

Association of Methionine Synthase (MTR) A2765G Gene Polymorphism with Homocysteine Levels and Enzyme Activity in Iraqi Patients with Myocardial Infarction

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ABSTRACT

Background and Objective: Myocardial infarction (MI) is a leading cause of morbidity and mortality among cardiovascular disease patients. Elevated plasma total homocysteine (tHcy) is a well-established risk factor for coronary artery disease (CAD), often linked to genetic mutations affecting homocysteine metabolism, including variations in the Methionine Synthase (MTR) gene. The MTR A2765G polymorphism has been implicated in MI pathogenesis due to its impact on methionine synthase enzyme activity, which is crucial for homocysteine metabolism. This study aimed to evaluate the association between MTR A2765G polymorphism, methionine synthase activity, and homocysteine levels in Iraqi patients with MI. **Methods:** This case-control study was conducted between December 2023 and March 2024, involving 116 participants: 58 MI patients (24 females, 34 males; mean age 56.91 ± 9.15) and 58 healthy controls (24 females, 34 males; mean age 56.53 ± 9.02). The MTR A2765G polymorphism was analyzed using the TETRA-ARMS PCR technique. Serum homocysteine and methionine synthase levels were measured using enzyme-linked immunosorbent assay (ELISA). **Results:** The genotype distribution of MTR A2765G significantly differed between MI patients and controls. Among MI patients, the frequencies were 27.6% (GG), 17.2% (AG), and 55.2% (AA), whereas in controls, the distribution was 8.6% (GG), 17.2% (AG), and 74.1% (AA). The G allele was more prevalent in MI patients (36.2%) compared to controls (17.2%). Furthermore, MI patients exhibited significantly higher homocysteine levels and lower methionine synthase activity than controls ($p \leq 0.01$). **Conclusion:** This study demonstrates a strong association between MTR A2765G polymorphism and elevated homocysteine levels in Iraqi MI patients. The presence of the G allele appears to increase MI risk by impairing methionine synthase activity, leading to homocysteine accumulation. These findings highlight the potential role of genetic screening for MTR polymorphisms in cardiovascular disease risk assessment and management.

Keywords: Myocardial Infarction (MI), Methionine Synthase (MTR), Gene Polymorphism, Homocysteine (Hcy), coronary artery disease (CAD).

INTRODUCTION

Myocardial infarction (MI) is a heart attack that occurs when blood supply to a specific area of the heart is reduced or completely blocked, resulting in damage to the heart muscle, its significant variable that contribute to morbidity and mortality in-patient with heart diseases [1, 2]. The risk of experiencing a myocardial infarction increases with advancing age, low physical activity, obesity, Hypertension, genetic variation and elevated cholesterol levels [3]. Homocysteine is a sulfur-containing amino acid that is produced when the essential amino acid methionine undergoes demethylation. Homocysteine can be metabolized by transsulfuration, a process that relies on the enzyme cystathionine β -synthase (CBS) and is dependent on vitamin B6. Alternatively, the enzyme methionine synthase (MTR), which relies on vitamin B12, can transform homocysteine into methionine through the process of re-methylation. The enzyme methylenetetrahydrofolate reductase (MTHFR) is responsible for reducing 5,10-methylenetetrahydrofolate to create 5-methyltetrahydrofolate, which acts as a methyl donor for the latter enzyme [4]. Vitamins B12 and B6 are crucial for controlling the metabolic processes of remethylation and transsulfuration of Hcy[5]. Supplementing with Vitamin B12 and B6 may be beneficial in lowering Hcy levels in high-risk patients with Hhcy [6]. Conversely, a lack of vitamin B6 and vitamin B12 would lead to Hhcy[7]. Elevated homocysteine concentrations are associated with increased risk of atherosclerosis and thrombosis, these elevated may caused by mutations in the genes responsible for the enzymes involved in tHcy

metabolism or to insufficient levels of vitamins necessary for tHcy elimination[8]. The MTR gene exon 21, located on chromosome 1q43, encodes the MTR enzyme, which converts homocysteine into methionine through remethylation and this conversion process requires vitamin B12 as a cofactor [9]. Mutations in the MTR gene can lead to effect to the activity of methionine synthase and therefore increased levels of homocysteine in the serum, which affects folic acid metabolism and can lead to the development of multiple diseases, such as myocardial infarction [10]. The sole known polymorphism in the MTR gene is an A>G transition at nucleotide 2756 (2756A>G), which leads to the substitution of an aspartate (A) residue with a glycine (G) at codon 919 (D919G) , This mutation has been identified as a genetic susceptibility factor for occlusive vascular disorders, such as myocardial infarction[11, 12]. Recently, it was suggested that MTR gene polymorphisms were involved in the pathogenesis of myocardial infarction, through the effect to the activity of methionine synthase, which contributes to homocysteine metabolism[4]. Previous study have suggested that individuals with the MTR GG genotype have reduced fasting homocysteine levels[13]. However, other research has indicated that there is no correlation between this MTR variation and tHcy concentration[14]. In another study conducted to investigate cardiovascular disease, it was shown that the presence of the methionine synthase gene polymorphism did not have a significant impact on plasma homocysteine concentration. However, those with the GG genotype had a four-fold higher likelihood of being part of the

disease cohort[12]. The primary objective of this study to investigate the effect of MTR gene polymorphism on homocysteine level in-patient with myocardial infraction and relationship between genetic variation in MTR and homocysteine metabolism in the context of MI in a sample of the Iraqi population.

Methiodology

Subjects

The study was performed between December 2023 to March 2024. The clinical Biochemistry and Chemistry Department at the University of Al-Qadisiyah, College of Medicine conducted a study on 118 individuals, including 58 patients diagnosed with (MI) from Merjan Hospital and Shaheed Al Mihrab Center. The study involved experiments at the Al-Ameen Center for Research and Advanced Biotechnologies in AL-Najaf Governorate and the Clinical Biochemistry Unit of the Laboratory Division at Al-Mahaweel General Hospital. The mean age of the patients (56.91 ± 9.15). The control group consisted of 58 unrelated healthy volunteers from the general population, with a mean age (56.53 ± 9.02). Explicit consent obtained from all participants, and the local Ethics Committee approved the study's design. Participants asked about familial and individual traits that increase the likelihood of coronary heart disease and their lifestyle choices.

Blood Sample Collecting

Each patient had 5 milliliters (ml) of blood drawn from a vein, and then separated into two test tubes: 2 ml with EDTA for genetic study, and 3 ml with a gel tube for biochemical analysis. The blood samples in gel tubes were centrifuged at 3000-x g for ten minutes to obtain serum. The serum was then stored at -20°C until used [15].

Inclusion and Exclusion Criteria

Inclusion criteria: The patients with MI were diagnosed by the cardiologist.

Exclusion criteria: The patients with renal, thyroid disease, Diabetes Mellitus, congestive heart disease, smoker, and patients who treats with vitamins B6 and B12.

Detection of Plasma Homocysteine Concentrations and the Genotype Rs1805087 Polymorphism

The genotyping of the MTR gene polymorphism performed using the TETRA-ARMS technology and a specific set of primers. While, the ELISA technique was employed to evaluate the serum homocysteine levels of all subjects.

DNA Extraction

RBC lysis is a process that involves obtaining fresh human blood, filling a microcentrifuge tube with 300 μl of blood, and centrifuging at 3000 xg for 10 minutes. The supernatants are removed, and the pellet is treated with 100 μl of RBC Lysis Buffer. The cells are pipetted back into suspension. Cell lysis involves agitating the sample mixture with 200 μl of FABG Buffer and leaving it undisturbed at room temperature for 10 minutes until it becomes transparent. DNA binding is achieved by introducing 200 μl of ethanol and pipetting the sample to facilitate mixing. The FABG column is placed within the collection tube, and the sample is meticulously put into it. The column is then subjected to centrifugation at 18,000 xg for one minute, after which the previous collecting tube is disposed of. The column is then dehydrated and moved to a 1.5-mL microcentrifuge tube, exposed to a pre-heated elution solution consisting of 100% buffer (TE). The column is placed in an incubator set at 37°C for 10 minutes, and the DNA is extracted using centrifugation at the highest speed for one minute at 18,000 xg.

MTR Genotyping: A – Selection of the SNP and the Primer

TETRA-ARMS PCR (tetra amplification-refractory mutation system) was used to determine the genotype of the MTR gene. They designed four primers two forward (Outer, Inner), and two Reverse (Inner, Outer). The Primer set described in Table (1). The SNP being studied in MTR genotyping is referred to as A2756G polymorphism (rs1805087). The amplification of this single nucleotide polymorphism (SNP) was accomplished by employing outer and reverse inner primers. The mutant nucleotide was amplified using Forward Outer (FO) and Reverse Inner (RI) primers, while the wild-type nucleotide was amplified using Forward Inner (FI) and Reverse Outer (RO) primers.

Table 1: The Set of Primers Employed in MTR Genotyping [16].

Gene	Type Primer	Sequence
MTR	Forward Outer	5'-GTGTTATCAGCATTGACCATTACTAC-3'
	Forward Inner	5'-TGGAAGAATATGAAGATAATTAGACATGA-3'
	Reverse Outer	5'-GAAGACCTCTGATTGAACTAGAGA-3'
	Reverse Inner	5'-ACTTACCTTGAGAGACTCATAATTGC-3'

Statistical Analysis

The present study uses the Statistical Package for the Social Sciences (SPSS version 21), Microsoft Excel 2019 to summarize, analyze, and presenting data. Continuous variables were represented by mean $\pm$ SD, and a student t-test was used to a comparison between patients and a control group. The Pearson correlation coefficient (r) was employed to quantify the strength and direction of the correlation among variables. Chi-square testing was used to determine allelic and genotypic frequencies, while odds ratios (OR) were used to evaluate the relationship between genetic patterns and the control group. Kruskal-Wallis and Mann-Whitney tests were used to demonstrate the association between biochemical markers and methionine synthase genotypes. A P-value of ≤ 0.05 indicate significance.

Results

The Result of Biochemical Parameters and Demographic Characteristics

The (mean $\pm$ SD) variances of age in the G1patient group were (56.91 ± 9.15) range (37- 70 Years) and in the G2 control group was (56.53 ± 9.02) range (37 - 69 Years), which are statistically non-significant at ($P > 0.05$). The sex variance among the G1 consisted of 34 males (58.6%) and 24 females (41.4%), while the G2 consisted of 34 males (58.6%) and 24 females (41.4%), which show no statistical differences ($P > 0.05$). As indicated in Table (2). In concerning BMI, the (mean $\pm$ SD) variances of BMI in the G1 group were (28.49 ± 1.16 Kg/m²) and in the G2 group was (27.46 ± 1.34 Kg/m²) which are

statistically highly significant at ($P \leq 0.01$), and the comparison of BMI between G1 and G2 as shown in Figure (1). As shown in Table (2) above, the (mean $\pm$ SD) of Homocysteine level in the G1 group were (10.43 ± 4.63 nmol/ml) and in the G2 group was (6.84 ± 1.50

nmol/mL), and Methionine synthase level in the G1 group were (3.03 ± 0.78 ng/mL) and in the G2 group was (3.64 ± 1.64 ng/mL), which show statistically highly significant difference for both at ($P \leq 0.01$), ($p \leq 0.05$) between G1 and G2. As shown in figure (1), (2) respectively

Table 2: A Comparison of Demographic Characteristics and Biochemical Parameters between Study Groups.

Demographic Characteristics and Biochemical Parameters	G1 No. 58 (Mean $\pm$ SD)	G2 No. 58 (Mean $\pm$ SD)	p
Age (Years)			
Mean $\pm$ SD	56.91 $\pm$ 9.15	56.53 $\pm$ 9.02	0.823 NS
Range	37 - 70 Years	37 - 69 Years	I
Sex			
Male	34 (58.6 %)	34 (58.6 %)	0.982 NS
Female	24 (41.4 %)	24 (41.4 %)	C
BMI (Kg/m ²)			
Mean $\pm$ SD	28.49 $\pm$ 1.16	27.46 $\pm$ 1.34	P = 0.001**
Biochemical Parameters			
Homocysteine(nmol/mL)	10.43 $\pm$ 4.63	6.84 $\pm$ 1.50	P = 0.001**
Methionine Synthase (ng/mL)	3.03 $\pm$ 0.78	3.64 $\pm$ 1.64	P= 0.013*

SD: Standard Deviation, I: Independent T-Test, C: Chi-Square ** Highly Significant ($P \leq 0.01$), * Significant ($P \leq 0.05$), NS: Not Significant, G1: Patient Group, G2: Control Group.

The Diagnostic Efficacy of Serum Homocysteine and Methionine Reductase in Determining Individuals with Myocardial Infarction

Receiver operating characteristic (ROC) curve analysis to find the best cutoff value of serum Homocysteine, Methionine reductase to predict a diagnosis of Myocardial Infarction as shown in Figures (3).

The results of the ROC curve analysis concerning serum Homocysteine, Methionine reductase, as shown in Table (3). The cutoff value of Homocysteine was >7.48 nmol/mL with 89% sensitivity, 72.3 % specificity, and 83.7 % accuracy. The cutoff value of Methionine reductase was >3.66 ng/ml with 93.1% sensitivity, 75.0% specificity, and 88.7% accuracy.

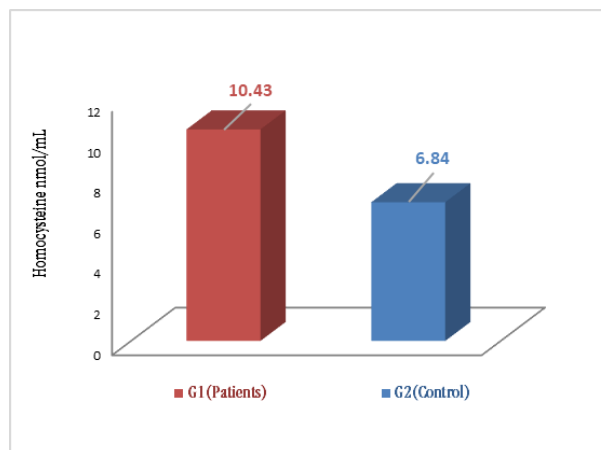


FIGURE 1: Comparison of Homocysteine between G1 and G2 at ($P \leq 0.01$)

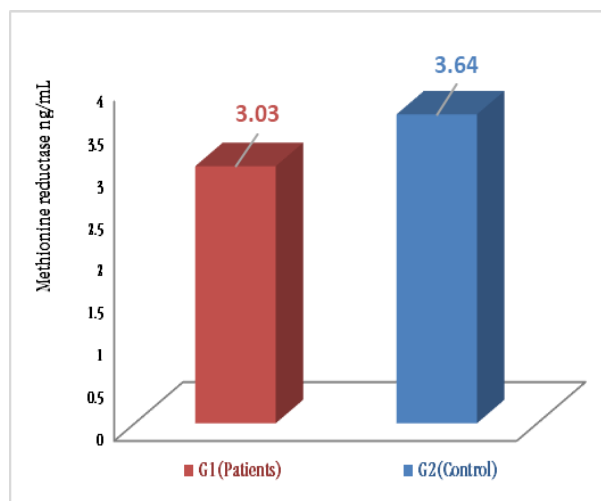
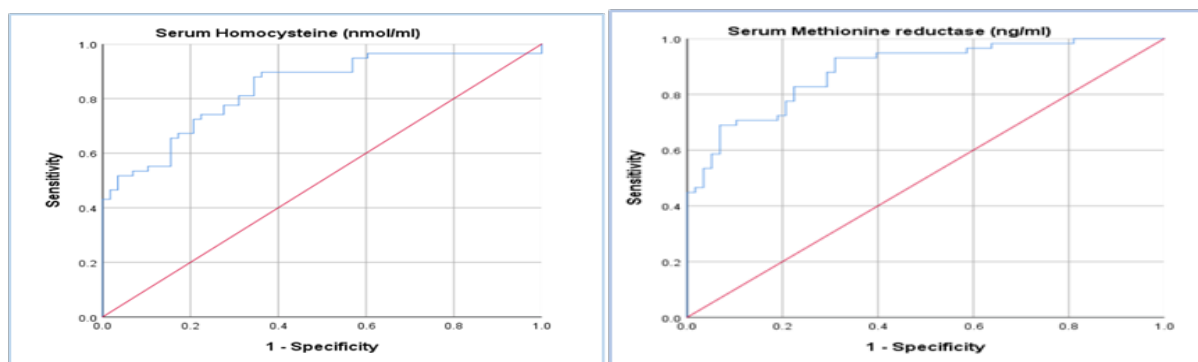


FIGURE 2: Comparison of Methionine Synthase between G1 and G2 at ($P \leq 0.01$).



FIGURES 3: ROC Curve Analysis to Find the Best Cutoff Value of Serum Homocysteine, Methionine Synthase to Predict a Diagnosis of Myocardial Infarction.

TABLE 3: Results of an Analysis of the Serum of Serum Homocysteine, Methionine Synthase Utilizing a Receiver Operating Characteristic (ROC) Curve.

Markers	Characteristic						
	Cutoff	AUC	95 % CI	P-Value	Sensitivity %	Specificity %	Accuracy %
Homocysteine	> 7.48	0.837	0.763 - 0.910	<0.001**	89 %	79.3%	83.7 %
Methionine reductase	> 3.66	0.887	0.829 - 0.945	<0.001**	93.1%	75 %	88.7 %

AUC: Area Under the Curve; **: High Significant at $P \leq 0.001$; CI: Confidence Interval.

Correlation of Serum Homocysteine with Demographic and Biochemical Parameters in Patient Group

As indicated in Table (4), show the correlations of serum Homocysteine to demographic and laboratory characteristics of patients with Myocardial Infarction. Serum Homocysteine was positively correlated to BMI and age. Serum Homocysteine was

negatively correlated to Methionine reductase as shown in figures (4,5 and 6).

Gene Polymorphism: DNA Detection

To verify the presence of a product and give information about how accurate the extraction process was, every sample of DNA that was isolated in electrophoresis as shown in Figure (7).

TABLE 4: Correlations of Serum Homocysteine to Demographic and Laboratory Characteristics of Patients with Myocardial Infarction.

Characteristic	Serum Homocysteine	
	r	P. Value
Age	0.512	0.32 NS
BMI	0.097	0.081 NS
Methionine reductase	- 0.721	0.021*

r: Correlation Coefficient Using Pearson Correlation, **: Highly Significant ($P \leq 0.01$), *: Significant ($P \leq 0.05$), NS: Non-Significant ($P > 0.05$).

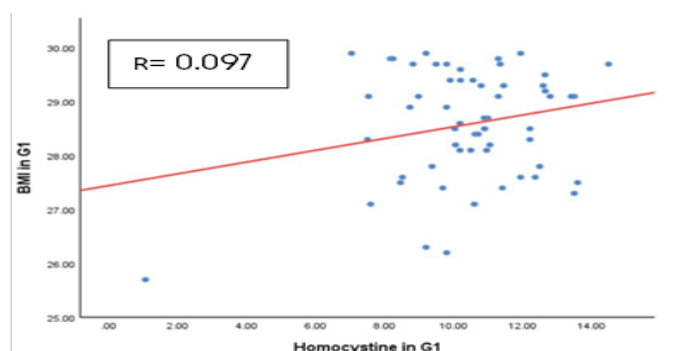


FIGURE 4: Correlation of Homocysteine Concentration with BMI In G1

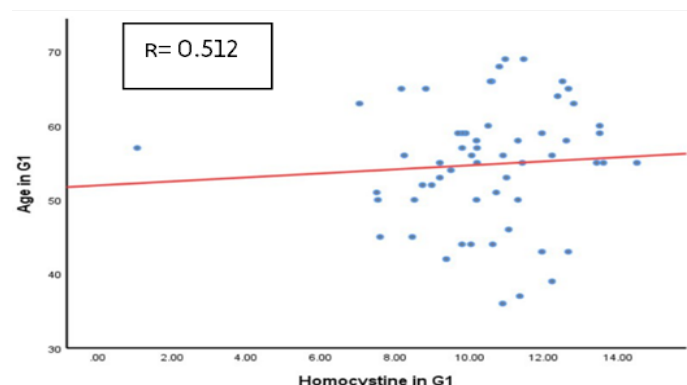


FIGURE 5: Correlation Of Homocysteine Concentration with Age in G1

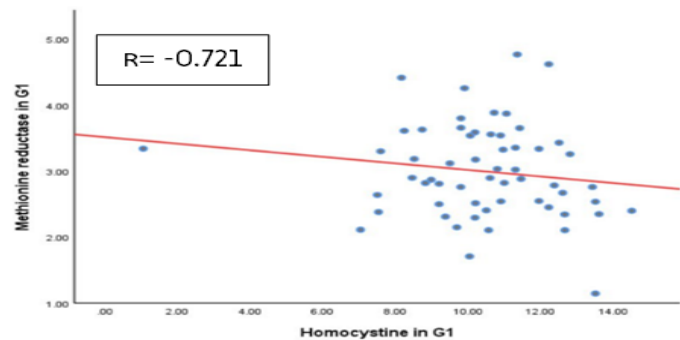


FIGURE 6: Correlation of Homocysteine Concentration with Methionine Synthase in G1.

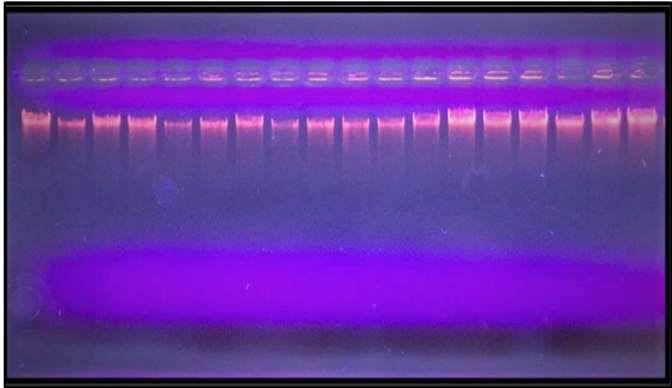


FIGURE 7: Demonstrates the Process of DNA Isolation by Injecting 5 μ l Of Isolated DNA into Each Well During Electrophoresis of the Extracted DNA on a 1.5 Percent Agarose Gel at a Voltage Of 85 V For a Duration Of 60 Minutes.

The Alleles of Methionine Reductase Gene Polymorphism

As shown in Table (5) Using TETRA-ARMS-PCR shown the result in Figure (8), 116 samples were amplified, showing a significant difference in MTR polymorphisms ($P = <0.001$). The G mutant (179 bp) allele was associated with a 0.367 times higher risk of developing

complications of myocardial infarction disease compared to the wild (203 bp) allele.

This finding highlights the importance of understanding the genetic makeup of individuals to prevent complications in patients with myocardial infarction.

Table 5: The Allele Frequency of MTR Gene Polymorphism Among Study Groups.

Allele	G1		G2		OR (95% CI)		P-Value
	N	%	N	%			
A wild (203 bp)	74	63.8%	96	82.8%	0.771 (0.657-0.905)		
G mutant (179 bp)	42	36.2%	20	17.2%	2.10 (1.31 - 3.34)	0.367 (0.199 -0.677)	<0.001**
Total	116	100 %	116	100%			C

***.* High Significance at $P \leq 0.001$; C: Chi-Square Test; OR: Odds Ratio; CI: Confidence Interval; N: Number of Alleles; %: Percentage

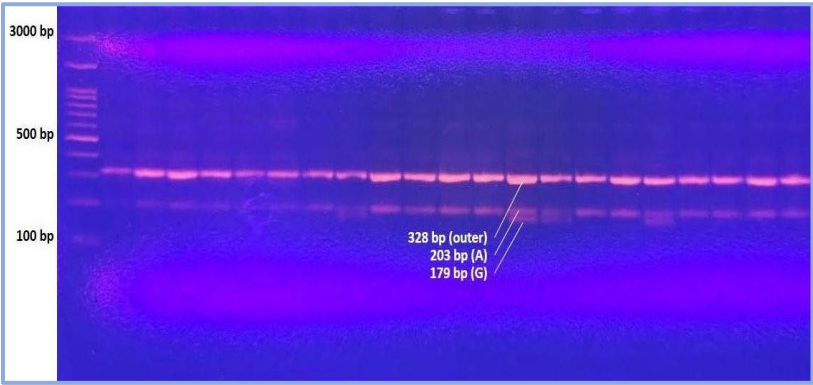


FIGURE 8: The Product of PCR of MTR Gene Polymorphism, the Ladder: 100-1500 Bp. Control 328 Base Pair, Mutant Allele 179 Bp, Wild Allele 203 Base Pair.

The Genotype of MTR Gene Polymorphism

As indicated in (Table 6), 116 samples were applied to gel electrophoresis after being amplified using TETRA-ARM-PCR. Gel

electrophoresis has shown three types of genotypes: homozygous AA at 203 bp, homozygous GG at 179 bp, and heterozygous AG at 203 bp and 179 bp. The frequency of the MTR gene polymorphism genotype differs

significantly between the two study groups at ($P \leq 0.05$), as indicated by Figures (10) and (11).

Association of MTR Genotypes with Results of Some Biochemical Markers in G1 And G2 by using the Kruskal – Wallis Test

As indicated in Table (7), a statistically significant association between methionine synthase genotypes and homocysteine was revealed by the Kruskal-Wallis's test. Specifically, significant associations were observed between MTR genotypes and homocysteine. To determine the association between any two groups of MTR

genotypes, a subsequent statistical analysis, such as the Mann-Whitney test, must be performed. Further insight into the nature of the association between the methionine reductase genotypes and the outcome measures of interest will be provided by this additional analysis. As indicated in Table (8), the Mann-Whitney test revealed a highly significant association between the MTR genotypes (GG and AG) with homocysteine. Similarly, a significant association observed between MTR genotypes (AA and GG) and homocysteine and methionine synthase. A non-significant association was also found between MTR (AA and AG) and homocysteine

Table 6: The Frequency of the MTR Gene Polymorphism Genotype Among the Study Groups.

Genotype	G1		G2		P-Value
	N	%	N	%	
AA	32	55.2 %	43	74.1 %	0.025* C
GG	16	27.6 %	5	8.6 %	
AG	10	17.2 %	10	17.2 %	
Total	58	100 %	58	100 %	

*: Significance at $p \leq 0.001$; C: Chi-Square Test.

Table 7: Relationship of Methionine Synthase Genotypes with Biochemical Marker in G1 And G2.

Marker	Genotypes	N0.	Mean Rank	df	X ²	P-Value
Homocysteine	AA	75	56.67	2	9.651	0.001**
	GG	21	66.29			
	AG	20	57.18			
Methionine Reductase	AA	75	59.42	2	9.420	0.001**
	GG	21	54.07			
	AG	20	59.70			

χ^2 (Kruskal – Wallis Test), df (Different Groups), **: HIGHLY SIGNIFICANT ($P \leq 0.01$), NO (Number of Allele).

Table 8: Comparison of Methionine Synthase Genotypes with Homocysteine.

Marker	Methionine Reductase Genotype	No	Mean Rank	U Test	P- Value
Homocysteine	AA	75	46.72	93.5	0.035*
	GG	21	54.86		
Methionine Reductase	AA	75	49.51	88.5	0.029*
	GG	21	44.88		
Homocysteine	AA	75	47.95	488.5	0.375 NS
	AG	20	48.18		
Methionine Reductase	AA	75	47.91	279	0.180 NS
	AG	20	48.35		
Homocysteine	GG	21	22.43	45	0.005 **
	AG	20	19.50		
Methionine Reductase	GG	21	20.19	68	0.002 **
	AG	20	21.85		

U: Mann–Whitney test; *: Significant when ($P \leq 0.05$); **: Highly Significant ($P \leq 0.01$); NS: Non-Significance ($P > 0.05$).

Discussion

The study found no statistically significant difference in mean age and gender variance between the two study groups ($p > 0.05$). This indicates that the demographic composition related to age and gender was comparable across the patient and control groups. However, there was a significant increase in BMI in the patient group compared to the control group ($p \leq 0.01$). Homocysteine (Hcy) showed a strongly positive correlation with BMI ($r = 0.097$), as presented in Table 4. Increased BMI was also associated with abnormal lipid levels, such as elevated LDL cholesterol and triglycerides, and reduced HDL cholesterol. Dyslipidemia is a significant risk factor for atherosclerosis, which can lead to myocardial infarction (MI) [17]. The result of the current study shown founded that as obesity levels increase in a group of patients with myocardial infarction (MI), the risk of MI also increases. A part of this study highlights the significant between obesity and the risk factors profile in patients with MI [18]. The results indicated that higher obesity levels in MI patients correlated with

increased MI risk. This finding aligns with previous studies demonstrating a positive correlation between BMI and MI. For instance, a recent study found a statistically significant correlation between BMI and MI [19]. while another study in 2021 also noted significant BMI differences between MI patients and control groups [20]. A 2020 study concluded a higher mean BMI in MI patients compared to healthy controls [21]. Overweight and obesity contribute to various chronic diseases, including heart disease, nonalcoholic fatty liver disease, and inflammatory bowel disease [22]. The study showed a significant increase in serum homocysteine levels and a decrease in methionine synthase in MI patients compared to the healthy group ($p \leq 0.01$). Homocysteine had a strongly negative correlation with methionine synthase ($r = -0.721$), as depicted in Table 4 and Figure 6. The elevation of homocysteine may be due to lower methionine synthase activity, encoded by the MTR gene. Elevated homocysteine is linked to an increased risk of atherosclerosis and MI [23]. Recently in 2018, where identified elevated levels of Hcy in patients compared to controls and also the positive correlation between Hcy and MI [24]. As

shown in previous study there are a high correlation between homocysteine (Hcy), a significant marker, and coronary artery disease (CAD) as well as serious cardiovascular complications such as recurrent heart attack, the narrowing of blood vessels after Percutaneous coronary intervention (PCI) and increased mortality[25]. In addition, author studies shows that the individuals under the age of 40 demonstrated a positive correlation between Hcy levels and the incidence of CAD. The findings of the current investigation support this correlation[26, 27]. One of the most deleterious effects of elevated Hcy is the homocysteinylolation of proteins, which are mainly involved in the formation of coronary artery walls. This causes the structure of these arteries to alter, and this is known as the atherogenic effect of Hcy[28]. Homocysteine plays a role in promoting the differentiation of bone cells into osteoblasts and the deposition of calcium in the coronary artery, high levels of homocysteine in calcified human atheroma, indicating that elevated homocysteine contributes to the pathological process of vascular inflammation and damage, ultimately leading to vascular calcification. And, consequently, increases the risk of myocardial infarction (MI) occurrence[29]. The study examined the frequencies of A and G alleles in patients (G1) and controls (G2). The patient group (G1) with the G allele had higher homocysteine levels (Table 5). The genotype frequencies of AA, GG, and AG were also analyzed. The AA genotype was found in 32 individuals in G1 and 43 in G2, while the GG genotype was present in 16 individuals in G1 and 5 in G2. Both groups had 10 individuals with the AG genotype (Table 6). Individuals with the AA genotype of methionine synthase tend to have lower homocysteine levels, while those with the GG genotype have higher levels. This is due to the genotype's effect on methionine synthase activity, which plays a crucial role in converting homocysteine to methionine, leading to hyper homo cysteinemia. The combined genotypes of methionine synthase and homocysteine showed associations with methionine synthase levels, but the associations with homocysteine levels were not significant. The current study has demonstrated that patients with MI had a higher frequency of the G allele in the MTR gene than controls group. The MTR A2765G polymorphism refers to a specific variation in the gene encoding methionine synthase, where aspartate (A) is replaced by glycine (G) at position 2765[30]. Previous study found a significant difference in the MTR (A2756G) gene polymorphisms among patient with MI and control group[31]. According to present study, those with elevated homocysteine levels and the allele G of the MTR gene had been more likely to develop MI[32]. The MTR A2765G polymorphism can influence methionine synthase enzyme activity, potentially altering homocysteine metabolism. Individuals carrying the G allele may have lower enzyme activity compared to those with the AA genotype[30, 33]. Reduced MTR enzyme activity associated with the G allele can result in decreased conversion of homocysteine to methionine, leading to elevated homocysteine levels and hyper homo cysteinemia[34]. High homocysteine levels have been associated with an increased risk of

cardiovascular diseases, including myocardial infarction[35]. we discovered a strong and interdependent association between the G allele of the MTR gene and myocardial infarction (MI) [32]. So, according to the results of current study, the genotypes of methionine synthase can influence to methionine synthase and homocysteine levels. Individuals with the AA genotype of methionine synthase tend to have lower homocysteine levels, while individuals with the GG genotype have higher homocysteine levels. These results above of the present study agreement with the previous study, research has demonstrated a significant positive correlation between the MTR 2756 GG genotype and the risk of coronary artery disease (CAD). The presence of the GG genotype is associated with a four-fold higher susceptibility to coronary heart disease in comparison to the AA genotype.[36]. In contrast, recent study where found no significant correlation[37]. Also another study they found, the MTR (A2756G) gene as a weak predictor for CAD[38].

The current study reports that there was a strong significant correlation between the GG genotype of MTR (A2756G) gene polymorphisms and homocysteine. We suggest the GG genotype of methionine synthase effect to the activity of methionine synthase enzyme due to decrease conversion of homocysteine to methionine, leading to hyper homocystenemia and therefore MI. However, study limitations that my impact the study results was a small sample size and the geographical area specified for sample collection was within Babylon Governorate only. The recommendation to the future researches should aim to utilize a broader and more diverse sample population and employ a variety of techniques to confirm the genetic predisposition to elevated homocysteine levels in individuals with myocardial conditions.

Conclusion

In conclusion, the present study demonstrates that the patients with myocardial infraction have a significant mutation in the MTR gene as compared to the healthy group, these mutation effect to the activity of methionine synthase and therefore a high level of homocysteine concentration, which considered risk factor for myocardial infarction. This suggests that patients with MI have an agentic predisposition to elevated and accumulated homocysteine levels in the blood, which in turn is considered a major risk factor for MI.

Acknowledgment

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