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WORD COUNT 2286
TIME SUBMITTED 02-APR-2024 01:02PM
PAPER ID 108005952

Association of MTHFR C677T, MTHFR A1298C polymorphism in relation to patients with autism in Thi-Qar Governorate

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Abstract

Background: Recent data suggests that environmental factors may account for up to 40-50% of the variability in the risk of developing autism spectrum disorder (ASD). In this study, we conducted a comprehensive examination of systematic reviews and meta-analyses that focused on environmental risk factors associated with autism spectrum disorder (ASD). We evaluated every review to determine the quality of evidence and presented a concise summary of potential pathways of environmental risk factors for ASD.
Aim of this study: The purpose of this study was to examine the correlation between MTHFR polymorphism and the heightened susceptibility to autism in children with autism in Thi-Qar.
Material and Method: Blood samples were collected from a cohort of 100 individuals diagnosed with autism, along with 100 healthy individuals serving as a control group. The participants were divided into three groups. The first group, known as the control group, consisted of one hundred healthy people aged between 3 and 14 years. The second group consisted of one hundred autistic patients, ranging in age from 3 to 14 years old.
Results: The findings demonstrated a noteworthy elevation in the gene expression of MTHFR C677T and MTHFR A1298C in all groups of patients, in comparison to the control group.
Conclusion: The study data indicates a higher likelihood of ASD in individuals with the MTHFR C677T CT/CC and MTHFR A1298C AC/CC polymorphisms, suggesting a potential involvement of abnormalities in the folate/methylation cycle in autism.

Keywords: Autism spectrum disorder, Autism, (ASD), Gene, MTHFR C677T, MTHFR A1298C

Introduction

Autism, often known as autism spectrum disorder (ASD), is currently recognized as one of the most prevalent neurodevelopmental disorders [1]. These encompass issues related to communication, social interaction, and conduct. Currently, there remains a significant portion of the population who lack a clear understanding of the concept of ASD. Consequently, ASD is frequently perceived in a negative light, with some individuals even classifying it as an illness. They frequently exhibit aberrant conduct [2][3]. MTHFR is an enzyme that has been linked to various intricate psychiatric mental health disorders. The enzyme converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate and is involved in the conversion of folate and homocysteine, which is linked to DNA methylation [4][5][6]. Multiple variations of the MTHFR gene have been identified [7][8]. Two frequent polymorphisms, C677T and A1298C, have been proven to decrease enzyme activity. The MTHFR C677T mutation is caused by a substitution of cytosine with thymine at position 677 of Exon 4. This substitution leads to the replacement of alanine with valine, resulting in an enzyme that is sensitive to changes in temperature and has decreased activity [9][10][11][12]. For example, the presence of the homozygous C677T (TT) condition is linked to elevated levels of Hcy and reduced levels of folate. The MTHFR A1298C mutation is caused by a substitution of adenine for cytosine at position 1298 of exon 7. This alteration occurs in the substitution of glutamic acid with alanine, leading to a significant decrease in activity in individuals with the homozygous 1298CC disease [13].

Material and Method

Patients

This study was conducted in the Autism Center in Nasiriyah, Thi-Qar Governorate, by the Biochemistry Laboratory in the College of Science. The study took place from December 2022 to June 2023. The study consisted of 200 cases, 100 control subjects, and 100 patients.

This study comprised a total of 100 male and female volunteers, both control and patients with trace elements, who were between the ages of 3 and 14 and had autism spectrum disorder (ASD). They split into two factions as follows:

Control: The study consisted of one hundred (100) participants who were in good health and ranged in age from 3 to 14 years old.

Autistic patients: The study included a total of one hundred (100) patient volunteers aged between three (3) and fourteen (14) years old.

Collection of Blood Samples

Gene sequencing and alignment: The PCR results were subjected to amplification and subsequently sequenced using the Sanger sequencing method using dideoxynucleosides at Microgen Company in South Korea. The sequencing findings were analyzed using bioinformatics

analysis tools, such as Bio edits, after receiving them from the firm. This analysis revealed the polymorphisms of the investigated SNP.

Statistical Analysis

The data of this study was statistically analysis by using SPSS version 26, based in using Chi-square and Odds ratio at p. value < 0.05.

Results

The data presented in Table (1) indicate a statistically significant difference ($p < 0.05$) between the genotypes observed in autism patients and the control group. The greatest genotype observed in both groups was CT, with a prevalence of 85% in autism patients and 1.43% in the control group. Conversely, the lowest genotype observed was TT, with a prevalence of 5% in autism patients and 1.43% in the control group. A non-significant difference was seen within the haplotype, with a p-value of less than 0.05. The control group had the highest allele frequency of C at 51.35%, whereas the autism patients had a frequency of T at 48.65%. The odds ratio analysis revealed that there was no statistically significant difference in the gene frequency between autism patients and the control group.

Table (1): Genotype and allele frequency of MTHFR C677T and MTHFR A1298C gene.

Gene	Genotype	Patients		Control		OR	CI95%	p. value
		No.	%	No.	%			
MTHFR C677T	CC	10	10.0	68	97.14	0.003	0.001-0.013	< 0.001
	CT	85	85.0	1	1.43	5.61	72.5-4335	< 0.001
	TT	5	5.0	1	1.43	5.21	0.59-45.4	0.097
	Allele	Patients		Control		OR	CI95%	p. value
MTHFR C677T	C	95	51.35	69	97.18	0.032	0.010-0.180	< 0.001
	T	90	48.65	2	2.82	31.0	9.22-104.5	< 0.001
Gene	Genotype	Patients		Control		OR	CI95%	p. value
		No.	%	No.	%			
MTHFR A1298C	AA	11	11.0	68	97.14	0.004	0.001-0.014	< 0.001
	AC	85	85.0	2	2.86	183.2	51.2-654.6	< 0.001
	CC	4	4.0	0	0.00	2.04	1.77-2.35	0.043
	Allele	Patients		Control		OR	CI95%	p. value
MTHFR A1298C	A	96	51.89	70	97.22	0.034	0.010-0.113	< 0.001
	C	89	48.11	2	2.78	29.8	8.86-100.4	< 0.001

Discussion

Several studies [14] [15] [16] [1] [17] [18] [19] [20] The findings indicated a substantial correlation between the C677T gene variant and autism spectrum disorder (ASD). ASD, or autism spectrum disorder, is a chronic neurological condition that results in difficulties with social relationships, deficits in communication, and repetitive activities [21]. Research has shown that ASD has a strong hereditary component, with both rare and common genetic variations contributing to the chance of developing the disorder [22]. Consequently, the genetic inclination towards ASD can vary among individuals. The precise etiology of ASD remains unknown, and certain hypotheses, such as the involvement of both rare and common single nucleotide polymorphisms (SNPs), have generated debate [23].

Table (2) presents the findings of the study, which examined the presence of a significant difference at a p-value of less than 0.05. The results indicate that the greatest genotype observed in both autism patients and the control group was AC, with a prevalence of 85% and 54% respectively. On the other hand, the lowest genotype observed was CC, with a prevalence of 4% in autism patients and 0% in the control group. A significant difference was seen within the haplotype, with a p-value of less than 0.05. The control group had the highest allele, C, with a frequency of 97.22%, whereas the autism patients had the highest allele, A, at a frequency of 48.11%. The odds ratio analysis revealed that there was no statistically significant difference in gene frequency between autism patients and the control group.

The primary aim of this study is to examine the correlation between MTHFR polymorphism and the heightened susceptibility to autism in children residing in Thi-Qar. This study is the first genetic investigation in Thi-Qar to examine such a connection. autistic is a complex illness influenced by multiple factors, including environmental, epigenetic, and genetic factors. These factors contribute to the frequency and severity of autistic symptoms [24][25]. Epigenetic pathways exert a significant influence on the manifestation of autism phenotypes. Furthermore, these systems are subject to modulation by drugs and nutrition. A study conducted by Meguid and colleagues found a correlation between the MTHFR 1298 AC/CC SNP and disruptions in the folate/methylation cycle, which in turn increased the risk of autism [26][27].

Conclusion

This data of study supports an increased risk for ASD in association with MTHFR C677T CT/CC, MTHFR A1298C AC/CC polymorphism and hence a role of folate/methylation cycle disturbances is suspected in autism.

Disclosure

None

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