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Research Article

Genetic Variability in Taste Receptors and Its Influence on COVID-19 Symptom Severity

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Abstract

The COVID-19 pandemic has impacted global health, economy, and society, highlighting the need for a deeper understanding of viral mechanisms and immunity enhancement strategies. This study investigates the relationship between genetic variability in taste receptors, particularly TAS2R38, and COVID-19 susceptibility, as well as the role of nutrition in modulating immune function. Influenced by genetic diversity, taste perception plays a role in food preferences, which may affect immune responses. We collected data from 21 participants regarding their food preferences, COVID-19 history, and phenotypic classification of taste perception using phenylthiocarbamide (PTC) strips. Our findings indicate a non-significant negative correlation between body mass index (BMI) and COVID-19 symptom severity, with supertasters experiencing milder symptoms compared to tasters and non-tasters. Additionally, participants with a history of COVID-19 preferred sweeter foods, while those without a history favoured bitter-tasting foods. These results suggest that genetic variations in taste receptors and dietary choices may influence individual immune responses to viral infections. Although this study faced limitations due to sample size and genotyping challenges, it emphasises the potential role of personalised nutrition and genetic factors in enhancing immunity against COVID-19 and future health crises. Further research is recommended to explore genotypic variations and their interactions with dietary patterns in shaping immune responses.

Keywords: COVID-19, Taste perception, Sensory preferences, TAS2R38, BMI, Supertasters, Bitter-taste receptors, Nutritional impact on immunity

1. Introduction

The emergence of the COVID-19 pandemic took the global community by surprise, resulting in a significant impact that was previously unimaginable in the contemporary age. According to the World Health Organisation (WHO), as of October 2023, the global tally of confirmed COVID-19 infections exceeded 771 million, with a reported mortality rate of 6.9 million(WHO, 2023). The UK has recorded over 24 million cases and about 230, 383 deaths up until October 2023 (WHO, 2023)(Msemburi et al., 2023). The virus, which is transmissible among humans, has exhibited fast and unprecedented dissemination, which largely occurs by direct human contact or the dispersal of respiratory droplets (Yüce et al., 2021). The COVID-19 pandemic exacerbated human misery, destabilised the world economy, disrupted the lives of billions of individuals worldwide, and substantially impacted health, economics, the environment, and society (Mofijur et al., 2021). It is the worst health emergency the world has seen in over a century. Miya et al. (2022) highlighted the impact of the pandemic on public health, stating that it affects mental health. They also emphasised the impact of the pandemic on the environment, socio-economy, and the educational system. Shrestha et al. (2020) highlighted the effect of the pandemic on healthcare capacity, academic institutions, and the food and agricultural sector, stating the critical necessity of reevaluating public health responses and disaster preparedness in future health crises.

Given the dire consequences entrained by the pandemic, it is pertinent to gain a more profound understanding of the virus's mechanisms and explore pathways to enhance immunity against the virus and potential future health emergencies.

Vaccines against the disease as well as drugs that directly interfere with the virus replication pathway have now been produced, however, not only did it take months with millions of lives gone, but there have been recorded cases of adverse effects and waning immunity after about 4 – 6 months (Menni et al., 2022). Mey et al. (2023) discussed the importance of nutrition in mitigating diseases, boosting the immune system, and reducing the risk of SARS-COV-2. Adequate nutrition is pivotal in modulating the immune response of Covid-19 patients. Careful selection of appropriate dietary components is crucial for maintaining immune equilibrium and enhancing its efficacy. Moreover, a nutritionally optimal diet can effectively mitigate oxidative stress, thereby exerting a positive influence on the overall immune function (Miyah et al., 2022). Calcuttawala (2022) investigated the impact of dietary components on both susceptibility to SARS-CoV-2 infection and the amelioration of associated symptoms. She asserted that dietary nutrients have few adverse effects and provide several advantages to the immune system. For example, proteins, play a crucial role in the synthesis of antibodies. Various dietary elements, including omega-3 fatty acids, vitamin C, vitamin E, and phytochemicals like carotenoids and polyphenols, have been shown to possess anti-inflammatory and antioxidant activities (Calcuttawala, 2022).

1.1 Genetic Diversity and Taste Perception

Heredity and environmental influences influence the human body's physiological response to diseases. The human genome passed down from preceding generations, plays a significant role in shaping the body's response to many conditions, including viral illnesses (Parsa et al., 2021). COVID-19 has clinical symptoms ranging from asymptomatic to respiratory failure needing critical care, but therefore targeting of chemosensory systems with ensuing impairment of the perception of smell and taste is the distinctive feature of the infection, independent of variations (Mazzatenta, 2022). Taste perception can differ among individuals due to genetic variances in specific taste receptor genes. Genetic differences can result in varying taste perceptions and sensitivity thresholds for different taste qualities, influencing individual preferences for specific food types (Feeney et al., 2011). Taste perception is crucial in influencing individual food preferences and dietary habits. It is generally presumed that maintaining a healthy sense of taste is important in maintaining good health (Okayama & Watanabe, 2019). Poor eating habits have been linked previously to diseases such as obesity, cardiovascular diseases, type 2 diabetes, and metabolic syndrome (MetS), therefore, taste perception may have a significant role in determining the risk of developing chronic diseases through the individual choice of unhealthy meals (Chamoun et al., 2018).

1.2 Taste Receptors

The human perception of taste is classified into five primary flavour modalities, namely sweet, sour, bitter, salty, and umami (savoury) (Gravina et al., 2013) (Bachmanov et al., 2014). The taste buds serve as the principal sensory component of the taste system and are located underneath the keratinized layer of the papillae, with a taste pore that is exposed to the external environment. Taste receptors are located at the microvilli of taste buds, and are responsible for taste recognition, playing a pivotal role in generating sensory perceptions, and initiating physiological processes essential for nutrient absorption and metabolic adjustments (Roper & Chaudhari, 2017). There are a minimum of five distinct cell types that comprise a taste bud, including type 1, type 2, type 3 cells, basal cells, and neuronal processes. Types I–III are mature taste receptor cells that are visible to the oral cavity and can interact with taste inputs through taste receptor proteins. This exchange causes excitement that is sent through gustatory nerves that connect to the brain and make taste awareness possible (Bachmanov et al., 2014). The presence of genetic diversity within prototypical taste receptors serves as a predictive indicator of the variation in perception levels of taste stimuli amongst individuals. (Ponnusamy et al., 2022).

Although the primary role of taste receptors is to identify external chemicals and translate their chemical signals into biological responses, taste receptors have been found across the body, and they seem to play a role in a wide variety of control mechanisms including peripheral chemical sensing, cortical processing, performance, physiology, and the pathophysiology of disorders like diabetes (Gravina et al., 2013), emphasizing the importance of investigating taste receptors.

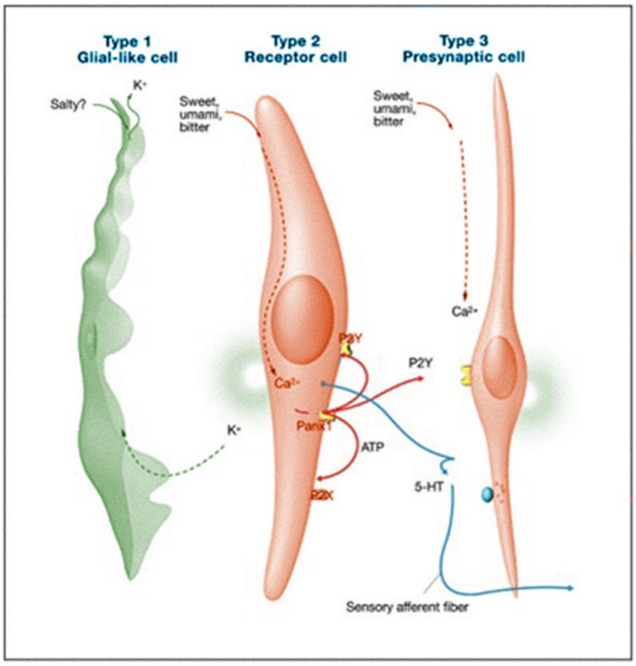


Figure 1: *Cell Types of Taste Buds. Type 1 taste buds produce salty flavours, while type 2 cells mediate sweet, umami, and bitter tastes. Type 3 presynaptic cells interpret sour tastes and communicate with type 2 cells via P2Y adenosine receptors, activating afferent neurons with serotonin.*

1.3 Genetic Variability in TAS2R38 and Implications for Respiratory Tract Defence

The TAS2R38 (T2R38) gene is in a subset of the TAS2Rs involved in taste perception and plays crucial roles in immune responses (Parsa et al., 2021). It is expressed in the ciliated cells of the human upper airways, the site where the coronavirus is known to replicate (Parsa et al., 2021). T2R38 also modulates the innate defence mechanisms of the human upper respiratory tract by generating nitric oxide, which stimulates mucus secretion aiding defence against pathogens (Lee & Cohen, 2015) (Parsa et al., 2021). There are two prevalent variants of this gene found globally, characterised by specific amino acids at positions 49, 262, and 296, encoded by three non-synonymous coding SNPs (rs713598 - G145C, Ala49Pro;rs1726866 - T785C, Val262Ala; rs10246939 - A886G, Ile296Val), which correspond to the PAV (Proline, Alanine, Valine, “phenylthiocarbamide PTC taster") and AVI (Alanine, Valine, Isoleucine, "PTC non-taster") haplotypes (Risso et al., 2016) (Parsa et al., 2021). Variations in the T2R38 gene, linked to different sensitivities to PTC, a bitter compound, also significantly influence the susceptibility of the upper respiratory tract to infections. Therefore, genetic alterations in T2R38 functionality are likely to cause individual differences in how airway cells respond to infectious agents. The TAS2R38 gene is.

The genetic basis of COVID-19 has been extensively studied, as reviewed by Cappadona et al. (2023) but the link between genetic variations in taste receptors and the severity of the disease remains largely unexplored. Barham et al. (2021) in a closely related study utilised PTC strips to determine the phenotypic expression of T2R38 and confirmed COVID-19 infection using PCR.

They also stated the need for further evaluating of the phenotypic expression of T2R38 as a factor associated with COVID -19. Kompaniyets (2021) found a non-linear relationship between Body mass index (BMI) and COVID-19 severity.

1.4 The Role of Nutrition in Enhancing Immune Function

An increasing body of research demonstrates how crucial nutrition is for enhancing immunity against pathogenic invasions. According to the World Health Organization's adult nutritional guidelines, maintaining a disease-free lifestyle involves eating a well-balanced diet rich in vitamins, minerals, dietary fibre, proteins, and antioxidants daily (Calcuttawala, 2022).

Dietary components like phytochemicals, micronutrients, and macronutrients strengthen the immune system. Macronutrients, such as proteins, fats, and carbohydrates, are needed in significant quantities, while micronutrients like vitamins and minerals are required in smaller amounts (Calcuttawala, 2022). Nutrients such as vitamins A and D, and their metabolites, directly control the expression of genes in immune cells, which are important for immune cell maturation, differentiation, and responsiveness.

One aspect of innate immunity is the production of damaging reactive oxygen species, which create a pro-oxidant environment (Calder, 2020). The host must be protected from these by providing antioxidant enzymes and classic antioxidant vitamins C and E. Thus, a balanced supply of these nutrients is necessary to trigger the right immune response (Calder, 2020).

Proteins

Amino acids play a crucial role in immune responses by controlling three processes: (i) the generation of antibodies, cytokines, and other cytotoxic substances; (ii) cellular redox state, gene expression, and lymphocyte proliferation; and (iii) the activation of T lymphocytes, B lymphocytes, natural killer cells, and macrophages. Research indicates that supplementing malnourished animals and humans with specific amino acids improves their immune systems, thereby lowering morbidity and mortality (Li et al., 2007). Key metabolic pathways of the immune response against infectious pathogens are also regulated by amino acids (Calcuttawala, 2022).

Carbohydrates

While not directly related to immunity, carbohydrates are essential for a healthy nutritional status, which in turn affects immune function. Maintaining a healthy nutritional status, including adequate carbohydrate intake, benefits both the prognosis of COVID-19 patients and overall immune function (Li et al., 2021). Additionally, water-soluble polysaccharides and polysaccharide-protein complexes can stimulate and enhance macrophage and complement system immune responses (Smith et al., 2015).

Lipids

Lipids are essential for the development of lipid rafts, specialised membrane microdomains that facilitate immune cell communication. These signalling events are critical for coordinating immune responses against pathogens such as SARS-CoV-2. Furthermore, lipid molecules like leukotrienes and prostaglandins act as signalling molecules that regulate inflammation, a crucial aspect of the immune response (Tran et al., 2022). Consuming omega-3 fatty acids through diet induces an anti-inflammatory response, while omega-6 fatty acids, like arachidonic acid, give rise to pro-inflammatory eicosanoids such as prostaglandins and leukotrienes.

Vitamins & Minerals

Table 1 summarises key vitamins and minerals, highlighting their specific functions in immune regulation and response. From the antioxidant properties of Vitamin C to the immune cell proliferation supported by Zinc, each nutrient plays a crucial part in maintaining and enhancing the body's defences against pathogens (Alpert, 2017).

The research is essential due to the continuing challenges in managing COVID-19, including waning vaccine efficacy and emerging variants. While vaccines and antiviral treatments are crucial, they are not sufficient alone. This research aims to address gaps in understanding how genetic variations, particularly in taste receptors like TAS2R38, influence COVID-19 susceptibility and immune responses. Additionally, the role of nutrition in modulating immune function and its interaction with genetic factors remains underexplored. By bridging these gaps, the study seeks to enhance personalised prevention strategies and treatment approaches, integrating genetic insights with nutritional strategies to bolster immune resilience against COVID-19 and future health crises. In trying to bridge this gap, we planned to collect data from participants on their food preferences, previous infection with COVID-19, weight, and height, to determine BMI, a crucial metric correlated with the severity of COVID-19 symptoms. Phenotypic testing using PTC strips was also planned to be carried out.

Table 1: Essential Vitamins and Minerals for Immune Function.

Vitamin/Mineral	Role in Immunity
Vitamin A	Regulates innate and cell-mediated immunity, enhances white blood cell function, reduces susceptibility to infections, improves antibody titers, and counters immunosuppressant effects of cortisone.
Vitamin B Complex	Works synergistically to support immune function, crucial for lymphocyte mitogenic response, lymphocyte maturation, and growth. Vitamin B6 and B12 deficiencies impair antibody production, T-cell function, and thymus size. Folic acid is essential for cell division and production in blood-forming organs. Vitamin B12 is critical for white blood cell maturation.
Vitamin C	Acts as a potent antioxidant, enhances leukocyte function, stimulates T lymphocyte proliferation, and increases immunoglobulin and cytokine production.
Vitamin D	Modulates innate and adaptive immune responses, is associated with autoimmunity prevention, and has immunosuppressant effects preventing autoimmune diseases.
Vitamin E	Boosts immune function especially in older adults, with a significant reduction in infections.
Copper	Essential for oxidation-reduction reactions, regulates energy production, iron metabolism, and connective tissue maturation, crucial for interleukin 2 and T cell proliferation, and neutrophil function
Iron	Necessary for immune cell proliferation and maturation, helps in generating responses to infection, and regulates iron availability to prevent infection and tumour development.
Selenium	Key in redox regulation and antioxidant function, protective against oxidative stress and heart damage from cytomegalovirus.
Zinc	Essential for immune cell proliferation, enhances skin and mucosal membrane integrity, has direct antiviral effects on rhinovirus replication, boosts innate immunity, antibody response, and cytotoxic CD8+T cell

1.5 Aims and Objectives

This research aimed to explore the relationship between BMI and the severity of COVID-19 symptoms, as well as examine sensory preferences and demographic characteristics in a sample population. The study also sought to investigate how taste perception might influence or be influenced by COVID-19, offering an exploratory insight into the role of sensory preferences during the pandemic.

This research work had the following objectives;

i. To investigate the correlation between BMI and COVID-19 severity

ii. To investigate the sensory preferences and demographic characteristics of a sample population, with an exploratory focus on taste perception in the context of COVID-19.

2. Materials and Methods

2.1 Ethics Approval

COSHH and risk assessment forms along with all relevant attachments were approved before any laboratory investigations took place. This research was conducted and approved by the Ethics Committee of Coventry University, with the approval code P146471. A participant questionnaire was created along with participant information sheets and informed consent forms: consent was given by all participants before taking part in the research. Participant data was anonymised using a coded system, as described below. All laboratory procedures were performed wearing PPE in the form of goggles and a lab coat.

2.2 Sample Collection and Processing

A random selection of volunteer students from Coventry University were recruited for this study. 21 participants between the ages of 18 and 35 were enlisted, and demographic data including age, sex, and biogeographic ancestry were gathered. For anonymisation, a random four-digit number generator was utilised to create participants' codes, with codes starting with a "Zero" eliminated. The JISC questionnaire system was utilised to create an online questionnaire, which comprised participants' preferences for food items that reflect both sensory preferences (bitter, sweet, savoury) and foodstuff preferences (Appendix 1). Other items included their COVID-19 predisposition, symptoms observed and the severity of the symptoms. Participants were also asked about their allergies and sensitivity to certain foods. 10 participants were recruited to validate this questionnaire before sample collection commenced.

2.3 Phenotypic Classification of Bitter Sensation Using PTC Strips

Participants were given taste test strips in the following sequence: first, the control strip was given, followed by the PTC strip. Participants were instructed to place the strips on their tongue until it was completely moistened. After this, they were directed to assess the taste quality and intensity, providing ratings on a scale of "taste nothing" to "very bitter."

2.4 Statistical Analysis

Participants' body mass index (BMI=weight [kg]/height [m]^2) was calculated using their height and weight data. The data were analysed using IBM SPSS statistics software. The relationship between COVID-19 symptom severity and BMI was assessed using Pearson's correlation and the COVID-19 symptom severity's association with Taster groups was examined using a box plot. The significance level was set as $P<0.05$.

3. Results

3.1 Participants Demographics

There were 21 participants recruited from Coventry University for the study. (Tab 2) shows the collected demographic data of participants, including their gender, age range, COVID-19 history, and ethnicity. There were slightly more female than male participants, most were below 30 years old. The majority were of Asian and Black descent with White, mixed, and Arabian ethnicities all having 4.8% participation. There was also a 9.5% whose ethnicity wasn't listed and didn't specify. In addition, concerning COVID-19 predisposition, 66.7% of the population had no covid history whilst 33.3% had been previously diagnosed with COVID-19.

3.2 BMI and COVID-19 Severity

The body mass index of participants was calculated using their height and weight data (Appendix 1) obtained from the questionnaire. The calculated BMI values ranged from 18.59 to 33.62kg/m^2, with a mean BMI of 24.93 kg/m^2. To investigate the relationship between and the severity of COVID-19 symptoms, the Pearson correlation coefficient was calculated (Fig 2a), only with data of participants with previous COVID-19 history and represented with a scatter dot plot (Fig 2b) which showed a non-significant negative correlation between both variables ($r=-.608$, $p > 0.05$). The symptoms observed by this cohort include high temperature, continuous cough, change and loss of taste, change and loss of smell, chest pain and running nose.

Table 2: Demographic data of participants.

Questions		Number of participants	Percentage (%)
Gender	Female	10	47.6
	Male	11	52.4
Age Range	19-24 years	7	33.3
	25-30 years	11	52.4
	31-34 years	1	4.8
	35-40 years	2	9.5
Mean age	24.4 years		
COVID-19 history	Participants with no history	21	66.7
	Participants with Covid history	7	33.3
Ethnicity	Asian or Asian British	11	52.4
	Black, Black British, Caribbean, African	5	23.8
	Mixed or multiple ethnic groups	1	4.8
	White, English, Welsh, Scottish, Northern Irish	1	4.8
	Arab	1	4.8
	Others	2	9.5

Correlations

		BMI	Covid_symptom_severity
BMI	Pearson Correlation	1	-.608
	Sig. (2-tailed)		.148
	N	7	7
Covid_symptom_severity	Pearson Correlation	-.608	1
	Sig. (2-tailed)	.148	
	N	7	7

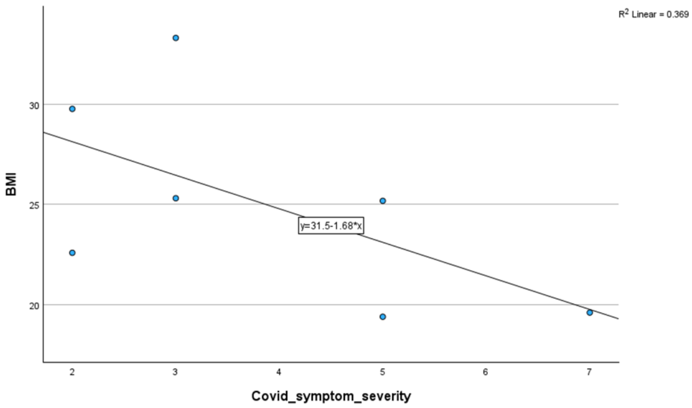


Figure 2: *BMI and COVID Symptom severity. (A) Pearson Correlation Coefficient for the Relationship Between BMI and COVID-19 Symptom Severity Among Participants with COVID-19 History (B) Scatter dot plot illustrating the correlation between COVID-19 symptom severity and BMI among participants with a history of COVID-19. The x-axis represents COVID-19 symptom severity, the y-axis indicates BMI values in kg/m².*

3.3 Taste Perception and COVID-19 Symptom Severity

All participants were assessed by phenotype taste testing and categorised into 3 groups (supertasters, tasters, and non-tasters) via phenotypic expression of TAS2R38 using the PTC strips: 33.3% were categorised as supertasters, 38.1% were categorised as tasters, and 28.6% were categorised as non-tasters (Appendix 1). In a bid to determine an association between Covid symptom severity across taster groups, a boxplot was plotted where it was observed that the median COVID-19 symptom severity was notably lower for the super tasters compared to both tasters and non-tasters. The interquartile range for super-tasters was also narrower, indicating less variability in symptom severity within the participants with COVID-19 history (Fig 3). While outliers were present, the overall pattern supports the hypothesis that supertasters had the least COVID symptoms, followed by tasters and non-tasters with the highest severity.

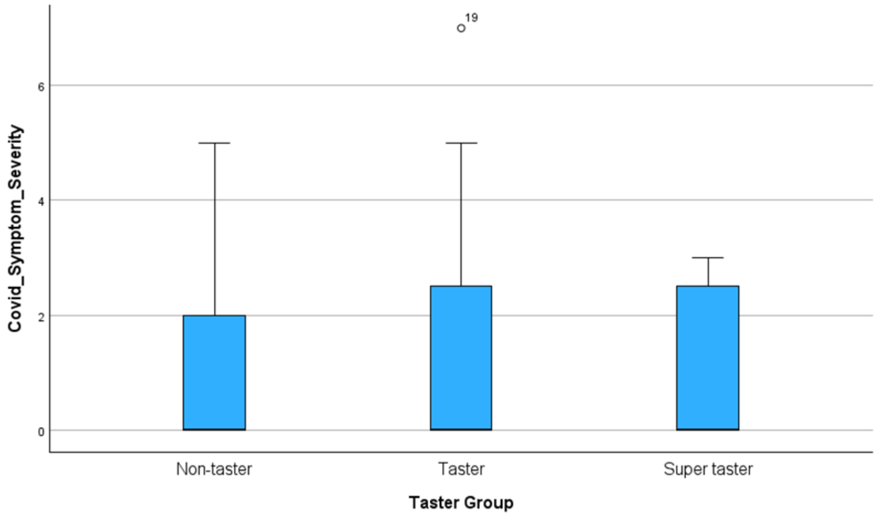


Figure 3: Boxplot of COVID-19 symptom severity across TAS2R38 phenotype groups. *From the PTC phenotypic test, participants who tasted nothing were classified as non-tasters, those who recorded "faint taste and noticeable bitterness" were grouped as tasters and the supertasters status was assigned to participants who experienced "bitter and very bitter" tastes.*

3.4 Dietary Questionnaire Responses

Participants stated their food and drink preferences from a list of 7 different drinks and 34 different foods including fruits. The data included their likes, dislikes and indifference towards these items, each participant had an option of "not applicable" for foods which they haven't tasted yet. The dietary preferences of participants with COVID-19 history and those without were compared, with emphasis on bitter foods hypothesizing a potential link between bitter taste perception and better immunity against Covid, aimed at uncovering patterns in dietary preferences that might contribute to the understanding of the relationship between taste perception and immune responses.

White wine was the most preferred drink by participants without a Covid history (43%), whereas vinegar was least preferred by the same cohort with 71%. Green tea and red wine (29%) had a seeming balance between the two cohorts for disliked drinks same as Coffee without sugar (14%) for liked drinks. Green tea with 57% was the most liked by participants with a Covid history whereas coffee without sugar with 71% was the most hated by the same group (Tab 4).

Table 3: Participants' drink preferences based on their COVID-19 history.

	% Who disliked		% who were in-different		% Who liked		% Not applicable	
Drink	covid history (%)	No covid history (%)	covid history (%)	No covid history (%)	covid history (%)	No covid history (%)	Covid history (%)	No Covid history (%)
Beer	29	21	-	29	29	36	43	7
Coffee without sugar	71	50	14	29	14	14	-	-
Green tea	29	29	14	36	57	36	-	-
Vinegar	43	57	29	29	14	7	14	-
Whisky	14	36	-	14	29	36	57	7
Red wine	29	29	-	29	43	36	29	-
White wine	14	21	-	7	29	43	57	21

Participants with COVID-19 history (N = 7)

Participants without COVID-19 history (N = 14)

participants didn't select any option

NB: This table displays participants' drink preferences based on their history of COVID-19 infection. Drinks are categorized by the percentage of participants who disliked, were indifferent to, liked, or did not select an option ("Not Applicable"). The preferences are separated for participants with a history of COVID-19 and those without.

The food preferences results showed a trend among participants who previously had COVID-19. A higher proportion of them preferred sweeter foods compared to the non-covid-19 group. Foods like bananas, chips, mangoes, pomegranates, sweet cherries, pineapples, guava, jackfruits, and carrots at 86% were the most preferred by this cohort, whereas garlic was the most hated. In contrast, Peas (100%) and onions (93%), were most preferred by participants without a Covid history. Black olives (36%) and figs (29%) were the most hated (Tab 5). These findings align with the hypothesis suggesting a potential link between taste receptor variations, specifically those related to bitter tastes, and better immunity. Notable preferences were observed for, bananas, chips, pineapples, and guava, suggesting that these fruits might be universally appealing, regardless of COVID-19 exposure.

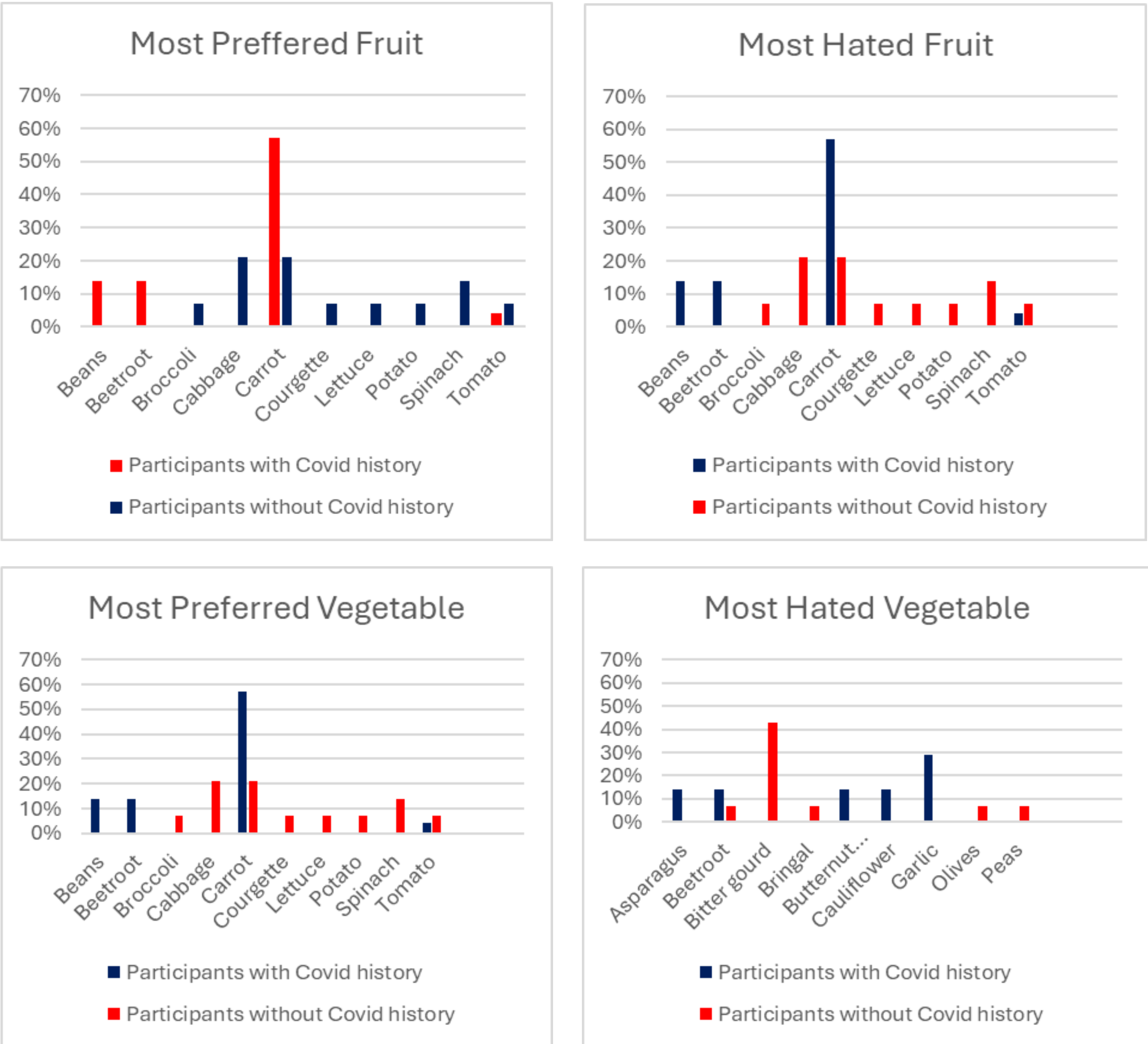
Table 4: Participants food/fruit preferences based on their COVID-19 history.

	No. Who disliked		No. who were indiffer-		No. Who liked		Not applicable	
Food/Fruit	covid history (%)	No covid history (%)	covid history (%)	No covid history (%)	covid history (%)	No covid history (%)	covid history (%)	No covid history (%)
Banana	14	7	-	7	86	86	-	-
Black olives	43	36	-	14	14	14	57	21
Apples Granny smith	29	7	14	14	57	71	-	-
Apples Royal gala	29	7	14	14	57	79	-	-
Apple Pink lady	29	7	14	14	43	57	14	21
Chips	14	7	-	21	86	71	-	-
Doughnut	14	7	14	21	71	71	-	-
Garlic	71	14	-	36	29	43	-	-
Grapefruit	14	7	14	21	71	64	-	7
Kiwi	14	7	14	7	57	57	-	29
Mango	-	7	14	-	86	86	-	7
Brussels Sprouts	14	21	57	7	14	50	14	14
Figs	14	29	43	-	14	29	29	43
Pomegranates	14	7	-	21	86	50	-	21
Sweet cherries	14	7	-	7	86	64	-	21
Passion fruits	-	14	-	7	43	79	57	-
Pineapples	14	-	-	7	86	79	-	14
Blueberries	14	14	29	-	43	86	14	-
Strawberries	14	7	29	-	71	71	-	-
Starfruits	29	14	-	7	43	50	29	29
Guava	14	7	0	0	86	86	14	0
Jackfruits	-	14	-	7	86	57	14	21
Asparagus	14	14	14	7	29	29	43	29
Beetroot	29	21	-	7	43	64	-	14
Broad beans	14	14	43	29	43	29	-	21
Broccoli	43	21	29	14	29	57	-	-
Carrots	14	7	-	14	86	79	-	-
Butternut squash	57	29	-	21	29	7	14	43
Cauliflower	57	-	-	7	43	71	-	14
Kale	43	14	14	29	0	29	14	29
Mushroom	43	14	-	14	57	64	-	7
Onion	14	7	-	-	71	93	14	-
Peas	14	0	29	0	29	100	29	-
Spinach	43	0	14	14	29	79	14	-

Participants with COVID-19 history (N = 7)
Participants without COVID-19 history (N = 14)
- participants didn't select any option

The online questionnaire ended with participants stating their most preferred and hated fruits and vegetables. Results for the most preferred fruits show participants with a COVID-19 history exhibiting a clear affinity for mangoes at 36% (Fig 4a). Conversely, those without a COVID-19 history equally preferred oranges and pineapples (29%). Assessment of the most hated fruits yielded insignificant results amongst those who never had COVID-19. In contrast, (Fig 4b) shows that participants with a COVID-19 history demonstrated a shared dislike for Passion fruits (29%). For vegetables, participants previously diagnosed with COVID-19 exhibited a dual preference for cabbage and carrots (21%), while those without Covid history predominantly favoured carrots at 57% (Fig 4c). Bitter gourd (43%) emerged as the most disliked vegetable for participants with a covid history, while garlic (29%) took the unfavourable lead among those without a COVID-19 history (Fig 4d).

A B



C D

Figure 4: Participants' Fruit and vegetable preferences based on COVID-19 history. *Bar chart presenting the percentage distribution of most preferred and hated fruits (A&B) and vegetables (C&D) among participants with and without a COVID-19 history. Participants with COVID-19 history (N = 7). Participants without COVID-19 history (N = 14).*

4. Discussion

The study was carried out to provide insight into the relationship between taste receptor variations and COVID-19 outcomes, aimed at emphasizing the importance of genetic predispositions in shaping individuals' preferences for certain tastes and its implications on immunity against the COVID-19 virus. The main findings of this study showed firstly, a non-significant negative correlation between BMI and COVID-19 symptom severity ($r=-.608$, $p > 0.05$) (Fig 2), secondly, that supertasters had the least COVID symptoms, as opposed to non-tasters with the highest symptom severity (Fig 3). Thirdly, a higher number of participants who previously had COVID-19 preferred sweeter foods compared to those without a COVID-19 history (Tab 4&5). Genotypic categorization of participants was hindered due to qPCR failure, and as such the study was not able to identify SNPs and their impact on physiological responses, and asses the influence of taste receptor genetic variations on COVID-19 symptoms, however, the study relied on phenotypic characterization of participants.

The population for this study was youthful, with a mean age of 24.4 years (Tab 2). Studies have shown that age is a great factor in immunity, as immunity is strongest at a youthful age and progressively weakens with age (Lawton, 2020). The immune system undergoes dynamic changes during life, often stronger in youth allowing for the rapid detection and combating of infectious diseases (Simon et al., 2015). This could explain why the cohort had more participants without a Covid history. Bajaj and his group stated that the elderly population (age>65years) were more significantly impacted by the COVID-19 pandemic, primarily because of genetic factors, comorbidities, and alterations in the immune system, stating that the modifications identified as immunosenscence and inflame-aging, contribute to a weakened immune response against infections and diminished effectiveness of vaccines (Bajaj et al., 2021). In addition, studies have also shown that age also impacts dietary preferences, and not just immunity. (Bawajeeh et al., 2020) in their meta-analysis, reported no clear relationship between taste perception and food choices in adolescents (mean age 10-19.9 years). Several studies that examined taste preferences and dietary habits in adults and younger individuals found that adults who were sensitive to bitter tastes expressed a greater affinity for and consumption of bitter-tasting vegetables compared to the younger cohort with a similar sensitivity. Conversely, when the focus shifted to sweet tastes, younger participants exhibited a stronger preference for sweet foods compared to adults (Bawajeeh et al., 2020).

4.1 Exploring the Relationship between BMI and COVID-19 Symptom Severity

BMI is currently used to define adults' anthropometric height and weight characteristics. It is also commonly used as an indicator of a person's fatness and is widely used as a risk factor for the development or prevalence of several health problems and in making public health policies (Nuttall, 2015). A BMI equal to or exceeding 25 kg/m^2 is classified as overweight, while that equal to or above 30 kg/m^2 is classified as obese (Nagar et al., 2022). The weight and height data provided by participants from the questionnaire was used to compute their BMI using the SPSS system after which a Pearson's correlation was carried out, to determine the relationship between the BMI and COVID-19 symptom severity and this yielded a non-significant negative correlation amongst participants with a history of COVID-19 (Fig 2). Although not statistically significant, the negative correlation suggests that higher BMI may be associated with less severe COVID-19 symptoms. (Nuttall, 2015) observed a higher prevalence of obesity (BMI≥30kg/m^2) in patients with critical COVID-19 conditions than in those with non-critical COVID-19 conditions (implying that higher BMI values meant higher COVID-19 symptom severity), which opposes the findings of this research. Similarly, (Gao et al., 2021) also documented an increased risk of hospital admission, intensive care unit admission, and mortality for every excess BMI (BMI ≥23 kg/m^2). Several other literature agree that higher BMIs ≥30kg/m^2 which are regarded as obese are associated with higher COVID-19 symptom severity and higher chances of ICU admission and death (Lighter et al., 2020) (Simonnet et al., 2020). In a meta-analysis conducted by (Du et al., 2021), researchers looked at 16 observational studies with a combined sample size of 109,881 participants and found that those with obesity (BMI ≥ 30 kg/m^2) had a 2.35-fold increased risk of critical COVID-19 and a 2.68-fold increased risk of COVID-19 in-hospital mortality. However, it is pertinent to note that the range (18.5≥ BMI ≥24.9) is deemed healthy by the WHO and as such higher BMI values within this range could mean healthier participants and hence the negative correlation with covid symptom severity as reported in this research (mean BMI 24.9kg/m^2) and that the sample size of this study was relatively modest with participants' self-reporting of height and weight data which may have introduced inaccuracies due to recall bias. Taste preferences can impact food choices, influencing caloric intake and subsequently higher BMI. Individuals with specific taste receptor variations might exhibit preferences for certain foods, leading to dietary patterns that contribute to being overweight or obese which could ultimately lead to risks of more severe COVID-19 symptoms.

4.2 PTC Sensitivity, Taste Phenotypes and C0VID-19 Severity

The ability to taste PTC is a classic phenotype that varies in human populations and is associated with the capacity to detect other bitter compounds, some of which are toxic, making this phenotype intriguing from a genetic, epidemiological, and evolutionary perspective. (Wooding et al., 2004). Increased sensitivity to PTC has been linked to dietary behaviour that is low in vegetables, especially, bitter-tasting vegetables such as cruciferous vegetables which are high in health-related bioactive compounds (Bawajeeh et al., 2020). Participants were made to taste the PTC strips and provide their taste perception after which they were categorized into the three taster groups following the model as described by (Bartoshuk et al., 2004). These observed taster groups were then correlated against COVID-19 symptom severity for participants with a COVID-19 history, focusing directly on the population of interest. The boxplot analysis revealed a pattern in COVID-19 symptom severity across the taster groups as supertasters exhibited a significantly lower median symptom severity compared to tasters and non-tasters (Fig 3). The interquartile range for supertasters indicates a more consistent, less variable experience of COVID-19 symptoms within this group. This consistency may be attributed to the potential protective role of the supertaster phenotype in mitigating the impact of the virus (Zhao et al., 2022). The overall trend supports the hypothesis that taste sensitivity, as indicated by the supertaster phenotype, correlates with milder COVID-19 symptoms. (Barham et al., 2021) their study also described a positive correlation between Supertasters and milder COVID-19 symptoms in a hospital setting, stating that non-tasters had a much higher chance of testing positive for SARSCoV-2, being hospitalised after infection, and exhibiting symptoms for a longer period. Further research on Barham's results, by (Wickham et al., 2023) with a much younger cohort and questionnaire data (like the one used in this research) also stated that non-tasters were at higher risks of developing COVID-19 than the other taster groups, which is also in agreement with the findings of this study. Whereas these findings contribute to the growing body of evidence supporting a connection between taste receptor genetics and respiratory tract infections, future investigations should explore the potential implications of taste sensitivity on COVID-19 outcomes.

4.3 The Role of Taste Preferences on Immunity

Adequate consumption of essential nutrients within a diverse dietary regimen is imperative for the maintenance and optimal performance of cellular entities, encompassing immune cells (HAVARD, 2022). Food preferences were obtained from participants from the online questionnaire however participants' genotypes were not assessed due to qPCR failure to determine if their genotypes aligned with their preferences. In exploring the dietary preferences of participants, the study examined a comprehensive list of drinks and foods, with a particular focus on bitter tastes. The investigation was based on the hypothesis that taste perception, especially sensitivity to bitter foods, could be linked to enhanced immunity against COVID-19. Participants were surveyed on their likes, dislikes, and indifference toward a range of drinks and foods. Comparative analyses were conducted between those with and without Covid history. Among participants without a COVID-19 history, white wine was the most preferred drink, while vinegar ranked as the least favoured (Tab 3). Notable shifts were observed in participants with a COVID-19 history, favouring green tea and exhibiting a strong aversion to coffee without sugar which has been ascribed to providing antioxidants and maintaining a healthy heart (Moreno, 2023). For food preferences, a higher preference for sweeter foods was evident in the COVID-19 cohort, with bananas, chips and mangoes standing out (Tab 4). Conversely, non-COVID-19 participants showed a pronounced liking for peas and onions. Analysis of participants' dietary preferences unveiled patterns that may have implications for immune function and overall health. The preference for sweeter foods among participants with a history of COVID-19 suggests a potential link between sweet taste perception and the body's response to viral infections as bitter-tasting foods are seen to have innate immune abilities.

The dislike for bitter foods amongst participants with no COVID-19 history suggests a potential role of bitter taste perception in the immune response. Research has shown that bitter compounds, are often associated with health-promoting properties and may influence the immune system's ability to mount a strong defence against infections (Daniela Bertollo, 2018). As stated by (Rezaie et al., 2021), Most nutritious and healthful foods, such as plant-based foods and extracts from various plants, contain naturally bitter-tasting compounds and can activate hosts' immune responses. Isothiocyanates, which come from brassica glycosylates, have physiological effects on the host's immune and metabolic systems. Many studies have shown that these isothiocyanates can reduce inflammation and free radicals by activating the Nrf2 and NF-κB pathways (Zhao et al., 2022). (Fig 4C) shows that none of the participants with COVID-19 history preferred broccoli, which is rich in vitamin C, boosts collagen production and strengthens the immune system. Two of broccoli's components, indole-3-carbinol and diindolylmethane, have immunological effects, regulating the immune response and lowering inflammation levels.

(Fig 5) shows that aside from their role in immunity, cruciferous vegetables contribute to the delay and prevention of various chronic diseases, such as cardiometabolic disorders, neurological disorders, musculoskeletal conditions, and specific types of cancers (Connolly et al., 2021). The dietary choices of participants from this study were not strong enough to conclude probably due to the low number of participants, however, in a cross-sectional study of about 250 COVID-19 participants, Varjagah and his team stated that the risk of severe COVID-19 was lower in patients who consumed more fruits, vegetables, and fibre-rich foods as they also had a reduced risk of higher COVID-19 symptoms, shorter convalescence, and hospitalisation periods (Tadbir Vajargah et al., 2022). A further study on the dietary relationship with COVID-19 symptom severity reported a reduced likelihood of COVID-19 severity and symptoms were associated with greater adherence to the Mediterranean diet, which is rich in olive oil, nuts, seeds, vegetables, fruits, whole grains, low-fat dairy, and low consumption of meats and dairy products (Zargarzadeh et al., 2022). Results from this study due to the small sample size limits conclusive statements on the link between taste perception, food choices and immune responses, however, cruciferous vegetables well known for their bitter taste, and the Mediterranean diet are dietary recommendations for boosting the immune system and maintaining a healthier lifestyle.

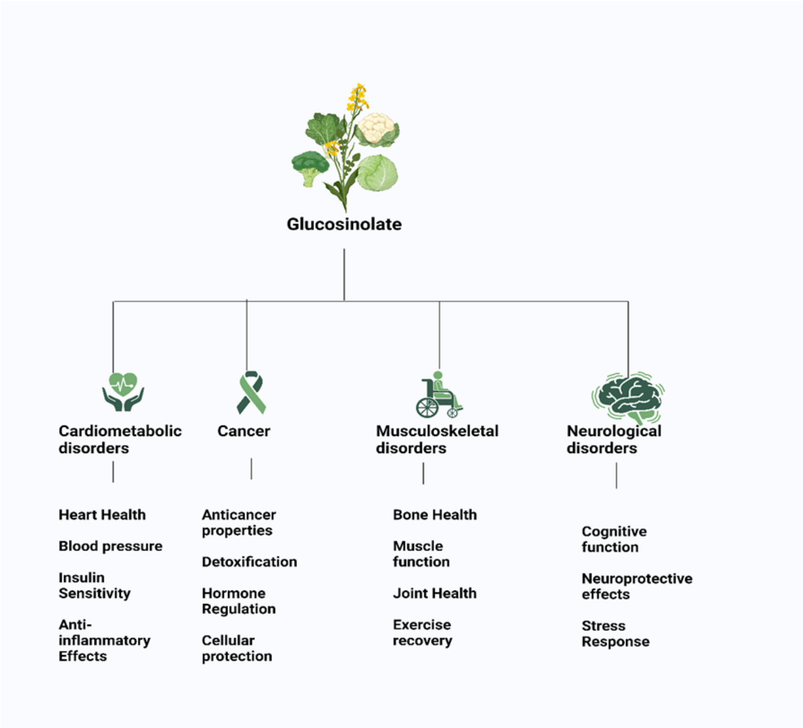


Figure 5: *Health benefits of cruciferous vegetables.*

5. Conclusion

This study investigated the connection between taste receptor variation and COVID-19 outcomes. The non-significant negative correlation between BMI and COVID-19 severity observed in this study challenges previous studies linking higher BMI values to more severe outcomes and prompts further examination of the relationship between body composition and immune responses. The study also highlights the importance of considering factors including age and dietary preferences, when evaluating the influence of genetic variation on susceptibility to COVID-19. The study also adds to the growing literature that supports Super tasters experiencing milder COVID-19 symptoms relying on phenotypic expressions. Dietary preferences of participants showed that participants without a COVID-19 history preferred more bitter foods than those with a history of COVID-19, although no established link was found between food and drink preferences and immune responses due to the small sample size.

Limitations

The most notable limitation of this study was the non-genotyping of participants, which limited the study to phenotypic characterization, preventing the exploration of specific genetic variations and their impact on the COVID-19 virus. The reliance on self-reported height and weight data introduces potential inaccuracies. The sample size was small, impacting the statistical power of the study, and limiting the generalizability of findings across various demographic groups. Additionally, the study's population was youthful affecting the extrapolating of these findings to older populations as age is a critical factor in both immunity and taste perception.

Suggestions for Future Studies

Future research should include genotyping methods such as Whole genome sequencing, which can provide a more comprehensive understanding of the genetic factors influencing taste perception and its overall consequence of immunity against the COVID-19 virus. Researchers should measure the height and weight data of participants. Expanding the sample size, including participants from diverse backgrounds, would allow for the generalizability of the findings.

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Appendix 1

PTC STRIP 1 Please rate how bitter the strip tastes.	10. PTC STRIP 2 Please rate how bitter the strip tastes.	Taster Groups		Percentage
0- Taste nothing	3- Bitter	Super Taster	7	33.33333333
0- Taste nothing	1- Faint taste	Taster	8	38.0952381
0- Taste nothing	0- Taste nothing	Non-taster	6	28.57142857
0- Taste nothing	2- Noticeable bitterness		21	
0- Faint taste	3- Bitter			
0- Taste nothing	2- Noticeable bitterness	Key		
2- Noticeable bitterness	2- Noticeable bitterness	Taste nothing = Non-taster		
0- Taste nothing	3- Bitter	Faint taste & Noticeable bitterness = Taster		
0- Taste nothing	0- Taste nothing	Bitter = Super taster		
0- Taste nothing	2- Noticeable bitterness			
0- Taste nothing	3- Bitter			
0- Taste nothing	0- Taste nothing			
0- Taste nothing	0- Taste nothing			
0- Taste nothing	0- Taste nothing			
0- Taste nothing	2- Noticeable bitterness			
0- Taste nothing	3- Bitter			
0- Taste nothing	1- Faint taste			
0- Taste nothing	3- Bitter			
0- Taste nothing	2- Noticeable bitterness			
0- Taste nothing	0- Taste nothing			
0- Taste nothing	3- Bitter			