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Association Between TCF7L2 Gene Polymorphism (rs34872471) and Increased Risk of Gestational Diabetes Mellitus in Samples of Iraqi Women

Ahood Abd Ali*, Sanaa Jasim Kadhim

Institute of Genetic Engineering and Biotechnology, University of Baghdad, Baghdad 10071, Iraq

Corresponding Author Email: ahoud.abd2100m@ige.uobaghdad.edu.iq

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ABSTRACT

Gestational diabetes mellitus (GDM) refers to a state of raised blood glucose levels SP during pregnancy especially in the second and third trimesters and is associated with complications in the pregnancy and fetal health. The current work aims at comparing the relationship between physical activity in pregnant women with GDM and the control group. The analysis showed that there were ties between TCF7L2-related SNPs (rs34872471) and other risk alleles, which also have an association with GDM. Samples were further analyzed for genotyping of the variant rs34872471 by using High Resolution Melting technology.The biochemical test of renal functions (Urea, Creatinine) was determined automatically by COBAS C111 analyser System, while blood parameters (WBC, Hb and PLT) was determined automatically by Haematology analyser Sysmex. The results of genotypes and alleles frequencies at TCF7L2 gene (rs34872471) single nucleotide polymorphism (SNP), in Women with GDM and healthy control showed the heterozygous genotype TC and the homozygous mutant genotype CC were found to have a high frequency and were statistically significant (P=0.0006** and P=0.0001**, respectively) in patients compared to the control group. Furthermore, allele frequency had a statistically significant difference between women with and without GDM at p value=0. 0001**. HWE showed how this genetic variant has mutated affecting the Iraqi context. The investigations of Biochemical parameters showed that, the parameters of Urea and Creatinine were measured from blood serum of all samples, it can be concluded by the observation that there was no significant change in the overall average serum Urea and Creatinine concentrations in the women with as well as without GDM and therefore the difference concluded was statistically insignificant. The association between WBC, Hb, and PLT and the risk of GDM was not statistically significant as per our result with p-value (0.2, 0.4 and 0.9) respectively. The result also appear showed that the comparison between the means of (Urea, Creatinine, WBC, Hb, PLT) and the genetic variant rs34872471, there were no significant difference between patient and control for all of them and all allele. When looking at the correlation findings of the blood types and GDM it was seen that there was no correlation and same was the case with the blood types and polymorphism were also not showing significant differences. Overall, the present study establishes that CC and TC genotype of the TCF7L2 gene (rs34872471) gene significantly raise the likelihood of GDM in the Iraqi pregnant women.

1. INTRODUCTION

Gestational diabetes mellitus (GDM) is a form of diabetes on which a woman is diagnosed while pregnant and commonly in the second or third trimester [1]. Diabetes during pregnancy is defined as any degree of glucose intolerance in a woman newly discovered during pregnancy regardless of the level of the high blood sugar. Later on in pregnancy, the degree of insulin resistance increases, less insulin will be produced by the pancreas than is needed to deal with this resistance [2]. The development of gestational diabetes mellitus (GDM) occurs when the pancreatic β-cells are unable to increase their output of insulin to match the decrements in sensitivity to insulin during pregnancy [3].

Since GDM of pregnancy undergoes permanent vessel alteration, it is shown that women with previous history of GDM are at a higher risk for cardiovascular diseases including ischaemic heart disease, myocardial infarction, coronary angioplasty, CABG and other cardiovascular diseases [4]. The above proximal causes of GDM are according to the International Diabetes Federation whereby in the year 2019 it emerges that hyperglycemia affects 16% of live births with 84% of them being caused by GDM thus meaning that GDM affects one out of six births [5].

GDM also affects the future mother's kidney function as being a risk factor that stepping up with repeated GDM cases. Pregnancy itself also affects GFR and creatinine and uric acid levels, and these raises by about 50% during pregnancy [6]. Insulin resistance in GDM belongs to metabolic syndrome; increased levels of uric acid [7].

About 95 genes have been found that could be potential candidates for GDM and one of them is TCF7L2. To do this we tested the rs34872471 variant in the TCF7L2 gene which earlier established to have a strong relation with GDM. This association can perhaps provide some clues as to the development of GDM in later years, particularly in reference to the physiological pathways that concern the β-cell [8].

The TCF7L2 gene is found in humans at a specific locus on the long arm of chromosome number 10 at position 25.3 and generates a HMG box containing transcription factor that plays a role in controlling the blood glucose levels. The purpose of this investigation is to determine whether there is a connection between the TCF7L2 gene polymorphism (rs34872471) and the presence of GDM among the sampled Iraqi women and, secondly [9], to establish the effect of the above genetic variant on selected blood biochemical parameters [10].

2. METHODOLOGY

The research work was carried out in the laboratory of the Institute of Genetic Engineering and Biotechnology for post graduate studies of the University of Baghdad, as well as in private external laboratories, and in the laboratories of Yarmouk Hospital and Iraqi Hereditary Company in Al-Harthya-Baghdad. The study involved blood samples that were collected from November 2022 to February 2023. The total samples collected were 100 samples from all pregnant women (with GDM and without GDM), samples were collected early in the morning after a fasting period of approximately 7-10 hours. It was divided into two groups that included pregnant women aged between 18-46 years.

In this study exclusion criteria that included:

- Any cases of chronic diabetes (type one).
- The cases of diabetes before pregnancy, whether it was type one or type two.
- If the decomposition of the blood sample occurred during or after the withdrawal.
- If the patient had inherited diabetes from one of the parents or both (for the control group).

The total amount of blood withdrawn from each volunteer was 5 milliliters, using a standard single-use syringe. This amount was divided into two parts:

1. The first part, 2 ml, was inoculated immediately into a sterile Vacutainer EDTA and placed at -20℃ for molecular investigations.

2. The second portion, 3 ml, was allocated into a gel tube that was allowed to coagulate for 10 minutes at room temperature ranging from 20 to 25℃ and centrifuged for 10 minutes at 3000 rpm to get the serum. To be more precise, the serum was loaded into groups: 0. In 5 ml Eppendorf tubes and kept at -20℃ for the biochemical tests of renal functions ([UREA], [CREAT]).

Blood samples collected from all pregnant women, whether GDM or non-GDM, had a whole blood sample collected for DNA extraction using the Wizard Genomic DNA Purification Kit (Genomic DNA KIT EE121). Finally, the DNA extracted was utilized in PCR to enhance the copies of the desired fragment of interest. Chosen primers utilized in the study were derived based on the reference sequence available in NCBI database. All the primers used were obtained from Alpha DNA Company and were all in the form of picomolar concentration of lyophillized materials. The sequences of these primers are listed in Table 1.

Table 1. Primer of polymorphism genotyping

TCF7L2 rs34872471 T>C			
Primer	**Sequence (5′→3′ Direction)**	**Product Pb**	**Company Origin**
Forward	TGTGGATTTGCCTGTTCTTG	20	Alpha DNA-Canada
Reverse	CAGACAGACACAAAAGCCCATA	22	

High Resolution Melting (HRM) is a detection technique used on closed-tube PCR products post PCR reaction and deals with the changes in the dsDNA to ssDNA at different temperatures and concentrations. It is even possible to distinguish PCR products by sequence, size, GC content or accordance with the Template-Strand-Protocol up to single base pair differences. The PCR conditions for amplifying single nucleotide polymorphisms (SNPs) fragments were as follows: Compare to the positive control PCR run at 40 cycles PCR at 94℃ for 10 sec., 60℃ for 15 sec., and 72℃ for 20 sec.

The biochemical tests for urea and creatinine were performed on the COBAS C111 analyzer system with fully automated method while blood parameters were also tested by using average and fully automated method E-1900, Sysmex.

SPSS Statistics 26 was used to run the significance tests for the purpose of determining the influence of various factors on study variables. Multiple comparisons of means were again done using one way ANOVA and T-test at the probability value of 0. 05 and 0. 01 and for percentage differences the Chi-square test was used. The odds ratios, along with the 95% confidence intervals were calculated in this study. The creation of figures in the manuscripts was done using the GraphPad Prism 9 software for the figures and WINPEPI and SPSS programs were used for genotyping analysis.

3. RESULTS AND DISCUSSION

One hundred blood samples of the volunteers, which were pregnant women were drawn and grouped thus: fifty pregnant women with GDM, and fifty apparently healthy pregnant individual controls. Biochemical markers renal function tests (Urea, Creatinine), blood parameters (WBC, Hb and PLT) and blood groups ABO tests. The age range in both patient and healthy groups was 17 to 49 years.

3.1 Biochemical parameters

Table 2 shows the results of examining and analyzing kidney function (Urea and Creatinine) in the blood in the samples of this study, the results of which did not indicate the existence of a correlation or statistical significance between the levels of Urea and Creatinine in normal and GDM pregnancies.

Table 2. Comparisons were made between patients and controls based on the kidney functions

Groups		Urea	Creatinine
Patients	Mean	19.5434	0.5196
	Std. Deviation	7.32446	0.18609
	Std. Error of Mean	1.03583	0.02632
Control	Mean	19.2846	0.5404
	Std. Deviation	7.52319	0.23225
	Std. Error of Mean	1.06394	0.03284
p-value		**0.8**	**0.6**

Alyas et al. [11] also noted that creatinine in a kidney profile did not differ significantly between women who later were diagnosed with GDM and those whose condition did not change. This study also indicated that there was no a statistically significant difference in creatinine levels between the two groups and therefore supports the findings of this study.

These results are in contrast with the study done by Mishra et al. [12], on Creatinine activity where the authors considered the result statistically significant at p <0. 01 while the authors noted that urea level was insignificant with a p-value of > 0. 05) among women with GDM, which was also the same with our findings.

In 2006, Güngör et al. [13] also identified in a later research on Turkish women that those with GDM had statistically significantly higher level of creatinine compared to those with no GDM, unlike to our findings. The results also show that the creatinine of GDM population even within the normal range has a common feature of acting as a predictor of the oncoming kidney disease. Sadly, acute kidney injury is often not noticed clinically until it occurs and creatinine levels fluctuate until it approaches 50 mL/min for clearance.

This means that, throughout pregnancy, renal blood flow rises in conjunction with glomerular filtration and consequently, urea and creatinine levels are lowest in the second trimester [11, 12]. While the development of kidney morbidity in GDM patients is less comprehensively documented, it has been observed with an overt diabetes [14].

Azotemia is a condition where nitrogenous end products are built up in the blood that was once synthesized by tissues. Creatinine and Urea are measured to estimate azotemia but neither of them possess significant toxicity attribute to its buildup [15, 16].

The findings of this study are similar to another study that Hadi and Al-hashemi did with urea level in 100 confirmed gestational diabetic pregnant women attending antenatal clinic in Baghdad between 28-33 weeks pregnancy. They established that the urea level decreased remarkably in both groups but was greater in the vials that contained dextrose. But their results on creatinine levels provided contrary argumentation to the research of the current study.

Several studies done internationally by Ntemka et al. [17] on albino rats with Alloxan-induced diabetes revealed that metformin when used at various concentrations greatly reduced P < 0. It was also possible to observe small differences in creatinine and urea levels in all three groups that received metformin three times a day.

A possible explanation for the findings of the current study is a relation between levels of these compounds and the consumption of diabetes treatments known as insulin and metformin. In these studies, majority of the women suffering from GDM were under treatment with metformin.

Table 3 illustrates the findings of the study performed to compare the rate of WBC percentage in women with and without gestational diabetes. The findings of this study suggested there were no statistically significant differences between two groups.

Table 3. Comparison among patients and control groups in WBC

Groups	Mean	Std. Deviation	Std. Error of Mean	p-value
Patients	9.4796	2.55851	0.36183	0.2 NS
Control	10.1372	2.94511	0.41650	

The results agree with those of Aytan et al. [18], whose results were related to WBC similar in patients with GDM, so he described them as non-significant.

A recent study in Iraq, Ali et al. [14] polarised the WBC count, a highly significant increase in GDM and a significant increase in PGDM was seen which was not in parallel with the above findings.

Additionally, several previous studies like Pattanathaiyanon et al. [19]; Fashami et al. [20] and Ye et al. [21] had established that in patients with GDM there were difference in the mean WBC count between the pre-labor and post-labor groups (P>0.05).

Table 4 illustrates comparative analysis in this study of Hb and PLT values in normal and gestational diabetic pregnancies. the results of which did not indicate the existence of a correlation or statistical significance between the levels of hemoglobin at (p-value 0.4) and the levels of platelets at (p-value 0.9) in the study samples.

Table 4. Comparison of patients with other control groups in terms of their Hb and platelet concentrations

Groups		Hb	Plate
Patients	Mean	11.3120	221.6400
	Std. Deviation	1.17415	65.22012
	Std. Error of Mean	0.16605	9.22352
Control	Mean	11.4800	221.2400
	Std. Deviation	1.13623	51.72516
	Std. Error of Mean	0.16069	7.31504
	p-value	0.4	0.9

These results were parallel to the findings from the study done by Aytan et al. [18] and Hassan et al. [22]. These studies also found that WBC counts of every type including immature Granulocytes or IGR and PLT indices including PMI, NPR and LPR were comparable among GDM patients. Data analysis on the differences of the blood parameters showed insignificant variance between the two groups (with and without GDM) in the mean PLT of 24.

One of the reasons why this study had higher levels of platelet decrease and a number of other studies had comparatively lower levels could be due to the timing of these studies; while a number of those studies were

conducted in the first three months, our study had a higher number of cases in the second and the third trimesters where platelets are known to reduce.

Apart from their anticoagulant and procoagulant activities, there is growing evidence from experimental and clinical studies showing that platelets participate in paracrine communication, inflammation, and immunization processes [23].

3.2 Blood groups

This examination in Table 5 demonstrates the conclusion where no marked distinctions can be found when it comes to the correlation between the various blood groups and the women with GDM as opposed to pregnant women from the control samples.

Table 5. Differences in the distribution of patients and control groups on the basis of blood groups

Count		Groups		Total
		Patients	Control	
ABO	A-	2	2	4
	A+	24	15	39
	AB+	1	3	4
	B-	1	1	2
	B+	9	14	23
	O-	1	3	4
	O+	12	12	24
Total		50	50	100

This finding is similar to those reported [24-26]. However, the evidence on this is contradictory. While many previous studies do not agree with the results of this study, the findings varied among researchers.

For example, Rom et al. [27] compared pregnant women with gestational diabetes with pregnant women without gestational diabetes and reflected that the risk of developing gestational diabetics is independent of blood type O. In contrast, Zhang et al. [28] found the frequency distribution of blood types comparing two groups was insignificant, again mirrors the present study.

In another study by Huidobro et al. [29] conducted on Malaysian women reported an incidence of GDM of 11%, 10.8%, 10.6%, and 8%. From the image above, we are realized that percentage for a blood type A is 8% while that of blood type B is 8%, blood type O is 8%, and that of blood type AB is 8%. As for blood type, statistically significant differences were noted in the prevalence of gestational diabetes depending on the basically blood group, specifically, AB blood group with decreased risk of gestational diabetes compared to other blood group, P=0.038.

Similarly, Karagoz et al. [30] in their study on a group of Chinese pregnant women provide support to the findings [31]. They were given information that revealed blood type AB is associated with a decreased risk of gestational diabetes than women with A, B and O blood types because the latter sample experienced relatively high incidence rates of gestational diabetes in the study.

However, a study made on 5,424 Japanese pregnant women using case control study showed that group O, A and B were having lower risk on GDM as compared to group A mothers whose results was in contrast to a study done [32-34]. have also estimated the associations between GDM and blood groups, although a greater risk of GDM in the patients with blood group AB versus control was identified. Furthermore, contrary to previous findings, the MM-ELISA results established that patients with GDM and blood group O had a raised risk of developing DM.

Although the World Health Organization has recommended comprehensive screening for pregnant women, some countries still do not have the financial and human resources necessary to implement this procedure. Thus, knowledge of new risk factors or protective factors allows improving diagnosis in those countries that rely on specific criteria in research [35].

Besides immunohematology, a growing body of evidence has connected it with T2DM, making blood group ABO a suitable candidate for this study. However, literature review studies on this relationship have yielded mixed results [36].

3.3 Molecular study

3.3.1 Distribution genotype and allele frequency at TCF7L2 gene rs34872471 T>C SNPs

Many researchers have proven in their studies that DNA sequence variations in genomes are primarily and most frequently caused by single nucleotide polymorphisms (SNPs) [37]. Recent studies have highlighted the significance of genetic variants having an impact on epigenetic controls in maintaining cellular [38].

Likewise, the genetic polymorphism (rs34872471) shows the three genotypes which are: Homozygous TT as a wild type, CC as a Homozygous mutant and Heterozygous mutant TC genotype. The frequency of all genotypes analyzed between women who had GDM associated with those who served as a normal pregnant.

Table 6 demonstrates the genotypes and allele frequencies of the SNP candidate rs34872471 for the two studied groups of women who experienced gestational and those who did not, as the genotype TT is Homozygous genotype (Wild) as a reference was found in patient women and in healthy control [8, 35], the Heterozygous genotype TC (mutant) was found as a highly frequency and statistically significant at (P=0.0006**) in patient in comparison to control 13 and 7, respectively. Moreover, the Heterozygous genotype mutant CC was found high significant at (P=0.0001**) in patient 29 while in control was 8. In addition, the individual and the combined groups of women with and without GDM in the tested allele frequency groups at (P=0.001**) for both alleles T and C.

The odds ratio for the T and C alleles was calculated with TT genotype (Wild)(OR 1.00) serving as the basis for comparison. The significant odds ratio for the Heterozygous genotype(mutant) TC was (8.1), while the odds ratio for the Heterozygous genotype CC was (15.8). In addition, the odds ratio for the allele frequencies T and C was (1.00 and 8.1), respectively.

The results in Table 6 were consistent with those reported by Ding et al. [37], who stated that the genetic variant rs34872471 has a strong relationship with gestational diabetes.

Also, Wei et al. [36] reported in their study that both Ras polymorphisms of the T gene are associated with an increased risk of gestational diabetes, which is consistent with the results of this study.

Table 7 demonstrates the HWE of this genetic variant rs34872471 in this population, indicative of the rate of effect of this polymorphism in the study area, was evaluated and

was statistically highly significant when comparing between the GDM group and the non-GDM groups, that is, this polymorphism had an influence on the population of Iraq.

Cheung and Lafayette [39] stated that polymorphism rs34872471 of the TCF7L2 gene is associated with diabetes in general and GDM in particular, is located in the intronic region of the TCF7L2 gene, and they added that rs34872471 had a statistically significant association with GDM at (P=0.02 and OR=1.14), and this is consistent with the results of this study.

Table 8 appears that the relationship between the kidney function parameters (Urea and Creatinine), and the genetic variant (rs34872471), the differences were non-significant for both of them with all alleles for patients and controls, at (P=0.5 and 0.4) for the parameter Urea, respectively, and at (P=0.9 and 0.9) for the parameter Creatinine, respectively.

As our knowledge this study was the first one which linked between rs34872471 SNP of TCF7L2 gene and Kidney functions in GDM pregnant women.

In particular, high risk of development of T2D is marked in mothers with GD after pregnancy [40]. TCF7L2 is one of the most significant genetic associations found and T2D or other related diseases, as it has been proven to replicate itself in different populations with varying genetic structures [41]. Gestational diabetes mellitus is a metabolic disorder that resembles T2D in affected women, with a condition that is marked by increased insulin resistance and impaired insulin secretion. Since the pathophysiology of both T2D and GDM has a lot of similarities, there is a great deal of curiosity in identifying out markers that could lead to the identification of a likely common root cause of both ailments.

Table 6. T/C genotype and allele frequency comparison between the patient group and the control group for TCF7L2 gene SNP rs34872471

Genotype rs34872471 T/C	Patient Group NO.=50	Control Group NO.=50	p-value	OR	CI 95%
TT	8 (16%)	35 (70%)	--	1.00	(Reference)
TC	13 (26%)	7 (14%)	0.0006**	8.1	2.4531 to 26.9115
CC	29 (58%)	8 (16%)	0.0001**	15.8	5.2969 to 47.4846
Total	50 (100%)	50 (100%)	--	--	--
		Allele Frequency			
T	0.29 (29)	0.77 (77)	--	1.00	(Reference)
C	0.71 (71)	0.23 (23)	0.0001**	8.1	4.3426 to 15.4701

Table 7. T privileging number and proportion frequencies of alleles as well as HWE of TCF7L2 gene (rs34872471 T/C) genotypes between control group and patients

	Patient Group		Control Group	
	Observed	Expected	Observed	Expected
Wild TT	8	4.205	35	29.645
Hetero TC	13	20.590	7	17.710
Mutant CC	29	25.205	8	2.645
Total	50	50	50	50
p-value	**0.009****		**0.001****	

Table 8. Relationship between TCF7L2 gene polymorphisms (rs34872471 T>C) and kidney functions

Groups	rs34872471 T/C		Urea	Creatinine
Patients	Wild TT	Mean	18.0187	0.5113
		Std. Deviation	6.64806	0.24839
		Std. Error of Mean	2.35044	0.08782
	Hetero TC	Mean	18.3915	0.5269
		Std. Deviation	7.98106	0.19379
		Std. Error of Mean	2.21355	0.05375
	Mutant CC	Mean	20.4803	0.5186
		Std. Deviation	7.30384	0.17039
		Std. Error of Mean	1.35629	0.03164
	p-value		0.5	0.9
Control	Wild TT	Mean	18.3986	0.5400
		Std. Deviation	7.67912	0.23070
		Std. Error of Mean	1.29801	0.03900
	Hetero TC	Mean	21.4643	0.5586
		Std. Deviation	8.31137	0.24093
		Std. Error of Mean	3.14140	0.09106
	Mutant CC	Mean	21.2538	0.5263
		Std. Deviation	6.11968	0.26219
		Std. Error of Mean	2.16364	0.09270
	p-value		0.4	0.9

Table 9. Relationship between TCF7L2 gene polymorphisms (rs34872471 T>C) and blood parameters

Groups	rs34872471 T/C		WBC	Hb	Plate
Patients	Wild TT	Mean	9.5250	11.5500	253.5000
		Std. Deviation	1.38431	1.14268	70.22413
		Std. Error of Mean	.48943	.40400	24.82798
	Hetero TC	Mean	9.4615	11.4846	220.8462
		Std. Deviation	2.76693	1.76911	50.85739
		Std. Error of Mean	.76741	.49066	14.10530
	Mutant CC	Mean	9.4752	11.1690	213.2069
		Std. Deviation	2.77390	.83285	68.83748
		Std. Error of Mean	.51510	.15466	12.78280
	p-value		0.9	0.6	0.3
Control	Wild TT	Mean	9.8509	11.4000	225.1429
		Std. Deviation	2.65403	1.25347	52.49658
		Std. Error of Mean	.44861	.21187	8.87354
	Hetero TC	Mean	10.6071	11.9429	229.2857
		Std. Deviation	3.79159	.93960	49.17558
		Std. Error of Mean	1.43309	.35514	18.58662
	Mutant CC	Mean	10.9788	11.4250	197.1250
		Std. Deviation	3.56932	.63189	49.64283
		Std. Error of Mean	1.26195	.22341	17.55139
	p-value		0.5	0.5	0.3

Table 10. Relationship between TCF7L2 gene polymorphisms (rs34872471 T>C) and blood groups

Groups			rs34872471 T/C			Total
			Wild TT	Hetero TC	Mutant CC	
Patients	ABO	A-	1	0	1	2
		A+	2	7	15	24
		AB+	0	1	0	1
		B-	0	1	0	1
		B+	4	1	4	9
		O-	0	0	1	1
		O+	1	3	8	12
	Total		8	13	29	50
Control	ABO	A-	2	0	0	2
		A+	11	1	3	15
		AB+	2	1	0	3
		B-	1	0	0	1
		B+	9	3	2	14
		O-	3	0	0	3
		O+	7	2	3	12
	Total		35	7	8	50

Moreover, women with GDM also have an inflammatory state, in addition to the previously mentioned insulin resistance, may impact the gene expression of the placenta, therefore, programming the fetus. These abnormalities, if sustained throughout life as consistently observed in this model, lead later on to develop several metabolic diseases including glucose intolerance, metabolic syndrome and conditions related to above factors [42]. The existence of maternal diabetes mellitus is also linked to the increased likelihood of macrosomia in offspring because of insulin insensitivity and elevated intrauterine glucose concentrations. It has also been noted that, an increased fetal birth weight came along with higher second and third trimester postprandial glucose values [43].

GDM also leads the causing of a dyslipidemic state which is in line with insulin resistance [44]. Further, decreased levels of serotonin and higher level of triglyceride were observed in the GDM group (P<0.001). We found that compared to the normal group, total protein, albumin, creatinine, urea, and uric acid were significantly different between the groups (P<0.001), however, they did not show an abnormal distribution within groups; Furthermore, they did not have any apparent clinical manifestation of kidney disease, or other diseases. Kidney related issues undergo a change during pregnancy and alters almost all the physiological processes. Nonpregnant renal plasma flow rises by 50% while the filtration rate rises by 40%, hence, GFR decreases, serum creatinine, urea and uric acid levels come down [45, 46]. Slightly elevated urinary albumin excretion rates, and early enhancement of GFR have also been observed in patients who have recently developed diabetes themselves [47, 48].

In Table 9, the value of (P=0.9, 0.6 and 0.3) for the parameters WBC, Hb and PLT for patients and (P=0.5, 0.3 and 0.3) for controls to measure blood parameters in the mother's body also revealed that none of these genotypes were activating any conceivable differences between the groups. in this rs34872471 multiple genetic form [49].

As our knowledge this study was the first one which linked between rs34872471 SNP of TCF7L2 gene and blood parameters in GDM pregnant women [50].

Therefore, the lack of association between the genetic variant rs34872471 in the TCF7L2 gene and the outcomes of interest could be used to negate or at least significantly tone down the findings presented in Table 10, it can be noted that there is an increase in type (A+) for the three genotypes (TT,

TC and CC), especially the homozygous mutation for the risk allele C, which amounted to 15% in the group of patients on The opposite of control was 0, followed by type (O+), which had a lower risk of 8% in patients, and 3 in control, for the S allele compared to the rest of the other types of types, which seemed to have no clear effect [51].

4. CONCLUSION

Several epidemiologic and genetic investigations in regard to the relation between ABO blood and T2DM A, as to the best of our knowledge, none of the current studies has identified a connection between the genetic variant rs34872471 of the TCF7L2 gene and blood groups among GDM pregnant women.

These genetic variant (rs34872471) do not significantly influence the vital measures of kidney function (Urea and Creatinine) and blood parameters WBC, Hb, and PLT, blood groups ABO, whereas the C allele of the SNP (rs34872471) of TCF7L2 could imply an allusion for GDM progression, and on the other hand TT could be considered protecting genotype among selected Iraqi women.

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