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Polymorphism of Human Insulin Receptor INSR Gene Rs1366600 in Iraqi Patients with Type2 Diabetes Mellitus

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KEYWORDS

investigate, polymorphisms, polymorphisms

ABSTRACT:

The aim of this study was to investigate the association of polymorphisms of human insulin receptor gene INSR rs1366600 to the susceptibility of type2 diabetes mellitus in diabetic patients from Wasit province using TaqMan SNP genotyping assay. A total of 80 participants (45 confirmed patients with type2DM and 35 healthy individuals as controls) were selected by using a convenient sampling method. The results of the current study displayed that in both in patients and control groups, the distribution frequencies of the genotypes and alleles of human insulin receptor gene rs1366600 A/G were not consistent with Hardy Weinberg equilibrium P<0.05. G allele is a major one in the studied groups. This allele is common in T2DM patients (65.56%) and controls (91.43%) with a highly significant difference, p-value =0.00012. The main genotype is GG in the patients and controls Groups. Notably, a significantly higher frequency of the homozygous AA genotype and heterozygous AG genotype was observed when T2DM patients were compared with controls 26.60% and15.62% respectively in patients vs. (2.85%) and(11.43%) in controls 3for each genotype respectively, p=0.0095. Moreover, frequency of homozygous GG genotype was lower when compared T2DM patients (57.78%) and healthy controls (85.72%) at tested position. These results suggest that the G allele might be a protective against the disease whereas the A allele may be considered as a risk factor in the disease. The association analysis revealed that the homozygous GG genotype reduces significantly the likelihood of contracting T2DM with OR= 0.2281 (CI95% [0.0747 to 0.6965]) p = 0.0095. The AA genotype increases the association significantly with T2DM with OR=12.3636 (CI95% [1.5208 to 100.5106]) ,p = 0.0187. The heterozygous genotype AG increases also the association with T2DM with OR=1.4276(CI95% [0.3826 to 5.3277]),p = 0.5962. The subgroup analysis displayed that the T2DM risk of females with 1366600A/G AA genotype was 2.6471 times higher than that in controls OR= 2.6471 (CI 95% [0.2481 to 28.2409]),p= 0.4203,. GG genotype decreases the probability of contracting the disease with OR = 0.6190 (CI 95% [0.1441 to 2.6594]) p = 0.5190. AG genotype increases slightly the association with T2DM with OR= 1.11 (CI95% [0.2047 to 5.7336], P = 0.9250. The polymorphism of INSR rs1366600 of the AA genotype increases significantly T2DM risk among the male patients OR= 22.4545 (CI95% [1.2129 to 415.6955]), p = 0.0367. The heterozygous AG genotype also increases the association with the disease OR= 2.4545 (CI95% [0.2347 to 25.6699]) ,p = 0.4534. While, the homozygous GG genotype decreases significantly the association with the disease OR= 0.0602 (CI95% [0.0069 to 0.5225]), p= 0.0108. In conclusion, human insulin receptor gene rs1366600 has possible roles in type2 diabetes mellitus susceptibility.

Introduction

Type 2 diabetes mellitus (T2DM) is an expanding global health problem closely linked to the epidemic of obesity (De Fronzo *etal*.,2015). This problem is considered a severe public health problem in terms of human life and average life expectancy (Khan *etal*.,2020). In recent years, there has been an incidence increase, affecting individuals of all ages. The global burden of T2DM on people 20–79 years old is projected to increase to 629 million in 2045 compared to 425 million in 2017 (Al-Rifai *etal*.,2019). The breakthrough discovery of a new family of naturally endogenous, small (~22 nucleotides), microRNAs that are

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small, conserved non-coding RNA molecules which are involved in most cellular processes through interaction with 3'-UTR region of the genes.(Ameres and Zamore,2013). MiRNAs regulate RNAs and gene expression in various common diseases such as T2DM (Kong *etal*.,2011) .MiRNAs seem to play a role in the development of pancreatic islets and differentiation of insulinproducing cells (Poy *etal*.,2007) . Single nucleotide polymorphisms (SNP) are variations in single nucleotides of genomic DNA sequence, which have modified potentials on gene functions (Shen *etal*.,2013). SNPs affect the miRNA binding efficiency, giving rise to increased or decreased miRNA regulation (Ghaedi *etal*.,2015). Single-nucleotide polymorphisms that reside in the microRNA target site can affect the binding of miRNA to mRNA, which can either create illegitimate-binding sites or abolish existing-binding sites(Chen *etal*.,2008). Recent studies have indicated that polymorphisms in miRNA target sites can affect gene and protein expression and lead to influence the risk of certain human diseases, including Tourette's syndrome and cancers(Abelson *etal*.,2005:Chin *etal*.,2008). Limited data are available that has investigated the association between gene polymorphisms in miRNA-binding sites and susceptibility to type2 diabetes mellitus especially *human insulin receptor* gene INSR rs1366600 .

The present study was designed to analyze the polymorphism of *INSR* rs1366600, and to determine whether there is an association between this polymorphism and the type2 diabetes mellitus phenotype in an Iraqi population from Wasit province.

Materials and Methods

This is a case –control study, The participants included 45 confirmed type2 diabetes mellitus patient (25males and 20 females) their age 40–70 years (mean ± standard deviation: 51.92± 51.50 years, median= 51 years). The control group comprised of 35 healthy individuals (19males and 16 females), their age 40-70 years (mean ± standard deviation: 51.52 ± 47.18 years, median=48years). Data collection encompassed a range of factors, including demographic details, medical history, and sample collection date, gathered from participants who met global diagnostic criteria. Samples were collected from Alzahraa Teaching Hospital in Kut, Iraq. For blood sample collection, 3 ml of blood was obtained via vein puncture from each participant, with the collected blood then transferred to sterile ethylenediaminetetraacetic acid –k3 (EDTA) tubes, labelled, and stored at -20°C for subsequent DNA extraction and genotyping.

Genomic DNA Extraction:

Genomic DNA was extracted from whole blood utilizing the Quick-DNA™ Blood MiniPrep kit (Zymo, USA) Catalogue Nos. D3024 & D3025. The quality of the extracted genomic DNA was assessed via Nanodrop, measuring the A260/A280 absorbance ratio within the range of 1.8 to 2.0, indicative of high quality.

SNPs Genotyping:

The TaqMan custom SNP genotyping assay from Thermo Fisher Scientific was utilized for genotyping the SNP rs1366600 in the human insulin receptor (INSR) gene. Real-time PCR was employed for the allele-specific discriminating approach. The reference and alternative alleles for rs1366600 were referred to from NCBI.

Statistical Analysis:

The data analysis was carried out using SPSS 21.0 software. The significance level (P-value) was categorized as follows: Sig. denoting Significant ($P<0.05$), and NS representing non-Significant. Analysis of variance (ANOVA) was employed to assess group differences.

Results

Forty-five Patients with type2DM (25males and 20 females) and 35 healthy individuals (19 males and 16 females)) were genotyped for of diabetes mellitus rs1366600 gene polymorphism .In both in patients and control groups, the distribution frequencies of the genotypes and alleles of *human insulin receptor gene* rs1366600 A/G were not consistent with Hardy Weinberg equilibrium $P<0.05$ The Chi-square test found a statistically significant difference of *insulin receptor gene* rs1366600 genotypes between two groups ($P <0.00953$).. The allele and genotype frequencies of rs1366600 gene polymorphisms were used to estimate the odds ratio (OR), confidence intervals (95% CIs), χ 2, and p-value. The distribution of genotypes and allele frequencies of *1366600 INSR* in T2DM patients is shown in Table (1). G allele is a major one in the studied groups. This allele is common in T2DM patients (65.56%) and controls (91.43%) with a highly significant difference, P-value =0.00012. The main genotype is GG in the patients and controls Groups. Notably, a significantly higher frequency of the homozygous AA genotype and heterozygous AG genotype was observed when T2DM patients were compared with control 26.60% and15.62% respectively in patients vs. 2.85% and11.43% in controls 3for each

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genotype respectively,P=0.0095. Moreover, frequency of homozygous GG genotype was lower compared between T2DM patients and healthy controls at tested position. The lower frequency in patient group (57.78%)compared to control group (85.72%).These results suggest that the G allele might be a protective against the disease whereas the A allele may be considered as a risk factor in the disease.

Table (1): Distribution of genotypes and allele frequency *human insulin receptor gene* of rs1366600 A/G in T2DM patients and controls

Groups	Genotype (%)			Allele frequency (%)	
	GG	AG	AA	G	A
Control	30(85.72)	4(11.43)	1(2.85)	(%91.43)64	(%8.57) 6
Patients	26(57.78)	7(15.62)	12(26.60)	(%65.56)59	(%34.44)31
Chi square	9.307			14.827	
***P*-value**	0.00953			0.00012	
Significance	**Significance ***			**Significance ***	

*P< 0.05

Susceptibility analysis of *human insulin receptor gene* rs1366600 gene A/G polymorphism with T2DM

Table (2) shows the association of each genotype of *insulin receptor gene* rs1366600 A/G with susceptibility toT2DM. The homozygous GG genotype reduces significantly the likelihood of contracting T2DM and controls with OR= 0.2281 (CI95% [0.0747 to 0.6965]) p-value = 0.0095.The AA genotype increases the association significantly with T2DM with OR=12.3636 (CI95% [1.5208 to 100.5106]) ,P = 0.0187. The heterozygous genotype AG increases also the association with T2DM with OR=1.4276(CI95% [0.3826 to 5.3277]),P = 0.5962.

Table (2): Odds ratio of human insulin receptor gene rs136600 A/G in T2DM patients and controls.

Genotypes	Control no.(%)	Patients no.(%)	OR	OR95%CI	p-value	Significance
GG	30(85.72)	26(57.78)	0.2281	0.0747 to 0.6965	0.0095	Sig. **
AG	4(11.43)	7(15.62)	1.4276	0.3826 to 5.3277	0.5962	Ns.
AA	1(2.85)	12(26.60)	12.3636	1.5208 to 100.5106	0.0187	Sig.*

*P< 0.05,ns: non-significant P>0.05

**P< 0.01

The odds ratio among females of human insulin receptor gene rs 1366600 A/G gene in studied groups

Association analysis showed that the T2DM risk of females with 1366600A/G AA genotype was 2.6471 times higher than that in controls OR= 2.6471 (CI 95% [0.2481 to 28.2409]),p= 0.4203, table (3) . GG genotype decreases the probability of contracting the disease with OR = 0.6190 (CI 95% [0.1441 to 2.6594]) P = 0.5190.AG genotype increases slightly the association with T2DM with OR= 1.11 (CI95% [0.2047 to 5.7336], P = 0.9250.

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Table (3): Odds ratio of human insulin receptor gene rs1366600 A/G among females T2DM patients and controls.

Genotypes	Control	Patients	OR	OR95%CI	P value	Significance
GG	12	13	0.6190	0.1441 to 2.6594	0.5190	Ns.
AG	3	4	1.11	0.2047 to 5.7336	0.9250	Ns.
AA	1	3	2.6471	0.2481 to 28.2409	0.4203	Ns.

ns: non-significant P>0.05

The Odds ratio among males of *human insulin receptor gene* rs1366600 A/G gene in studied groups

The association analysis showed that the polymorphism rs1366600 of the AA genotype increases significantly T2DM risk among the male patients OR= 22.4545 (CI95% [1.2129 to 415.6955]), P = 0.0367. The heterozygous AG genotype also increases the association with the disease OR= 2.4545 (CI95% [0.2347 to 25.6699]) P = 0.4534. While, The homozygous GG genotype decreases significantly the association with the disease OR= 0.0602 (CI95% [0.0069 to 0.5225]),P= 0.0108.

Table(4) Odds ratio among males of *human insulin receptor gene* rs1366600 A/G in studied groups

Genotypes	Control	Patients	OR	OR95%CI	P value	Significance
GG	18	13	0.0602	0.0069 to 0.5225	0.0108	Sig.**
AG	1	3	2.4545	0.2347 to 25.6699	0.4534	Ns.
AA	0.00	9	22.4545	1.2129 to 415.6955	0.0367	Sig.*

*P< 0.05,ns: non-significant P>0.05

**P< 0.01

Discussion

To the best of our knowledge, this is the first study of blending analysis with case–control studies for analyzing genetic association of *insulin receptor* gene rs1366600 A>G among T2DM patients in Iraq. rs1366600 as a potential functional SNP in the INSR gene. SNPs located within miRNA-binding sites are likely to affect the expression of the miRNA targets that may contribute to the susceptibility to human diseases(Guay *etal*., 2011; Dehwah *etal*.,2012).In brief, an SNP may either abolish or weaken a miRNAs target or create a perfect sequence match to the seed of a miRNAs(Chen *etal*.,2008). miRNA binding site SNPs are considered goldmine for the genetic epidemiological studies and assumed to contribute to the susceptibility of multiple human diseases (Chen *etal*.و 2008). In previous studies that have investigated the association of polymorphisms of several factors and other biomarkers among patients with type2 DM from Wasit province, (Yousif and Ghali,2021), revealed that IL-10 is a major contributor to the onset of type 2 diabetes mellitus and there may be a correlation between low levels of interleukin-10 and type two diabetes(Al-Sarray and Ahmed ,2021) found that may be a correlation between high levels of TNF-α and type 2 diabetes mellitus.(Shamkhi and Ahmed ,2021), displayed that levels of SIRT1 may be not associated with type2 diabetes mellitus. Furthermore, the cell free mitochondrial DNA increases significantly in patients with type2 diabetes mellitus (Hussein and Ghali,2022). COX-1 is a major contributor to the onset of type 2 diabetes and there may be an association between low levels of cyclooxygenase-1and type 2 diabetes (Jebil and Ghali,2021). The association analysis of IL-17AG197A gene polymorphism with T2DM displayed that heterozygous AG genotype of IL-17AG197A showed a risk association among T2DM with OR=1.24 CI95% (0.31 - 5.01) p-value =1.00 and the G allele was associated with an increased risk ofT2DM (Khidhum and Ahmed,2022). (Mahmood and Ghali,2022), revealed that there was an association between the polymorphism of Osteoprotegerin (OPG) polymorphism

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and susceptibility to type2 diabetes mellitus. (Mahmood and Ghali,2022b), found also that there may be a correlation between high levels of OPG and T2DM.

In the current study, the distribution frequencies of the genotypes and alleles of human insulin receptor gene rs1366600 A/G were not consistent with Hardy Weinberg equilibrium . A significantly higher frequency of the homozygous AA genotype and heterozygous AG genotype was observed when T2DM patients were compared with control. Moreover, frequency of homozygous GG genotype was lower in T2DM patients compared to healthy controls. Thus, the G allele might be a protective against the disease whereas the A allele may be considered as a risk factor in the disease. The association analysis showed that AA and AG genotypes are associated with T2DM .The subgroup analysis revealed that these genotypes are associated with the disease among females and it is more pronounced in males . Many previous studies have investigated the association of INSR gene with type 2 diabetes, and all previous studies have focused on the variant re1366600T>C. rs1366600CC, TC/CC of insulin receptor (INSR) gene contributed an independently increased risk for T2DM compared with rs1366600TT(Zhao *etal*.,2013).Similar results were reported by (Wang *etal*.,2017). According to previous studies, the 3′ UTR SNP located in the microRNA-binding site of HNF1B, WFS1 and various other genes were found to be associated with T2DM susceptibility in different population (Gong *et al*. 2014; Elek *et al*. 2015; Goda *et al*., 2015; Moszyńska A *et al*.,2017) reviewed the impacts of 3′ UTR SNPs in human diseases ranging from cancer to diabetes and presented that SNPs affecting microRNA-binding sites in the 3′ UTR regions can lead to disease pathogenesis via altering mRNA stability (Moszyńska A *et al*.,2017; Parvin *etal*.,201 9) showed that the minor allele of the microRNA-binding site polymorphism rs13666000 is associated with almost two-fold increased risk of T2DM, compared to the individual not carrying the minor allele 'C'. Dissecting analysis into different models of inheritance pattern showed that the dominant model (CC+TC genotype against the TT genotype), confers two fold increased susceptibility to T2DM in Bangladeshi population. The INSR gene encodes protein having direct role in insulin signaling pathway and is implicated in the insulin signal transduction and insulin sensitivity modulation. Some polymorphisms localized mainly on coding region of the INSR gene had shown correlation with insulin resistance (IR) and T2DM(Malodobra *et al*.,2011) showed that G/G genotype of rs3745551 on 3′-UTR of the INSR gene dominated in IR diabetic patients and had effect on insulin resistant phenotype development. Thus far, there has been little focus on the association between the SNP rs1366600 and the risk of T2DM(Malodobra *etal*.,2011;Zhao *etal*.,2013)found that the variant allele C of rs1366600 in 3′-UTR of the INSR gene may cause a loss of the binding site for the miR-20b by algorithms and identified that it is associated with higher diabetes risks. They hypothesized that the SNP rs1366600 in miR-20b target site can have an effect on INSR gene expression, further to change the function of the receptor. Although normal insulin secretion continues, the receptor cannot react to the existing insulin, ultimately leading to IR or T2DM.

Conclusion

A SNP located within miRNA-binding sites: *human insulin receptor gene* rs1366600 has possible roles in type2 diabetes mellitus susceptibility. Genotypes: AA and AG of human insulin receptor gene rs1366600 are associated with T2DM and the G allele might be a protective against the disease whereas the A allele may be considered as a risk factor in the disease. These genotypes are associated with the disease among females and it is more pronounced in males .

References

1. Abelson, J. F., Kwan, K. Y., O'Roak, B. J., Baek, D. Y., Stillman, A. A., Morgan, T. M. et al. Sequence variants in SLITRK1 are associated with Tourette's syndrome. Science 310, 317–320 (2005).
2. Al-Rifai, R.H.; Majeed, M.; Qambar, M.A.; Ibrahim, A.; AlYammahi, K.M.; Aziz, F. Type 2 diabetes and pre-diabetes mellitus: A systematic review and meta-analysis of prevalence studies in women of childbearing age in the Middle East and North Africa, 2000–2018. Syst. Rev. 2019, 8, 268.
3. Al-Sarray, A.J. and Ahmed, I.H., 2021. Serum TNF-A Concentrations In Type Two Diabetes Mellitus. NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal| NVEO, pp.540-546.
4. Ameres SL, Zamore PD. Diversifying microRNA sequence and function. Nat Rev Mol Cell Biol. 2013;14:475–88.
5. Chen K, Song F, Calin GA, Wei Q, Hao X, Zhang W (2008) Polymorphisms in microRNA targets: a gold

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(5), 76-82 | ISSN:2251-6727

mine for molecular epidemiology. Carcinogenesis 29:1306–1311.

6. Chin, L. J., Ratner, E., Leng, S., Zhai, R., Nallur, S., Babar, I. et al. A SNP in a let-7 microRNA complementary site in the KRAS 3'untranslated region increases Non–small cell lung cancer risk. Cancer Res. 68, 8535–8540 (2008).
7. De Fronzo, R.A.; Ferrannini, E.; Groop, L.; Henry, R.R.; Herman, W.H.; Holst, J.J.; Hu, F.B.; Kahn, C.R.; Raz, I.; Shulman, G.I.; et al. Type 2 diabetes mellitus. Nat. Rev. Dis. Prim. 2015, 1, 15019.
8. Dehwah, M. A., Xu, A. & Huang, Q. MicroRNAs and type 2 diabetes/obesity. J. Genet. Genomics 39, 11–18 (2012).
9. Elek Z, Nemeth N, Nagy G, Nemeth H, Somogyi A, Hosszufalusi N, SasvariSzekely M, Ronai Z (2015) Micro-RNA binding site polymorphisms in the WFS1 gene are risk factors of diabetes mellitus. PLoS ONE 10:e0139519.
10. Ghaedi H, Bastami M, Zare-Abdollahi D, Alipoor B, Movafagh A, Mirfakhraie R, et al. Bioinformatics prioritization of SNPs perturbing microRNA regulation of hematological malignancy-implicated genes. Genomics (2015) 106:360–6.
11. Ghali,.Z.H.and Jebil,H.D., 2021. Evaluation Of Serum Levels Of Cyclooxygenase-1 (COX-1) Among Patients With Type Two Diabetes Mellitus (T2DM). NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal| NVEO, pp.511-515.
12. Goda N, Murase H, Kasezawa N, Goda T, Yamakawa-Kobayashi K (2015b) Polymorphism in microRNA-binding site in HNF1B infuences the susceptibility of type 2 diabetes mellitus: a population based case–control study. BMC Med Genet 16:75.
13. Gong W, Xiao D, Ming G, Yin J, Zhou H, Liu Z (2014) Type 2 diabetes mellitusrelated genetic polymorphisms in microRNAs and microRNA target sites. J Diabetes 6:279–289.
14. Guay, C., Roggli, E., Nesca, V., Jacovetti, C. & Regazzi, R. Diabetes mellitus, a microRNA-related disease? Transl. Res. 157, 253–264 (2011).
15. Hussein, A.R. and Ghali, Z.H., 2022. Analysis Of Cell Free DNA And Cf-Mt DNA As Molecular Markers In Patients With Type-2 Diabetes Mellitus. NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal| NVEO, pp.444-449.
16. Kadhum, M.S. and Ahmed, I.H., 2022. THE INFLUENCE OF IL-17A GENETIC POLYMORPHISM ON THE SUSCEPTIBILITY OF TYPE 2 DIABETES MELLITUS IN IRAQI PATIENTS, Pages No: 288-291 .
17. Khan, M.A.B.; Hashim, M.J.; King, J.K.; Govender, R.D.; Mustafa, H.; Al Kaabi, J. Epidemiology of Type 2Diabetes—Global Burden of Disease and Forecasted Trends. J.Epidemiol. Glob. Health 2020, 10, 107–111.
18. Kong L, Zhu J, Han W, Jiang X, Xu M, Zhao Y, et al. Significance of serum microRNAs in pre-diabetes and newly diagnosed type 2 diabetes: A clinical study. Acta Diabetol. 2011;48:61–9.
19. Mahmood, D.Q. and Ghali, Z.H., 2022. ASSOCIATION OF OSTEOPROTEGERIN OPG T950C POLYMORPHISM TO SUSCEPTIBILITY OF TYPE 2 DIABETES MELLITUS, Pages No. 280-283 .
20. Mahmood, D.Q. and Ghali, Z.H., 2022. Evaluation of Osteoprotegerin (OPG) levels among Iraqi type2 diabetic patients, 6(S7), 517–521.
21. Malodobra, M., Pilecka, A., Gworys, B. & Adamiec, R. Single nucleotide polymorphisms within functional regions of genes implicated in insulin action and association with the insulin resistant phenotype. Mol. Cell Biochem. 349, 187–193 (2011)
22. Moszyńska A, Gebert M, Collawn JF, Bartoszewski R (2017) SNPs in microRNA target sites and their potential role in human disease. Open Biology 7:170019.
23. Parvin M, Jahan F, Sarkar PK, Howlader ZH, Nabi AHMN, Hosen MI. Functional Polymorphism Located in the microRNA Binding Site of the Insulin Receptor (INSR) Gene Confers Risk for Type 2 Diabetes Mellitus in the Bangladeshi Population. Biochem Genet. 2019 Feb;57(1):20-33.
24. Poy MN, Spranger M, Stoffel M. microRNAs and the regulation of glucose and lipid metabolism. Diabetes Obes Metab. 2007;9(Suppl 2):67–73.
25. Shamkhi, R.J. and Ahmed, I.H.,2021. Association between Sirtuin1 levels and Type2-Diabetes Mellitus. Turkish Journal of Physiotherapy and Rehabilitation, 32, p.3.
26. Shen H, Li J, Zhang J, Xu C, Jiang Y, Wu Z, et al. Comprehensive characterization of human genome variation by high coverage whole-genome sequencing of forty four Caucasians. PloS One (2013) 8:e59494.
27. Wang X, Li W, Ma L, Ping F, Liu J, Wu X, Mao J, Wang X, Nie M (2017) Investigation of miRNA-binding site variants and risk of gestational diabetes

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(5), 76-82 | ISSN:2251-6727

mellitus in Chinese pregnant women. Acta Diabetol 54:309–316.

28. Yousif, B.A. and Ghali, Z.H., 2021. Evaluation Of Serum Levels Of Interleukin-10 Among Patients With Type Two Diabetes Mellitus (T2DM). NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal| NVEO, pp.496-499.
29. Zhao, X., Ye, Q., Xu, K. et al. Single-nucleotide polymorphisms inside microRNA target sites influence the susceptibility to type 2 diabetes. J Hum Genet 58, 135–141 (2013).