as changing to C, G, or T nucleotide.[11]

SNP frequency and presence vary among population groups, which may lead to greater sensitivity to COVID-19 infection in populations having gene expression-related SNPs.[12] Although the genes and SNPs may be ranked according to their relative contributions, it may be difficult to quantify the strength of genetics' influence. In addition, because many SNPs affect the action of genes indirectly, this may not always apply to all people. Moreover, given that the COVID-19 pandemic was recently discovered and is still going on, the SNPs may not necessarily affect COVID-19 infection.[13]

OAS genes have a role in interferon-induced antiviral defense. The second messenger, 20–50-linked Oligoadenylate, is created by proteins upon dsRNA binding, and it activates ribonuclease L to break down viral RNA and prevent viral replication.[14] Through nonsense-mediated RNA degradation, rs1131454 controlled the expression of *OAS1* in functional investigations. The "Neanderthal" haplotype isoform resulted in lower nonsense-mediated degradation, which raised *OAS1* levels.[15]

OAS1 isoforms shared a similar reduction in viral loads in cells expressing both isoforms, indicating that their anti-COVID-19 efficacy was not different in vitro. Both *OAS1* isoforms might be activated in vitro by interferons. In addition, genotyped *OAS1* haplotypes were connected to viral eradication in interferon-treated individuals. In the placebo group, viral clearance was slower with the risk (non-"Neanderthal") haplotype, but no correlation between therapy and viral clearance was seen, indicating that the benefits of interferon therapy exceed hereditary *OAS1* deficiencies.[16] In light of the mounting data supporting the significance of *OAS1*, pharmacological approaches to augment its action are predicted and may be repurposed for the treatment of COVID-19.[17]

Materials and Methods

The coronavirus infection in patient groups was checked validity in the hospital by RT-PCR assay, though nasopharyngeal swabs and 140 blood samples that had positive results of (RT-PCR) infected with (COVID-19) were provided by the medical staff of Marjan Teaching Hospital from December/2021 to February/2022. The severe patients were from urban (70 patients) and rural (70 patients) of Babylon province. In this investigation, venous blood samples from each patient totaled around 5 mL. The serum was collected and maintained in the freezer (−20°C) until it was needed. The blood was put in a gel tube for 30 min, followed by 15 min of centrifugation at 3000 rpm. DNA was "extraction from blood according to protocol of Imran and Al-Karrem"[18] to evaluate the concentration and purity of DNA. The restriction fragment length polymorphism (RFLP) technique was used for genotyping the *OAS1* (rs1131454).

Human DNA amplification was performed by using primer sequence (forward primer: 5′CCCCTCAGAGTGACTGAAGGAA3′; Reverse primer: 5′ CAGTGCTTGACTAGGCGGA TG3′. The cycling condition is predenaturation 95°C for 5 min., 30 cycles of 94°C for 15 s, 60°C for 15 s, and 72°C for 30 s. The amplification of the amplicon of *OAS1* gene size was (243bp), and the PCR product was treated with restriction enzyme (BstV1I) as directed by the manufacturer. This enzyme Bstv1I digested the PCR product into two bands, 208 and 35bp. The digested products were electrophoresed in a 2% agarose gel. The product was visualized by Ethidium Bromide using electrophoreses. Bstv1I typing band 208bp is usually cut after SNP rs1131454, and bands with length 208 bp indicate the GG genotype of *OAS1*. In comparison, bands at 115 and 93 bp indicated the AA genotype. Bands 208, 115, and 93 bp indicated the AG genotype.

Ethical approval

The study was conducted in accordance with the ethical principles. It was carried out with the patient's verbal and analytical approval before the sample was taken. The study protocol, the subject information, and the consent form were reviewed and approved by the University of Babylon, College of Science for Women, a local ethics committee according to document number 5907, on November 8, 2021, to get this approval.

Statistical analysis

The phenotypic odds ratio (OR) was estimated with the help of medcalc.net, and general statistical metrics like mean, standard deviation, percentage, and descriptive plots were carried out using Microsoft® Excel 2010 software. OR test was calculated according to © 2024 MedCalc

Software Ltd. (https://www.medcalc.org/calc/odds_ratio.php). IPM ® SPSS® software by IBM Company (https://www.ibm.com/spss), the phenotypic means, and the standard deviation were compared using the Student *t*-test. The SNPStats® online statistical program was used to calculate the genetic association parameters.[19]

Results

Genomic DNA extraction

The quality of the human DNA genome from whole blood of all samples under interest undergoing infection with COVID-19 was estimated by gel electrophoresis [Figure 1].

Amplification of targeted region of the *OAS1* included SNP rs1131454

The targeted region of the *OAS1* was amplified by a primer pair designed in this study covering SNP rs1131454 under interest. The primer pair span sequence region from 112910983 to 112911225 of chr12 illustrated the amplicon length with flanking regions of primers equal to 243bp [Figure 2].

RFLP-PCR genotyping

Screening of targeted sequence of *OAS1*gene polymorphisms was performed by RFLP-PCR assay using restriction enzyme BstV1I. This enzyme preliminary digestive the main amplicon 243 bp into bands 208 and 35 bp, and its hydrolysis after eight nucleotides of recognition sequence GCAGC (N_8), produced three genotypes (GG, GA, and AA), first: single band as homozygous genotype GG (208 bp) when no SNP (wild type), second: three bands representative heterozygous genotype GA (208, 115, and 93 bp) and the third one was two bands representative homozygous mutant genotype AA (115 and 93bp). The three digestive bands were visualized in [Figure 3].

Figure 4 visualizes the action of enzyme BstV1I to hydrolysis the amplicon 243 bp in the tube by RFLP-PCR assay to show three genotypes: Homozygous wild type genotype GG as single band 208 band in samples:1, 3, 5–7, 13, 16; heterozygous genotype GA representative by three bands (208, 115, 93 bp), and homozygous mutant genotype AA representative by two bands (115 and 93 bp). The bands 35 bp disappeared in gel due to their small size; this site of digestion occurs due to the presence of

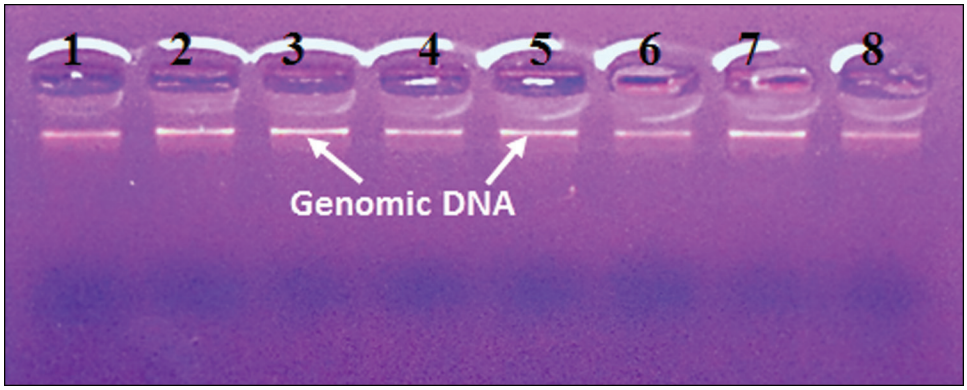

Figure 1: Profile gel electrophoresis of eight DNA samples as representative for patients with COVID-19; the genomic DNA was run in 2% gel at 100 v for 45 min

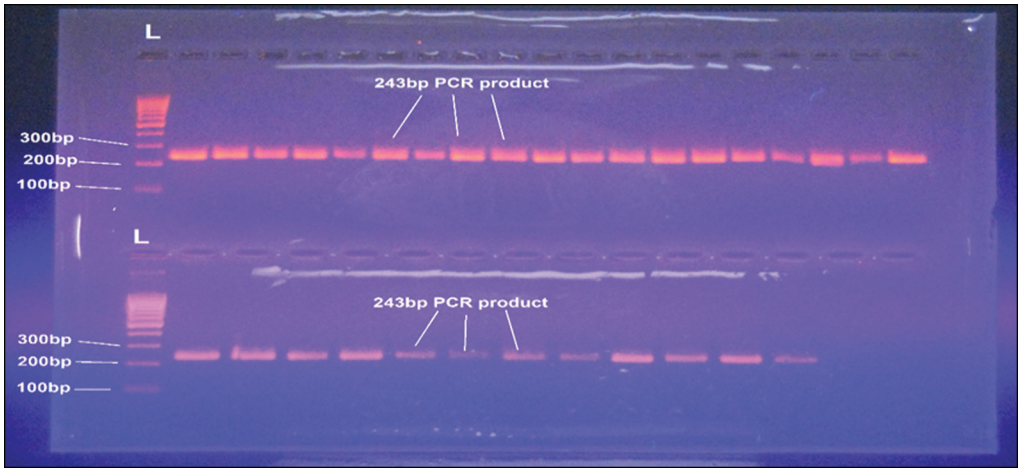

Figure 2: Profile of PCR product (243 bp) of the designed primers pair for rs1131454 genotyping. The electrophoresis carried on agarose gel (2%), lane *L* = 100 bp step ladder, other lanes = 243bp PCR products

Enzymes: BstV1I

Length	5' Enzyme	5' Base	3' Enzyme	3' Base	Sequence
115	BstV1I	94	BstV1I	208	TAACCCCCAA ATCTATGTCA AGCTCATCGA GGAGTGCACC GACCTGCAGA AAGAGGGCGA GTTCTCCACC TGCTTCACAG AACTACAGAG AGACTTCCTG AAGCAGCGCC CCACC
93	none	1	BstV1I	93	CCCCTCAGAG TGACTGAAGG AAATTCAGAG AAGAGCTGAC ACCTAAGTTG TAGATTTTGC CCGAACAGGT CAGTTGACTG GCAGCTATAA ACC
35	BstV1I	209	none	243	AAGCTCAAGA GCCTCATCCG CCTAGTCAAG CACTG

Figure 3: Illustration of virtual digest of enzyme BstV1I by online restriction way

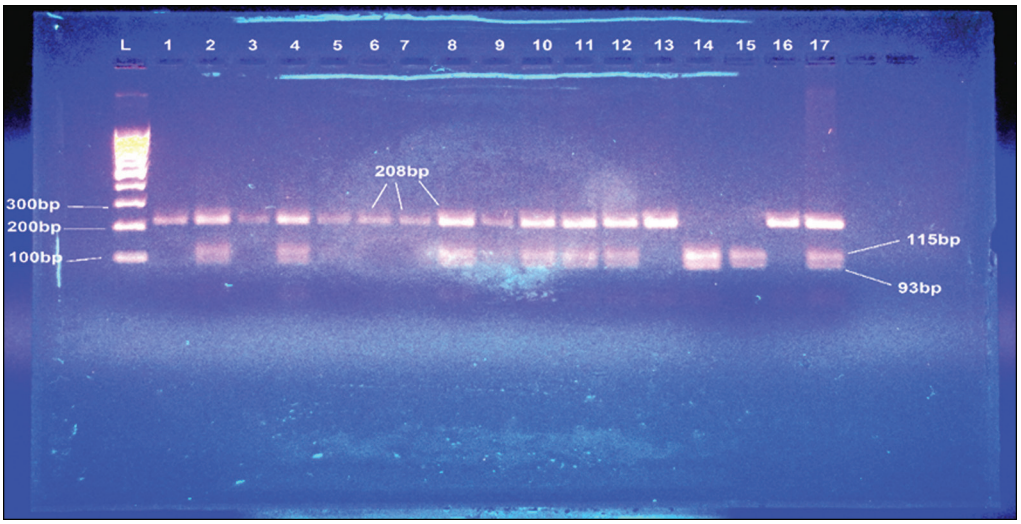

Figure 4: Agarose gel electrophoresis showing three genotypes of rs1131454 obtained by PCR-RFLP assay. Lane L: DNA ladder (100–1000 bp); Lanes 1,3,5–7: the GG genotype at 208 bp; Lanes 14–15: the homozygous mutant AA genotype 115 and 93 bp; Lanes 2,4,8–12, 17: the heterozygous mutant AG genotype 208, 115 and 93 bp.

Table 1: Genotype and allele frequency of *OAS1*gene polymorphisms rs1131454 G>A associated with urban patients COVID-19 infection and rural patients

Rs1131454 G>A	Patients urban area N = 70		Patients rural area N = 70	OR (95% CI)	*P*-value
Genotypes	GG	29 (41.4%)	32 (45.7%)	Reference group	
	GA	33 (47.1%)	37 (52.8%)	0.08 (0.04–1.5)	0.4
	AA	8 (11.4%)	1 (1.4%)	8.9 (1.08–73.2)	0.0.04
Allele frequency	G	91 (65%)	101 (72.14%)	0.71 (0.43–1.9)	0.1
	A	49 (35%)	39 (27.86%)	1.39 (0.84–2.3)	

recognized sequence GCAGC at sequence site 209 of the main amplicon 243bp.

The detailed information is clearest in Table 1. The genotyping findings for COVID-19 patients in urban areas and rural areas show the three genotypes (GG, GA, and AA). In compartmented with genotyping rs1131454 G>A in COVID-19 patients urban area infection. A significant appeared in OR and allele frequency in the two groups. The values of the OR supported the idea that the A allele in AA was correlated with disease under interest and considered a risk allele. The OR was higher in genotype AA OR = 8.9 (1.8–73.2) with a high significance *P* value of 0.04, and the allele frequency was higher with A allele 49 in the urban patient group with a high value of OR = 1.39 (0.84–2.3), *P* value = 0.1, while the allele frequency low 39 rural group Table 1. Unfortunately, no prior research mentioned the

relationship between this SNP and COVID-19. For the first time simultaneously, our investigation established the validity of this SNP in the examined population of interest.

Discussion

The consideration of this study is to give attention to the importance of SNP rs1131454 (*OAS1*; G > A), which is a missense mutation that codes for a different amino acid Gly162 to Ser; this mutation alters gene expression due to amino acid changed from Glycine to Serine. The result of this study showed a higher value of OR (OR = 8.9) for the A allele with a significant difference ($P = 0.04$) in genotype AA. The allele frequency of A allele in patients in urban of Babylon province was more frequent compared with rural (49 (35%) vs. 39 (27.86%)). Based on the value of OR (OR = 8.9), this study found A allele, considered a risk allele of SNP rs1131454 in *OAS1,* and mutation Guaine to Adinine (G > A) contribute to the severity of the COVID-19 infection in these populations.

Indicated that polymorphism of this gene (*OAS1*; G > A) correlated with COVID-19 infection. The polymorphism of this gene (*OAS1*; G > A) correlated with many human viral diseases.[20] Asian, European, and African individuals with chronic viral infections (HCV and COVID-19) were shown to have significantly higher frequencies of the "AA" and "AG" genotypes within the SNP rs1131454 (*OAS1*; G > A).[21]

Urbanization is affecting the patterns of mortality and morbidity worldwide, especially in developing countries, shifting the majority of cases from infectious to noncommunicable illnesses.[22] One of the most frequent forms of genetic variants found in the human genome is SNPs.[23] SNPs in genes that control immunity and DNA mismatch repair are linked to a hereditary predisposition to illness.[24]

Finding gene polymorphism and analyzing gene expression patterns are two methods for analyzing immune response variations between urban and rural populations since gene expression variability is influenced by both genetic and environmental variables.[25]

In our study, we observed marked differences in *OAS1* gene polymorphism correlated with COVID-19 among patients who lived in urban areas compared with those in rural areas the same patients. This gene polymorphism in SNP rs1131454 G>A may be correlated with Amino acid change Gly162 to Ser, leading to a change in gene expression and affected response to disease.

The results of this study are consistent with the results of many recent studies that highlight the occurrence of many diseases occurred in urban and rural people correlated with gene expression changes. Idaghadour *et al*.,[26,27] who employed whole-genome expression arrays and discovered a genome-wide expression signature of regional population disparities in Morocco, reported a similar discovery. The same outcomes were also seen in the gene expression patterns of Ghanaian students enrolled in urban and rural schools in Southern Ghana.[28] Despite its limitations, our investigation shows that patients in the two target groups exhibit considerable gene polymorphism due to the divergent environments generated by urban and rural features. Although there is not many research comparing patients from urban and rural regions, a recent study examined patients from both urban and rural locations as well as within urban areas.[26-28] Future research is required to understand the functional implications of the diverse *OAS* gene expression profiles reported in terms of disease patterns and vulnerability, as well as to discover specific triggers that activate certain immune pathways.[29-31]

Conclusion

Urbanization is altering the predominantly infectious death and morbidity patterns compared with rural habitats. The result of this study shows high frequency A allele in COVID-19 patients urban of Babylon province was high frequent compared with rural, and this study found A allele, considered a risk allele of SNP rs1131454 in *OAS1,* plays a role in the severity of COVID-19 infection in these populations.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hu J, Li C, Wang S, Li T, Zhang H. Genetic variants are identified to increase risk of COVID-19 related mortality from UK Biobank data. Hum Genomics 2021;15:10.
2. Tian X, Li C, Huang A, Xia S, Lu S, Shi Z, *et al*. Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody. Emerg Microbes Infect 2020;9:382-5.
3. Hadi A, Kadhom M, Hairunisa N, Yousif E, Mohammed S. A review on COVID-19: Origin, spread, symptoms, treatment, and prevention. Biointerface Res Appl Chem 7242;2020:7234.
4. Raheem R, Kadhom M, Albayati N, Alhashimie E, Alrubayee W, Salman I, *et al*. A clinical–statistical study on COVID-19 infection and death status at the Alshifaa Healthcare Center/Baghdad. Baghdad J Biochem Appl Biol Sci 2021;2:218-29.
5. Al-Kaif LA, Al-Saadi MA, Al-Charrakh AH. Effect of SARS-CoV-2 infection on HBV-infected patients: Reactivation. Med J Babylon 2022;19:736-46.
6. Shelton JF, Shastri AJ, Ye C, Weldon CH, Filshtein-Sonmez T, Coker D, *et al*; 23andMe COVID-19 Team. Transancestry analysis reveals genetic and nongenetic associations with COVID-19 susceptibility and severity. Nat Genet 2021;53:801-8.
7. Hajihosseinlo A, Hashemi A, Sadeghi S. Association between polymorphism in exon 3 of leptin gene and growth traits in the Makooei sheep of Iran. Livestock Res Rural Dev 2012;24:1-4.

8. Zhao J, You XY, Xu ZZ, Chen AL, Zhao Y, He WJ. Review on application of SNP detection methods in animal research. Trans Chin Soc Agric Eng 2018;34:299-305.
9. Hoskins RA, Phan AC, Naeemuddin M, Mapa FA, Ruddy DA, Ryan JJ, *et al*. Single nucleotide polymorphism markers for genetic mapping in Drosophila melanogaster. Genome Res 2001;11:1100-13.
10. Ismail S, Essawi M. Genetic polymorphism studies in humans. Middle East J Med Genet 2012;1:57-63.
11. AL-Miqdad M. The role of single nucleotide polymorphisms in diagnosis and treatment. J Lab Diagn Syria 2010;5:1-8.
12. Mollica V, Rizzo A, Massari F. The pivotal role of TMPRSS2 in coronavirus disease 2019 and prostate cancer. Future Oncol 2020;16:2029-33.
13. Siyeon S, Sol L, Ho G, Sanghyuk Y, Seunghwan P, Jihi C, *et al*. A systematic review on papers that study on single nucleotide polymorphism that affects coronavirus 2019 severity. BMC Infect Dis 2022;22:47.
14. Wang Y, Lu D, Chung YJ, Xu S. Genetic structure, divergence and admixture of Han Chinese, Japanese and Korean populations. Hereditas 2018;155:19.
15. Gaziano L, Giambartolomei C, Pereira AC, Gaulton A, Posner DC, Swanson SA, *et al*.; VA Million Veteran Program COVID-19 Science Initiative. Actionable druggable genome-wide Mendelian randomization identifies repurposing opportunities for COVID-19. Nat Med 2021;27:668-76.
16. Banday AR, Stanifer ML, Florez-Vargas O, Onabajo OO, Papenberg BW, Zahoor MA, *et al*. Genetic regulation of OAS1 nonsense-mediated decay underlies association with COVID-19 hospitalization in patients of European and African ancestries. Nat Genet 2022;54:1103-16.
17. Zhou Z, Ren L, Zhang L, Zhong J, Xiao Y, Jia Z, *et al*. Heightened innate immune responses in the respiratory tract of COVID-19 patients. Cell Host Microbe 2020;27:883-890.e2.
18. Imran ZK, Al-Karrem Z. Evaluation natural cloning of azole-resistant genes CDR1, CDR2, MDR and ERG11 between clinical and soil isolates of *Candida albicans* based on gene expression. Int J Pharm Tech Res 2016;9:229-36.
19. Sole X, Guino E, Valls J, Iniesta R, Moreno V. SNP Stats: A web tool for the analysis of association studies. Bioinformatics 2006;22:1928-9.
20. Kenney AD, Dowdle JA, Bozzacco L, McMichael TM, Gelais C, Panfil AR, *et al*. Human genetic determinants of viral diseases. Annu Rev Genet 2017;51:241-63.
21. Tanimine N, Takei D, Tsukiyama N, Yoshinaka H, Takemoto Y, Tanaka Y, *et al*. Identification of aggravation-predicting gene polymorphisms in coronavirus disease 2019 patients using a candidate gene approach associated with multiple phase pathogenesis: A study in a Japanese city of 1 million people. Crit Care Explor 2021;3:e0576.
22. WHO, Global status report on non-communicable diseases 2010. Geneva: World Health Organization, 2011.
23. Deng N, Zhou H, Fan H, Yuan Y. Single nucleotide polymorphisms and cancer susceptibility. Oncotarget 2017;8:110635-49.
24. Xu Q, Dong Q, He C, Liu W, Sun L, Liu J, *et al*. A new polymorphism biomarker rs629367 associated with increased risk and poor survival of gastric cancer in Chinese by up-regulated miRNA-let-7a expression. PLoS One 2014;9:e95249.
25. Zeller T, Wild P, Szymczak S, Rotival M, Schillert A, Castagne R, *et al*. Genetics and beyond—The transcriptome of human monocytes and disease susceptibility. PLoS One 2010;5:e10693.
26. Idaghdour Y, Storey JD, Jadallah SJ, Gibson G. A genome-wide gene expression signature of environmental geography in leukocytes of Moroccan Amazighs. PLoS Genet 2008;4:e1000052.
27. Idaghdour Y, Czika W, Shianna K, Lee S, Visscher P, Martin H, *et al*. Geographical genomics of human leukocyte gene expression variation in southern Morocco. Nat Genet 2010;42:62-7.
28. Amoah AS, Obeng BB, May L, Kruize YC, Larbi IA, Kabesch M, *et al*. Urban–rural differences in the gene expression profiles of Ghanaian children. Genes Immun 2014;15:313-9.
29. Hussein AA, Al-Mammori RTO, Hassan FG, Al Saeedi KRH, Al-Charrakh AH. Association of testosterone level and anti-SARS-CoV-2 antibodies in diabetic patients in Babylon, Iraq. Med J Babylon 2024;21:673-80.
30. Ali ZH, Al-Marzoqi AH, Rahmaan N, Al-Taee ZM. Sp110 gene polymorphisms associated with increased susceptibility to COVID-19 severity among the Hillah population. Med J Babylon 2024;21(Suppl 1):S16-20.
31. Abdul-Husseein HK. A review of the persistent burden of post-COVID headaches in children. Hilla Univ Coll J Med Sci 2025;3:Article 10. DOI: https://doi.org/10.62445/2958-4515.1053