Association between Blood Group and TAS2R Gene with COVID-19 Infection

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ABSTRACT

Background: COVID-19 is a widespread infection all over the world which could be affected by different biological, physiological and pathological parameters.

Aim: The study is conducted to investigate the relationship between COVID-19 infection and, the expression of the TAS2R38 gene and other physiological parameters (blood groups, age and gender).

Methods: A total of 105 persons participated in this study. They were subdivided into groups according to COVID-19 infection, age and gender. Phenylthiocarbamide (PTC) test paper was used to detect the distribution of the TAS2R38 gene allele in the whole participants (PAV/PAV homozygote, AVI/PAV heterozygote, AVI/AVI non-taster). Standard serological tests were used to determine the ABO and Rh blood groups.

Results: Up to 71% of homozygotes, 72% of heterozygotes and 68% of non-tasters of the participants tested positive for COVID-19. Both men and women had approximately the same percentage of having been infected with COVID-19. The percentage of having COVID-19 was reported to be significantly higher for middle-aged subjects in comparison with young subjects. Apart from a significant negative correlation with Rh blood grouping, no correlation was found between PTC test results, and having COVID-19 infection and the studied physiological variables.

Conclusion: The study indicates that there is no significant correlation between TAS2R38 polymorphism and the physiological variables age, gender and ABO blood grouping. The study shows the absence of a crucial role of the gene in susceptibility to COVID-19 infection.

Keywords: COVID-19, TAS2R38 gene, bitter taste, ABO blood group, Rh blood group.

العلاقة بين فصيلة الدم وجين التذوق وعدوى مرض كورونا

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الخلاصة

الخلفية: مرض كورونا هي عدوى واسعة الانتشار في جميع أنحاء العالم يمكن أن تتأثر بمعايير بيولوجية وفسيولوجية ومرضية مختلفة.

هدف الدراسة: أجريت الدراسة للتحقيق في العلاقة بين مرض كورونا العدوى والتعبير عن جين التذوق والمعلمات الفسيولوجية الأخرى (فصائل الدم والعمر والجنس).

طرق العمل: شارك في هذه الدراسة ١٠٥ أشخاص. تم تقسيمهم إلى مجموعات حسب مرض كورونا العدوى والعمر والجنس. تم استخدام ورقة اختبار الطعم الفينيل ثايوكارباميد للكشف عن توزيع أليل جين التذوق في جميع المشاركين تم استخدام الاختبارات المصلية القياسية لتحديد فصائل الدم حسب صنف ونوع الدم.

النتائج: تم اختبار ٧١٪ من الزيجوت المتماثل و ٧٢٪ من الزيجوتات غير المتجانسة و ٦٨٪ من غير المتذوقين للمشاركين إيجابيا ل مرض كورونا. كان لدى كل من الرجال والنساء نفس النسبة المئوية تقريبا للإصابة ب مرض كورونا. تم الإبلاغ عن أن النسبة المئوية للإصابة بـمرض كورونا أعلى بكثير بالنسبة للأشخاص في منتصف العمر مقارنة بالشباب. بصرف النظر عن وجود ارتباط سلبي كبير مع فصيلة الدم، لم يتم العثور على ارتباط بين نتائج اختبار الفينيل ثايوكارباميد ، ووجود عدوى مرض كورونا والمتغيرات الفسيولوجية المدروسة.

الاستنتاجات: تشير الدراسة إلى عدم وجود علاقة ذات دلالة إحصائية بين تعدد الأشكال جين التذوق والمتغيرات الفسيولوجية العمر والجنس وفصيلة الدم. تظهر الدراسة عدم وجود دور حاسم للجين في القابلية للإصابة بعدوى مرض كورونا

الكلمات المفتاحية : مرض كورونا ، جين التذوق ، طعم مر ، فصيلة دمABO , فصيلة دم Rh.

INTRODUCTION

Taste receptor is well known to be found on the tongue to aid in tasting and warning for unwanted ingested material. Interestingly these receptors are found in other tissues like the respiratory tract, gastrointestinal epithelium, brain, and pancreas. TAS2R38 presents with two haplotypes: the taster (PAV) and the non-taster (AVI).[1]

The function of these receptors remains unknown but data is suggesting a relation between sweet and bitter tests with innate immunity, as the taste in the tongue may help in avoiding unwanted ingested material. There is a different expression of (AVI) and (PAV) alleles in different individuals which may explain the difference in innate immunity responses among different individuals.[2]

TAS2R38 gene products (expression) are found in the respiratory tract which is considered an important entry to infectious microorganisms whether it is viral, bacterial or fungal. The extraoral taste receptors found in the respiratory tract may help the immune system detect unwanted pathogens.[3]

A bitter product by microorganisms may contribute to immunity regulation like enhanced microbial removal by mucous secretions, and antimicrobial peptide features. A genetic variation in bitter response may contribute to variation in response to respiratory tract infections.[4]

The TAS2R38 gene products can be affected by quorum molecules produced by these microorganisms triggering nitric oxide production from the respiratory tracts and helping in eliminating these microorganisms. In addition, cilia are present at the respiratory epithelium and it is part of innate immunity and plays a pivotal role in the elimination of unwanted harmful particles.

The bitter taste receptor family (T2Rs) have a role in stimulating sinonasal innate immunity.[5]

Coronavirus SARS-CoV-2 had a widespread infection all over the world which caused a crucial morbidity and mortality that has overwhelmed health systems worldwide.[6,7]

Many studies have been conducted to highlight the relationship between the coincidence of COVID-19 and different physiological parameters such as ABO, and Rh blood phenotypes.[8]

It is recommended to know whether persons with AVI are more prone to getting infection or not, as the data is not sufficient to confirm this link yet.[9]

Aim of the study: The study is conducted to investigate the relationship between COVID-19 infection and, the expression of the TAS2R38 gene and other physiological parameters such as blood groups, age and gender.

SUBJECTS AND METHODS

Subjects and study strategy: This cross-sectional study involved a total of 105 healthy students/staff volunteers from the College of Pharmacy/University of Mosul (Mosul City, Iraq) during period 01.01.2021 to 01.04.2021. A demographic questionnaire was used to collect the data about age, gender, as well as the medical history, signs and symptoms of having COVID-19 with positively confirmed through laboratory diagnosis. The participants are subdivided into groups according to their gender, age (young age 20s years versus middle age 40s years),[10-12] and blood groups (according to ABO system and Rhesus system). Blood grouping was measured using standard serological analysis.[13]

The volunteers were asked to taste Phenylthiocarbamide (PTC) paper to determine the heritable trait of having the TAS2R38 gene.[14] The participants were subdivided according to gene detection into 3 groups: homozygote (feel highly bitter taste), negative gene carrier (feel no taste at all), or heterozygote (feel slight to moderate bitter taste).[15,16]

Statistical analysis: The results were statistically analyzed using the GraphPad Prism program. The data were expressed as Mean ± Standard deviation. A one-way Analysis of Variance (Kruskal-Wallis Test ANOVA) and Chi-square test were employed to determine the statistical difference between various subgroups, using Tukey's multiple comparison tests as a post-hoc analysis. Spearman's non-parametric correlation was used to measure the correlation coefficient between PTC results and the different studied groups. A P-value of < 0.05 was considered significant.

RESULTS

Sample features: The average age of the 105 participants employed in the present study was 31.83 ± 10.72 yr. According to their age, the subjects were subdivided into young aged 19-25 yr (n=54) and middle-aged 30–50 years (n=51). With regard to gender, the subjects were distributed as follows: men (n=52) and women (n=53). The results of the PTC test showed that there were 24 homozygous (PAV/PAV) for the *TAS2R38* gene (22.85%), 38 negative gene carriers (AVI/AVI) (36.19%) and 43 heterozygous (AVI/PAV) for *TAS2R38* gene (40.95%). In addition, the prevalence of different blood groups was the following: blood group O (41.9%), group A (35.2%), group B (15.2%) and finally group AB (7.6%). Finally, most of the participants (89.5%) were tested Rh positive , table 1.

Distribution of *COVID-19* positivity among the study groups: The 74 subjects (70.5%) tested positive for COVID-19 out of 105 individuals enrolled in the present study. 71% of subjects (17 out of 24) tested as homozygous for the TAS2R38 gene tested positive for COVID-19 as well. 72% of heterozygotes (31 out of 43) and 68% of the negative gene carriers (26 out of the 38) tested positive for COVID-19.

With regard to ABO blood grouping, subjects with blood group O had the lowest percentage of Covid19 positivity (30/44, 68%) while those with groups B and AB had the highest percentage of Covid19 positivity (12/16, 75% and 6/8, 75%, respectively). Additionally, 70% of the subjects of blood group A were positive for COVID-19 (26 out of 37 individuals). Considering Rhesus blood grouping, among 94 of Rh-positive individuals 65 were tested as Covid19 positive (69%) while among 11 of the Rh-negative subjects 9 were shown positive for Covid19 (82%).

According to gender, both men and women had approximately the same percentage of having been infected with COVID-19 (37/52, 71% and 37/53, 70%, respectively). However, the percentage of having COVID-19 was reported to be significantly higher (86%) for middle-aged subjects in comparison with only (56%) for young subjects , figure 1.

Table 1. Descriptive data of the study groups.

Variables	Total (n=105)	*p-value*	COVID-19 positivity in each subgroup	*p-value*
	n (%)		n (%)	
TAS2R38				
PAV/PAV	24 (22.85%)		17 (70.83%)	
AVI/PAV	43 (40.95%)	> 0.9	31 (72.09%)	0.81
AVI/AVI	38 (36.19%)		26 (86.42%)	
Gender				
Male	52 (49.5%)		37 (71.15%)	0.59
Female	53 (50.47%)		37 (69.81%)	
Age				
Young	54 (51.42%)		30 (55.55%)	0.02 *
Middle age	51 (48.57%)		44 (86.27%)	
ABO blood group				
O	44 (41.9%)		30 (68.18%)	
A	37 (35.2%)	> 0.9	26 (70.27%)	0.89
B	16 (15.2%)		12 (75%)	
AB	8 (7.6%)		6 (75%)	
Rh blood group				
Rh+	94 (89.50%)		65 (69.15%)	0.63
Rh-	11 (10.47%)		9 (81.82%)	
Chi-square is used to calculate *the p-value*. * denotes that the p-value is <0.05.				

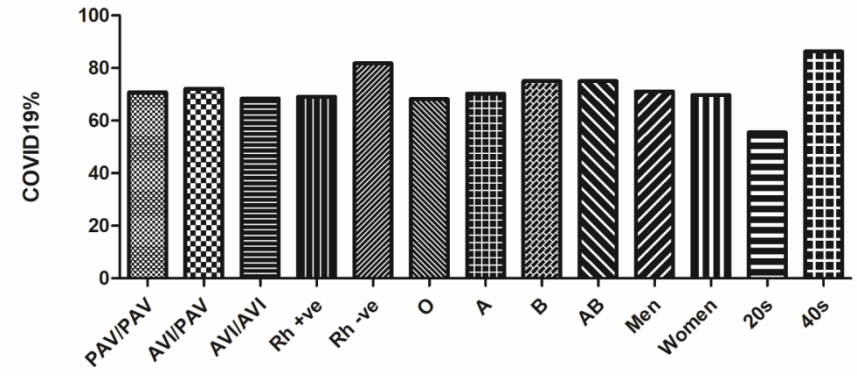

Figure 1: Percentage of COVID-19 positivity to the total number in each group.

Correlation of *TAS2R38* variants with study variables

There was no significant correlation (r=0.02) between PTC testing and COVID-19 positivity. Additionally, the results of the non-parametric Spearman correlation showed that there was no correlation between PTC testing and participants' ABO blood groups, age and gender (r=0.08, -0.1, and 0.02, respectively). However, PTC results were negatively (inversely) correlated to Rh blood grouping (r= -0.29, *p-value*=0.002). Table (2) summarizes the results of correlation between PTC results and different parameters in the study.

Table 2. Correlation of TAS2R38 with different measured variables.

Variables	Spearman r	95% confidence interval	P value (two-tailed)
COVID19	0.0201	-0.1778 to 0.2165	0.8387
ABO groups	0.08661	-0.1125 to 0.2791	0.3797
Rh groups	-0.2978	-0.4675 to -0.1068	0.002**
Sex	0.02961	-0.1686 to 0.2255	0.7643
Age	-0.102	-0.2933 to 0.09719	0.3005

DISCUSSION

The present study found no significant correlation between PTC taster status and COVID-19 infection, indicating that the TAS2R38 genotype does not directly influence disease susceptibility. Ashok et al. (2022) investigated the association between blood group, TAS2R38 gene variants, and COVID-19 susceptibility.[17] The TAS2R38 gene encodes for bitter taste receptors that bind bitter compounds such as phenylthiocarbamide (PTC). Individuals can be classified as PAV/PAV homozygotes, AVI/PAV heterozygotes, or AVI/AVI non-tasters based on their sensitivity to PTC.[18] The distribution of these genotypes varies globally, with the non-taster genotype being most prevalent in Africa and the Middle East.[19]

However, PTC taster status was inversely correlated with Rh-negative blood type. The Rh blood group locus is genetically linked to the TAS2R38 locus on chromosome 12,[20] which may explain this association. COVID-19 positivity rates were also similar across ABO blood groups in this cohort, contrasting some previous studies reporting increased risk in blood group A and protection in group O.[20,21] However, the small sample size of some blood groups (e.g. n=8 for group AB) may have obscured potential associations.

The present study confirmed that COVID-19 positivity was significantly higher in middle-aged (86%) versus young (56%) participants. This aligns with global data showing higher morbidity and mortality among older adults.[22,23] Age-related difference may reflect immunosenescence, higher rates of comorbidities, or socioeconomic factors that increase viral exposure risk in mid-life.[21] Further analysis of participant demographics, behaviours, and clinical factors could provide insight into the basis of age-related COVID-19 susceptibility.

A key limitation of this study was the lack of genetic analysis to confirm TAS2R38 genotypes. PTC paper testing is subject to user errors and cannot distinguish heterozygotes from homozygotes.[18] PCR-based genotyping should be employed to definitively assign genotypes. No specific variants reported conferring Rh-negative status, which could help explain the correlation with PTC taster status. Additionally, the study may have been underpowered to detect associations between blood groups or TAS2R38 genotypes and COVID-19, given the small sample size. Expanding the cohort could improve statistical power to find significant effects.

Nonetheless, this study provides initial evidence that age is a stronger predictor of COVID-19 risk than blood group or bitter taste receptor genetics in this population. The study also confirmed a positive linkage between the TAS2R38 and Rh loci suggesting further investigation. Replication in larger, genetically defined cohorts is needed to clarify the role of these genetic factors in COVID-19 susceptibility. Especially important is an assessment of diverse global populations, since blood group distributions and TAS2R38 genotypes vary significantly among ethnicities.[19,24] Additionally, clarifying the expression and function of bitter taste receptors across respiratory tissues could unveil mechanisms connecting this chemosensory system to SARS-CoV-2 infection.[25,26] Overall, this study highlights important areas for future research regarding host genetic factors influencing COVID-19 risk. Integrating analysis of blood groups, taste receptor genetics, and other biomarkers could eventually enable personalized prediction of disease susceptibility.

CONCLUSION

The present study checked to identify the association of TAS2R38 polymorphism with some physiological variables (age, gender, ABO blood group, and Rh blood group) alongside the correlation with COVID-19 susceptibility. A non-significant association were confirmed between the gene test and these variables. The taste positivity does not correlate with the susceptibility to COVID-19.

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Conflict of Interest

The authors declare no conflict of interest in publishing this manuscript.

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