CHAPTER 3
TO STUDY THE ROLE OF OMENTIN-1 IN TYPE 2 DIABETES

To study the role of Omentin-1 in Type 2 Diabetes

3.1 Introduction

The insulin resistance in peripheral tissues, liver, muscle and adipose tissue is the hallmark of T2D [Pramanik *et al.,* 2018]. In the past few decades, obesity has been recognized as one of the principal factors that lead to T2D. Adipose tissue secretes bioactive molecules called adipokines (pro- and anti-inflammatory) besides serving as an energy depository organ. The pro-inflammatory and anti-inflammatory adipokines are in a state of equilibrium, and they play a significant role in regulating lipid metabolism, insulin sensitivity, glucose metabolism, appetite and satiety [Blüher *et al.,* 2012]. *Omentin-1*, the anti-inflammatory adipokine gene, is located on chromosome 1q22-q23 and is secreted by visceral adipose tissue (VAT) [Yang *et al.,* 2006]. In subcutaneous fat, omentin-1 can enhance insulin action. It was related to down-regulated TNF-α induced expression of adhesion molecules in endothelial cells via NF-κB inhibition. Thus, omentin-1 may be of possible advantage due to its anti-inflammatory ability to attenuate endothelial dysfunction and atherosclerosis [Pramanik *et al.,* 2018]. Circulating omentin-1 levels were reported to be decreased in obese individuals and have been negatively correlated with markers of obesity, such as waist circumference, BMI, and circulating leptin [de Souza Batista *et al.,* 2007]. Omentin-1 has been involved in the insulin signalling pathway through Akt activation and consequently increasing insulin sensitivity [Schäffler *et al.,* 2005]. Reports suggest that reduced *omentin-1* gene expression and circulating plasma omentin-1 levels are associated with impaired glucose tolerance in T2D patients [Tan *et al.,* 2010; Yan *et al.,* 2011]. Moreover, fasting serum omentin-1 levels have been negatively correlated with HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) [Yan *et al.,* 2011].

There are limited studies on the genetic variants of *omentin-1* worldwide. *Omentin-1* Val109Asp rs2274907 has been exclusively studied in various populations, and it is associated with non-alcoholic fatty liver disease (NAFLD) [Kohan *et al.,* 2016], coronary artery disease (CAD) [Nazar et al., 2017; Yörük *et al.,* 2014], psoriasis [Zhang *et al.,* 2015], high calorie-diet intake [Splichal *et al.,* 2015], and breast cancer [Bahadori *et al.,* 2014]. Only one report is available on *omentin-1* 3' UTR rs1333062 in the Indian population showing an association with diabetes [Tabassum *et al.,* 2012]. Hence, we aimed to investigate *omentin-1* genetic variants (Exon 4 Val109Asp rs2274907 and 3' UTR rs1333062), *omentin-1* transcript levels in VAT along with its plasma protein levels, and genotype-phenotype correlation with various metabolic parameters.

3.2 Materials and Methods

3.2.1 Study subjects

Details regarding study subjects are described in **section 2.2.1** of chapter 2. Samples of visceral (omental) adipose tissue were taken from the individuals undergoing bariatric surgery and fasting clinical parameters of all the study subjects were considered. The individuals with FBG>125mg/dL and not suffering from any other diseases were recruited for the study as T2D patients.

3.2.2 Anthropometric parameters, Lipid profiling and DNA extraction

Details regarding anthropometric parameters, lipid profiling and DNA extraction are described in **section 2.2.2** of chapter 2.

3.2.3 Genotyping of *Omentin-1* gene polymorphisms

Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) was used for genotyping of *omentin-1* gene two polymorphisms. The primers details of genotyping of SNPs of *omentin-1* gene and monitoring *omentin-1* transcript levels are shown in Table 3.1. The reaction mixture (20µl) consisted of 3µl (50ng) of genomic DNA, 11µl of NFW, 2.0µl of 10X PCR buffer, 2.0µl of 2.5mM dNTPs (Sigma Chemical Co, St.Louis, Missouri, USA), 1.0µl each of 10µM forward and reverse primers (MWG Biotech, India) and 0.2µl of 5U/µlTaq Polymerase (Bangalore Genei, India). Amplification was executed using Applied Biosystems 96 well Thermal cycler (California, USA) as per the procedure of initial denaturation at 95°C for 5 minutes followed by 39 cycles each at 95°C for 30 seconds, 59-67°C (product specific, shown in Table 3.1) for 30 seconds and 72°C for 30 seconds, followed by final extension at 72°C for 10 minutes. The information of the REs (Thermo Fisher Scientific, Wilmington, DE, USA) and digested products are mentioned in Table 3.1. The amplified products (15µl) were digested with 1U of the corresponding RE in a total reaction volume of 20µl as per the manufacturer's instruction. The amplified PCR products (5µl) and digested products (20µl) were assessed by electrophoresis on a 3.5% agarose gel stained with EtBr along with a 50bp/100bp DNA ladder (MBI Fermentas, St.Leon-Rot, Germany). All the gels were visualized under UV transilluminator using Gel Doc EZ System (Bio Rad Laboratories, California, USA).

Table 3.1 Primers and REs used for genotyping for the studied polymorphisms and expression of *Omentin-1* gene.

SNP/Gene Primer	Sequence (5' to 3')	Annealing Temp	Amplicon Size (bp)	RE	Digested products (bp)
***Omentin-1* rs2274907** Val109Asp A/T	**FP:** CTTCTCCA GCCCATCCCAC **RP:** CCAGCGTGCA CGAGAATGAC	64.1°C	269	AccI	192 + 77
***Omentin-1* rs1333062** 3'UTR G/T	**FP:** GGTGAGTTAG GAAGGGTTTGG **RP:** CTCAAGGCTT GGTGTTTCTGTG	63°C	248	BfaI	198 + 50
Omentin-1 transcript	**FP:** CCTAGTGCAT TTGATGGCCTG **RP:** CCACCCCCAG AGGTCATG	64°C	86	-	-
GAPDH	**FP:** CATCACCATC TTCCAGGAGCGAG **RP:** CTGCAAATG AGCCCCAGCCT	64°C	122	-	-

FP: Forward Primer; RP: Reverse Primer; bp: base pairs

3.2.4 Determination of the transcript levels

Total RNA was extracted from VAT by Trizol method. RNA integrity and purity were confirmed by 1.5 % agarose gel electrophoresis/EtBr staining and O.D. 260/280 absorbance ratio 1.9 respectively. Further, RNA was treated with DNase I (Puregene, Genetix Biotech) before cDNA synthesis to avoid DNA contamination. One microgram of total RNA was used to prepare cDNA using the Transcriptor High Fidelity cDNA Synthesis Kit (Roche Diagnostic GmbH, Mannheim, Germany) according to the manufacturer's instructions in the Eppendorf Mastercycler gradient (USA Scientific, Inc., Florida, USA). The transcript levels of *omentin-1* and *GAPDH* (reference gene) were detected by LightCycler®480 Real-time PCR (Roche Diagnostics GmbH, Manneheim, Germany) using gene-specific primers (Eurofins, Bangalore, India) as shown in Table 3.1. The thermal cycling conditions comprised an initial activation step at 95°C for 10 min, followed by 45 cycles of denaturation (95°C for 10 sec.), annealing (60-69°C for 10 sec; shown in Table 3.1), and amplification (72°C for 10 sec.). The fluorescence data collection was accomplished during the extension step. At the end of the amplification phase, a melt curve analysis was carried out to validate the specificity of the products formed. The PCR cycle at which PCR amplification begins its exponential phase was considered as the crossing point (Cp) or cycle threshold (Ct). The ΔCt or ΔCp value was obtained as a difference between the Ct of *omentin-1* gene and Ct of *GAPDH* gene. The

difference among the two ΔCt values (ΔCt Controls and ΔCt patients) was considered as ΔΔCt to attain the value of fold expression ($2^{-\Delta\Delta Ct}$).

3.2.5 Determination of plasma omentin-1 protein levels

The plasma levels of omentin-1 were estimated by the enzyme-linked immunosorbent assay (ELISA) kit for human omentin-1 (RayBio, Norcross, GA, USA) with the sensitivity of 2ng/ml. All the plasma estimations were carried out in duplicates to ensure % CV below 10%. The readings were taken to estimate the protein levels against a standard curve using MultiSkan reader (Thermo Fischer, USA).

3.2.6 Statistical analyses

The clinical characteristics (metabolic and lipid profile, transcript and protein levels) were compared using the t-test or Mann Whitney test between controls and T2D patients followed by one-way ANOVA for multi-group comparison. Evaluation of the HWE was performed for all the polymorphisms in patients and controls by comparing the observed and expected frequencies of the genotypes using chi-square analysis. The distribution of the genotypes and allele frequencies of the studied polymorphisms for patients and control subjects were compared using the chi-square test with 2x2 contingency table. *p*-values less than 0.025 for genotype and allele distribution were considered as statistically significant as per Bonferroni's corrections. OR with respective confidence interval (95% CI) for disease susceptibility was also calculated. Haplotypes, LD coefficients (D'= D/Dmax) and r^2 values for the pair of the most common alleles at each site were obtained using http://shesisplus.bio-x.cn/SHEsis.html [Yong *et al.*, 2005]. For the genotype-phenotype association analysis, primarily all the parameters were checked for the normality test and accordingly further analyses were carried out. All the genotype-phenotype correlation analyses were carried out in T2D patients after adjusting for the disease susceptibility. Correlation analysis was performed by Spearman's correlation test. All the analyses were carried out in Prism 6 software (GraphPad, USA).

3.3 Results: Baseline characteristics

Clinical parameters varied significantly between controls and T2D patients (Table 2.1). Clinical parameters varied significantly between controls and T2D patients recruited for *omentin-1* transcript levels analysis (Table 3.2). Patients had significantly higher FBG (p=0.05), HbA1c (p=0.0106), and LDL levels (p=0.0256) as compared to controls. However, other parameters were not significantly different between the controls and patients.

Table 3.2 Clinical characteristics of the controls and T2D patients recruited for *omentin-1* transcript analysis.

	Controls (Mean ± SD)		**Patients (Mean ± SD)**	***P* value**
	(n =12)		(n =10)	
Age (years)	41.18 ± 10.23		56.67 ± 15.75	0.0312
Sex: Male	2		3	
Female	10		7	0.8410
FBG (mg/dL)	86.54 ± 7.04		157.7 ± 10.60	**0.05**
HbA1c (%)	5.1 ± 0.5		7.9 ± 1.2	**0.0106**
BMI (Kg/m^2)	44.90 ± 8.7		61.25 ± 41.93	0.2439
Total Cholesterol	166.4 ± 39.45		170.3 ± 42.29	0.8252
(mg/dL)	148.8 ± 101.2		137.8 ± 26.86	0.3884
Triglycerides	45.66 ± 8.26		56.90 ± 27.82	0.8252
(mg/dL)	64.05 ± 32.35		102.1 ± 28.30	**0.0256**
HDL (mg/dL)				
LDL (mg/dL)				

Data are presented as Mean±SD. Statistical significance was considered at $p<0.05$.

3.3.1 Genetic analysis of the *omentin-1* gene polymorphisms

The *omentin-1* SNPs were assessed using PCR-RFLP, and the representative gel images are shown in Figure 3.1. The genotype and allele frequencies of the explored *omentin-1* polymorphisms are summarized in Table 3.3. The distribution of genotype frequencies for the two polymorphisms investigated was consistent with HWE ($p>0.05$). Our results suggest no difference in genotype and allele frequencies of *omentin-1* two SNPs among diabetic patients and controls; and not associated with T2D risk ($p>0.05$). Hence discontinued after an initial assessment of 250 samples.

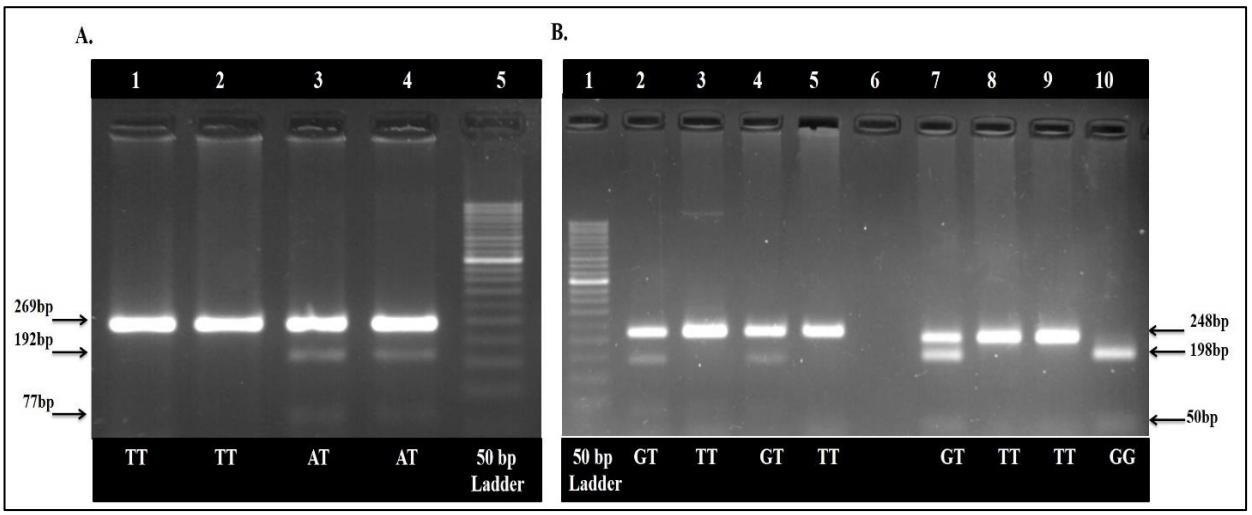

Figure 3.1 Representative gel images of *omentin-1* SNPs. A) PCR-RFLP analysis of *omentin-1* rs2274907 A/T polymorphism on 3.5% agarose gel: lanes 1 and 2 show homozygous (TT) genotypes; lanes 3 and 4 show heterozygous (AT) genotypes; AA genotype was not observed. Lane 5 shows a 50bp DNA ladder. B) PCR-RFLP analysis of *omentin-1* rs1333062 G/T

polymorphism on 3.5% agarose gel: lanes 2, 4 and 6 show heterozygous (GT) genotypes; lanes 3, 5, 8 and 9 show homozygous (TT) genotypes; lane 10 shows homozygous (GG) genotype. Lane 1 shows a 50bp DNA ladder.

Table 3.3 Genotype and allele frequencies distribution of *omentin-1* polymorphisms in controls and T2D patients.

SNP	Genotype /Allele	Controls	Patients	*p* for Association	OR	95% CI
(rs2274907) *Omentin-1* Val109Asp A/T		n=250	n=235			
	TT	206 (83.17)	189 (81.38)	R	-	
	TA	44 (16.05)	46 (17.66)	0.1992[a]	1.378	0.8436 to 2.250
	AA	0 (0.77)	0 (0.96)	-	-	-
	T	430 (0.93)	416 (0.90)			
	A	34 (0.07)	44 (0.10)	0.2212[b]	1.338	0.8381 to 2.135
(rs1333062) *Omentin-1* 3' UTR G/T		n=250	n=250			
	TT	45 (15.84)	35 (13.86)	R	-	-
	TG	109 (47.92)	105 (46.74)	0.4167[a]	1.239	0.7387 to 2.077
	GG	96 (36.24)	95 (39.40)	0.3681[a]	1.272	0.7526 to 2.151
	T	199 (0.40)	175 (0.37)			
	G	301 (0.60)	291 (0.63)	0.4119[b]	1.114	0.8602 to 1.444

n: number of patients/controls, R: reference group, CI: Confidence Interval, Odds Ratio: the allele frequency distribution, P: patients, C: controls, [a]Patients vs Controls (genotype) by the chi-square test with 2×2 contingency table. [b]Patients vs Controls (allele) by the chi-square test with 2×2 contingency table. Statistical significance was considered at $p<0.025$ as per Bonferroni's correction.

3.3.2 Haplotype analysis of the *omentin-1* polymorphisms

The haplotype frequencies obtained for *omentin-1* (global $p=0.853$) did not differ between T2D patients and controls (Table 3.4).

Table 3.4 Distribution of haplotype frequencies of *omentin-1* in controls and T2D patients.

Haplotype (rs2274907 A/T, rs1333062 G/T)	Patients (Freq. %; n=230)	Controls (Freq. %; n=250)	*p* for Association	$p_{(global)}$	Odds Ratio [95%CI]
TT	142 (0.307)	135 (0.322)	0.064	0.853	1.296 [0.983~1.707]
TG	276 (0.597)	249 (0.595)	8.60×10^{5}		1.641 [1.283~2.099]
AT	28 (0.06)	29 (0.069)	0.684		1.116 [0.654~1.905]

CI represents the Confidence Interval. (Frequency<0.03 in both control & case has been dropped and was ignored in the analysis).

3.3.3 Linkage disequilibrium analysis of the *omentin-1* polymorphisms

The LD analysis revealed that the polymorphisms of *omentin-1* (rs2274907 A/T; rs1333062 G/T) were in moderate linkage (D'=0.56, r^2= 0.05) (Figure 3.2).

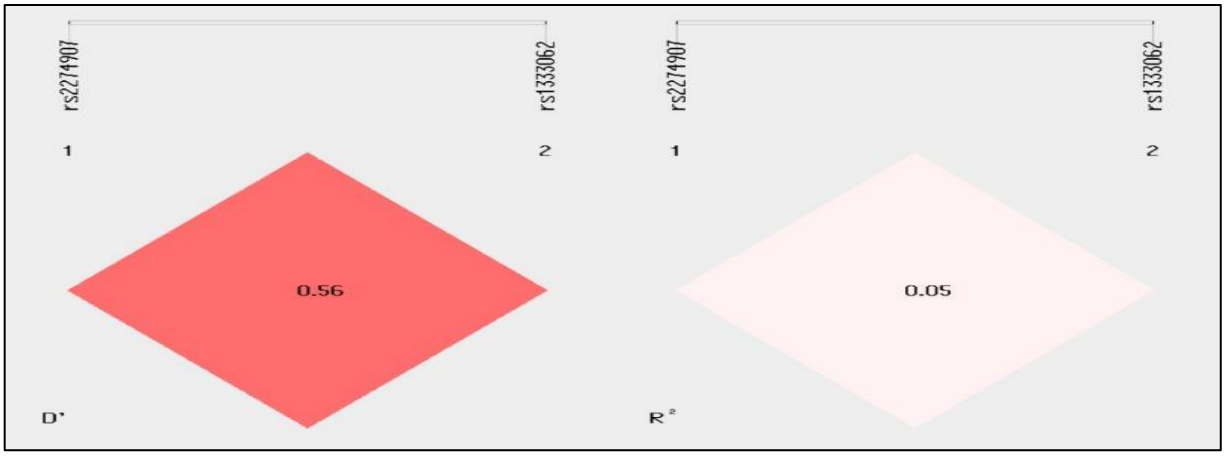

Figure 3.2 Linkage disequilibrium block: LD block with respect to *omentin-1* rs2274907 A/T and rs1333062 G/T polymorphisms in Gujarat population.

3.3.4 The analysis of the association of the *omentin-1* polymorphisms with the metabolic profile

Omentin-1 rs2274907 AA genotype was associated with elevated BMI levels (*p*=0.0247); however, it was not associated with other parameters (*p*>0.05). In comparison, *omentin-1* rs1333062 G/T did not show an association with the metabolic profile (*p*>0.05) (Table 3.5).

Table 3.5 Genotype-phenotype association analysis of *omentin-1* polymorphisms with metabolic profile.

Genotype	FBG (mg/dl)	BMI (kg/m^2)	TG (mg/dl)	TC (mg/dl)	LDL (mg/dl)	HDL (mg/dl) Male	HDL (mg/dl) Female
***Omentin-1* Val109Asp A/T (rs2274907)**							

TT	118.7(45.5)	25.6(5.4)	157.0(85.5)	161.3(36.8)	100.1(29.8)	36.4(9.9)	41.3(9.6)
AT	127.8(45.1)	27.0(5.5)	168.6(86.1)	166.3(32.7)	106.1(28.8)	33.8(7.6)	41.3(8.6)
AA	-	-	-	-	-	-	-
p value	0.1369	**0.0247**	0.1763	0.2010	0.0825	0.1248	0.8184
***Omentin-1* 3'UTR G/T (rs1333062)**							
TT	119.7(54.2)	25.4(6.0)	144.6(74.9)	162.0(37.5)	101.8(25.1)	36.0(9.1)	41.8(11.1)
TG	120.1(43.2)	25.9(5.3)	155.8(88.8)	163.0(34.1)	103.6(32.2)	36.5(10.4)	41.9(9.4)
GG	120.3(41.2)	25.8(5.2)	163.9(88.5)	159.3(37.1)	98.7(29.8)	35.8(8.1)	40.8(8.5)
p value	0.9150	0.4323	0.1852	0.3773	03678	0.8933	0.5850

Data are presented as Mean ±SE; Statistical significance was considered at $p<0.05$.

3.3.5 *Omentin-1* transcript levels and their association with *omentin-1* polymorphisms, and a correlation with the metabolic profile

After normalization with *GAPDH* expression, a 4.2-fold ($p=0.0127$) increase in the expression of *omentin-1* transcript levels was observed in T2D patients by $2^{-\Delta\Delta Cp}$ analysis (Figure 3.3A). However, there was no association between *omentin-1* transcript levels and their polymorphisms ($p>0.05$) (Figure 3.3B). Spearman's correlation analysis showed no correlation between *omentin-1* transcript levels and metabolic profile ($r^2=0$, $p>0.05$) (Table 3.6).

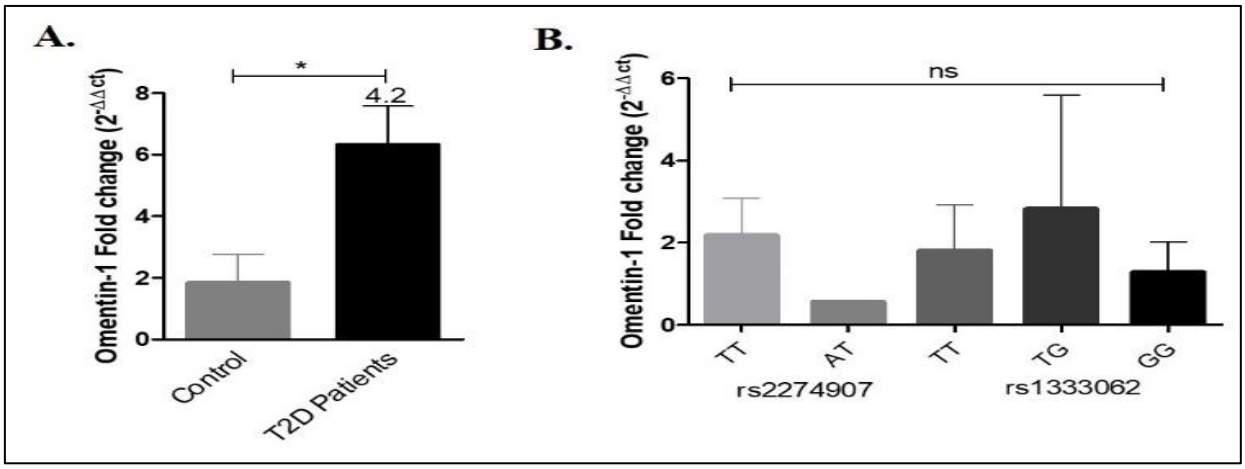

Figure 3.3 A) Relative fold change of *omentin-1* transcript levels in adipose tissue of controls and patients. T2D patients showed 4.2-fold ($p=0.0127$) increase in *omentin-1* transcript levels as estimated by the $2^{-\Delta\Delta Cp}$ method (Controls n=12; T2D patients n=10). **B) Association of *omentin-1* polymorphisms with their transcript levels.** *Omentin-1* polymorphisms showed no association with their transcript levels ($p>0.05$).

Table 3.6 Correlation analysis of *omentin-1* transcript levels with the metabolic profile.

Parameters	***r*²**	***p-value***
BMI (Kg/m²)	0.2571	0.6583
FBG (mg/dL)	-0.4000	0.7500
TG (mg/dL)	0.4000	0.7500
TC (mg/dL)	0.3491	0.7568
HDL (mg/dL): Male Female	0.5678 0.9876	0.6789 0.5678
LDL (mg/dL)	0.4000	0.7500

$p>0.05$, non-significant. n=10

3.3.6 Plasma omentin-1 protein levels and their association with *omentin-1* polymorphisms and metabolic profile

Plasma omentin-1 protein levels showed a significant decrease (p<0.0001) in T2D patients (Figure 4.4A). Our results showed no association of *omentin-1* polymorphisms with plasma omentin-1 protein levels. (p>0.05) (Figure 3.4B). Spearman's correlation analysis revealed no correlation between omentin-1 protein levels and the metabolic profile parameters (p>0.05) (Table 3.7).

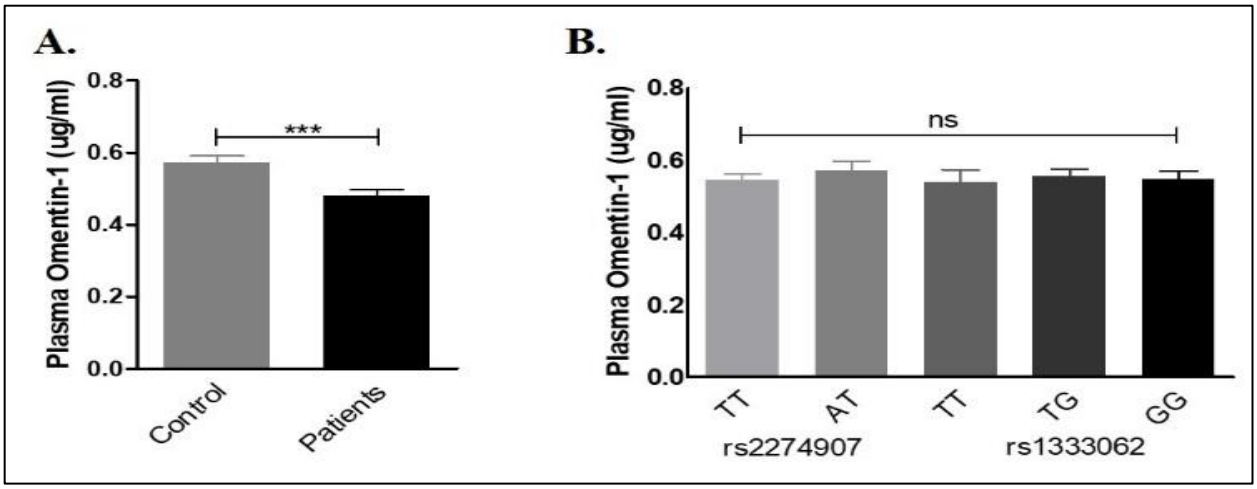

Figure 3.4 Plasma omentin-1 protein levels in A) controls vs patients. Our results showed a significant decrease in plasma omentin-1 protein levels in T2D patients (p<0.0001) compared to controls (Controls n=40; T2D patients n=40). **B) Association of *omentin-1* polymorphisms with plasma omentin-1 protein levels.** *Omentin-1* polymorphisms showed no association with omentin-1 protein levels (p>0.05)

Table 3.7 Correlation analysis of plasma omentin-1 protein levels with the metabolic profile.

Parameters	r^2	*p-value*
BMI (Kg/m^2)	-0.0127	0.9020
FBG (mg/dl)	0.2427	0.1538
Triglycerides (mg/dl)	0.1728	0.2401
Total Cholesterol (mg/dl)	0.0940	0.4865
HDL (mg/dl): Male Female	0.1420 0.3000	0.4541 0.1642
LDL (mg/dl)	0.1192	0.4520

p>0.05, non-significant. n=40

3.4 Discussion

There are several reasons to investigate o*mentin-1* SNPs with the risk of T2D, as omentin-1 secreted from adipose tissue is associated with peripheral insulin resistance. There are numerous population-based studies on o*mentin-1* genetic variants, but only a few in the Indian population.

The present study was attempted to determine genetic risk factors from one of the strongly linked chromosomal regions i.e., 1q21-23 in the Gujarat population for T2D.

Our results reveal that the genetic variants of *omentin-1 (*rs2274907 A/T and rs1333062 G/T) are not associated with T2D. Our results are in agreement with the Caucasian population [Schäffler et al., 2007; Isakova *et al.,* 2018] though not in the Polish and North Indian population [Mrozikiewicz-Rakowska et al., 2017; Tabassum *et al.,* 2012]. Further, our association studies showed rs2274907 AT genotype to be significantly associated with increased BMI in T2D patients. In this context, an association with increased risk towards NAFLD is reported [Kohan *et al.,* 2016]. *Omentin-1* rs2274907 polymorphic (A/T) site is present in exon-4 and is described as a change of amino acid from Asp (GAC) to Val (GTC) at position 109 [Schäffler *et al.,* 2007]. Interestingly our *in-silico* analysis revealed that the site as benign, having no significant structural effect on protein activity.

The transcript and protein expression levels of omentin-1 painted quite an intriguing picture of elevated mRNA levels and reduced protein levels in T2D patients. Although the studies carried out by other researchers are in discord with our transcript results [de Souza Batista et al., 2007; Tan *et al.,* 2008; Cai *et al.,* 2009], these groups have not monitored the protein levels. Our results on the transcript levels agree with the report of Schäffler *et al.* [Schäffler *et al.,* 2005], who showed an increased *omentin-1* transcript levels as a response to elevated levels of pro-inflammatory adipokines. The best explanation could be a defence mechanism that gets stimulated due to obesity-induced changes in adipose tissue micro-environment [Schäffler *et al.* 2005, Jeffery *et al.,* 2016]. Li *et al.* have explained this elevated anti-inflammatory adipokine levels could be due to stimulation induced by various pro-inflammatory cytokines. Moreover, there are differential binding frequencies of NF-κB, a primary adipokine regulator [Li *et al.,* 2012]. Our observation of increased expression of pro-inflammatory adipokines such as TNF-α [Patel *et al.,* 2019], IL1β [Patel *et al.,* 2016] and resistin [Rathwa *et al.,* 2019] is in agreement. Furthermore, epigenetic modifications like DNA methylation and post-translational modifications coupled with miRNA regulation, have also been suggested to regulate mRNA expression of adipokines [Li *et al.,* 2012; Kokosar *et al.,* 2016; Guzik *et al.,* 2017]. In this context, the observed increase in mRNA expression of *omentin-1* could be due to any of the above reasons.

As opposed to the transcript levels, plasma omentin-1 levels seem significantly reduced in T2D patients. A similar trend was reported by other research groups on protein levels [de Souza Batista *et al.,* 2007, Abd-Elbaky *et al.,* 2016]. There are numerous explanations put forward for

the decreased circulatory omentin-1 levels in diabetic patients. First of all, reduced omentin-1 in the circulation could result from either repressed translation or reduced stability of mRNA/protein. Secondly, Yan *et al.* [Yan *et al.,* 2011] have shown a direct association between circulating omentin-1 and adiponectin levels.

Interestingly, we have observed reduced adiponectin levels in our population [Palit *et al.*, 2020], and it may have a regulatory influence on omentin-1 levels [Jaikanth *et al.,* 2013]. However, future studies are needed in this direction to unravel the complicated associations, if any. Dysregulation of blood glucose levels with an increased inclination towards T2D and diabetic complications stands linked with sleep turmoil [Kawakami *et al.,* 2004]. Moreover, reports show that circadian rhythms can impact adipose tissue metabolic processes, particularly adipokines expression and secretion [Gómez-Santos et al., 2009; Johnston *et al.,* 2012]. Such regulation is likely to be mediated by melatonin through its membrane receptors or via action by the sympathetic nervous system on VAT [de Farias *et al.,* 2015]. The potential mechanism of action of melatonin on omentin-1 may be through direct involvement with adiponectin levels. From our previous study, we have observed reduced plasma melatonin levels in T2D patients [Patel *et al.,* 2018]. The reduced omentin-1 levels might contribute towards the progression/development of T2D. The underlying mechanism for the differential expression of mRNA and protein levels needs investigation in depth through *in-vivo* studies.

As discussed above, there are altered pro-inflammatory (TNF-α) and anti-inflammatory (adiponectin) adipokine levels in obesity-induced diabetic patients. Omentin-1 reportedly manifests its anti-inflammatory activity by inhibiting TNF-α through the JNK pathway in healthy individuals [Kazama *et al.,* 2012]. Circulatory omentin-1 levels serve as a biomarker of diabetes, obesity, atherosclerosis, inflammatory diseases, metabolic syndrome and cancer [Blüher *et al.,* 2012; Tan *et al.,* 2010]. However, its polymorphic sites are not associated with T2D. The current study suggests that *omentin-1* might be regulated by multiple factors at transcriptional and translational levels, while genetic polymorphisms are not associated with T2D. There was an association of the AT genotype of rs2274907 with increased BMI levels. Increased pro-inflammatory adipokines and epigenetic modifications might influence the reduced plasma omentin-1 levels. These factors are known to be induced by a sedentary lifestyle and an unhealthy diet. The plasma omentin-1 protein levels might also be regulated by anti-inflammatory adipokines and melatonin. Thus, all these factors could be involved in developing dyslipidemia and obesity induced T2D (Figure. 3.5).

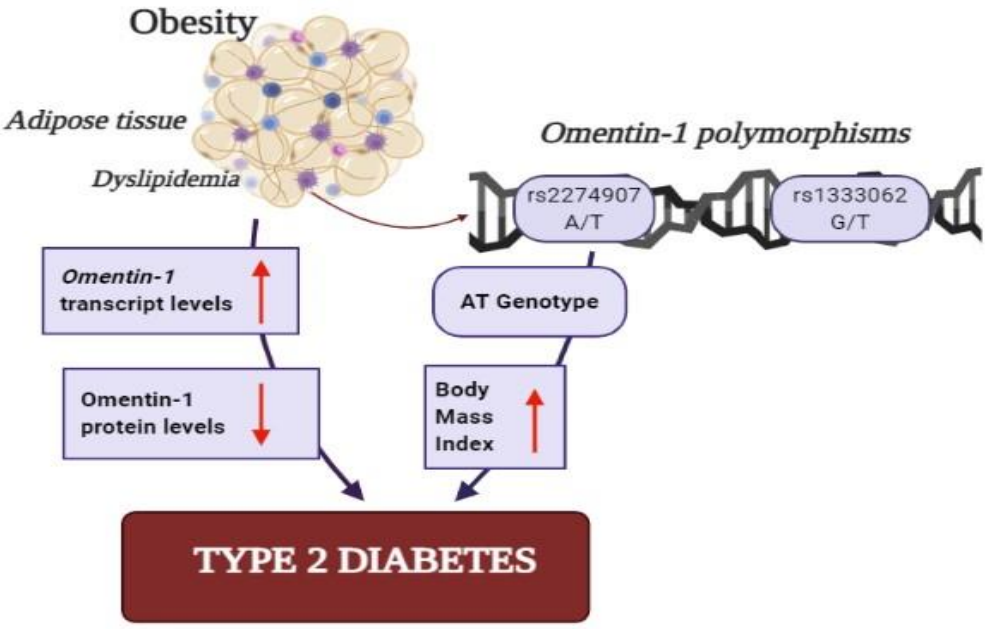

Figure 3.5 Role of Omentin-1 in T2D: The genetic variants of *omentin-1* are not associated with T2D susceptibility, however, the AT genotype of rs2274907 A/T is associated with increased BMI. Besides, in T2D individuals, *omentin-1* transcript levels are increased, but the protein levels are reduced. Altogether, the above factors contribute to the increased risk of T2D in Gujarat population.

References:

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