Supplementary Tables File (Manuscript: UJMS-2019-0257.R2)

Table 1 Comparison of continuous variables between overall cases (OW+OB) and normal weight controls

Continuous variables	All (males and females) N = 612			Males N = 336			Females N = 276		
	OW+OB N = 306	Controls N = 306	*P*-value	OW+OB N = 168	Controls N = 168	*P*-value	OW+OB N = 138	Controls N = 138	*P*-value
Anthropometric parameters									
Weight (Kg)	445.80	167.20	**<0.001***	203.93	73.07	**<0.001***	248.66	88.34	**<0.001***
Height (cm)	301.14	311.86	0.453	129.32	147.68	0.056	167.77	169.23	0.890
BMI (Kg/m^2)	459.46	153.54	**<0.001***	207.46	69.54	**<0.001***	252.50	84.50	**<0.001***
WC (cm)	449.83	163.17	**<0.001***	202.17	74.83	**<0.001***	248.56	88.44	**<0.001***
HC (cm)	146.14	166.86	**<0.001***	202.58	74.42	**<0.001***	244.34	92.16	**<0.001***
WHR	410.81	202.19	**<0.001***	188.01	89.99	**<0.001***	224.84	112.16	**<0.001***
Biceps SFT (mm)	414.30	198.70	**<0.001***	190.34	86.66	**<0.001***	233.67	103.33	**<0.001***
Triceps SFT (mm)	436.04	176.96	**<0.001***	194.15	82.85	**<0.001***	243.31	93.69	**<0.001***
Abdominal SFT (mm)	432.75	180.25	**<0.001***	194.62	82.38	**<0.001***	239.34	97.66	**<0.001***
Supra-iliac SFT (mm)	427.17	185.83	**<0.001***	190.29	86.71	**<0.001***	242.48	94.52	**<0.001***
Thigh SFT (mm)	437.17	175.83	**<0.001***	195.22	81.78	**<0.001***	243.89	93.11	**<0.001***
Sub-scapular SFT (mm)	430.26	181.33	**<0.001***	198.16	78.84	**<0.001***	233.66	101.95	**<0.001***
% Body fat	442.22	170.78	**<0.001***	195.82	81.18	**<0.001***	247.19	89.81	**<0.001***
Metabolic parameters									
Systolic BP (mmHg)	343.71	269.29	**<0.001***	165.13	111.87	**<0.001***	178.43	158.57	**0.052***
Diastolic BP (mmHg)	344.25	268.75	**<0.001***	152.89	124.11	**0.002***	192.01	144.99	**<0.001***
VAI (mmol L-1)	352.83	260.17	**<0.001***	195.11	141.89	**<0.001***	158.89	118.11	**<0.001***
LAP (mmol L-1)	428.87	184..13	**<0.001***	237.72	99.28	**<0.001***	191.29	85.71	**<0.001***
TyG index	363.06	249.94	**<0.001***	204.41	132.59	**<0.001***	158.64	118.36	**<0.001***
FBG (mg/dL)	334.92	278.08	**<0.001***	153.49	123.51	**0.002***	182.44	154.56	**0.009***
Insulin (µl U/mL)	372..00	241.00	**<0.001***	155.06	121.94	**0.001***	217.29	119.71	**<0.001***
HOMA-IR	374.31	238.69	**<0.001***	157.30	119.70	**<0.001***	217.75	119.25	**<0.001***
HOMA-IS	238.69	374.31	**<0.001***	119.25	217.75	**<0.001***	119.74	157.26	**<0.001***
Cholesterol (mg/dL)	333.31	279.69	**<0.001***	143.05	133.95	0.343	190.57	146.43	**<0.001***
Triglycerides (mg/dL)	357.87	255.13	**<0.001***	155.37	121.63	**<0.001***	203.10	133.90	**<0.001***
HDL-C (mg/dL)	316.98	296.02	0.142	134.79	142.21	0.440	183.15	153.85	**0.006***

LDL-C (mg/dL)	366.06	246.94	**<0.001***	155.25	121.75	**<0.001***	210.98	126.03	**<0.001***
VLDL-C (mg/dL)	354.62	258.38	**<0.001***	153.98	123.02	**0.001***	201.35	135.65	**<0.001***
CHR	317.88	295.12	0.111	143.68	133.32	0.280	174.25	162.75	0.278
CRI	317.92	295.08	0.110	174.14	162.86	0.287	143.73	133.27	0.276
AI	354.13	258.87	**<0.001***	198.25	138.75	**<0.001***	156.78	120.22	**<0.001***
TG/HDL-C	345.27	267.73	**<0.001***	192.46	144.54	**<0.001***	153.71	123.29	**0.002***

Continuous variables are expressed in mean ranks and compared by Mann–Whitney U test between cases and controls. Abbreviations; OW+OB: overweight and obese cases, BMI: body mass index, WC: waist circumference, HC: hip circumference, WHR: waist-to-hip ratio, SFT: skin fold thickness, BP: blood pressure, VAI: visceral adiposity index, LAP: lipid accumulation product, TyG: product of triglyceride and glucose, FBG: fasting blood glucose, HOMA-IR: homeostasis model assessment of insulin resistance, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, VLDL-C: very low density lipoprotein cholesterol, CHR: cholesterol HDL-C ratio, CRI: Coronary Risk Index, AI: Atherogenic Index, TG/HDL-C: triglyceride-to-HDL-C ratio.*A P-value <0.05 was considered significant and shown in bold.

Table 2 Comparison of categorical variables between overall cases (OW+OB) and normal weight controls

Categorical variables	Response	All (males & females) N = 612			Males N = 336			Females N = 276		
		OB+OW N = 306	Controls N = 306	*P*-value	OB+OW N = 168	Controls N = 168	*P*-value	OB+OW N = 138	Controls N = 138	*P*-value
Demographic characteristics										
Parental consanguinity [a]	Yes	74 (24.2%)	67 (4.9%)	0.565	45 (26.8%)	38 (22.6%)	0.448	29 (21.0%)	29 (21.0%)	1.00
	No	232 (75.8%)	239 (78.1%)		123 (73.2%)	130 (77.4%)		109 (79.0%)	109 (79.0%)	
Family history of obesity [b]	Yes	185 (60.5%)	105 (34.3%)	**<0.001***	89 (53.0%)	50 (29.8%)	**<0.001***	96 (69.6%)	55 (39.9%)	**<0.001***
	No	121 (39.5%)	201 (55.7%)		79 (47.0%)	118 (70.2%)		42 (30.4%)	83 (60.1%)	
Eating behavior										
Eating timing	Random	200 (65.4%)	163 (53.3%)	**0.003***	111 (66.1%)	86 (51.2%)	**0.008***	89 (64.5%)	77 (55.8%)	0.176
	Specific	106 (34.6%)	143 (46.7%)		57 (33.9%)	82 (48.8%)		49 (35.5%)	61 (44.2%)	
Diet unconsciousness	Yes	226 (73.9%)	210 (68.6%)	0.152	134 (79.8%)	115 (68.5%)	**0.025***	92 (66.7%)	95 (68.8%)	0.797
	No	80 (26.1%)	96 (31.4%)		31 (20.2%)	53 (31.5%)		46 (33.3%)	43 (31.2%)	
TFDF	High	113 (36.9%)	59 (19.3%)	**<0.001***	68 (40.5%)	38 (22.6%)	**0.002***	45 (32.6%)	21 (15.2%)	**0.003***
	Moderate-low	193 (63.0%)	247 (80.7%)		100 (59.5%)	130 (77.3%)		93 (67.4%)	117 (84.6%)	
Ethnicity										
Urdu speaking		172 (56.2%)	169 (55.2%)		94 (56.0%)	81 (48.2%)		78 (56.5%)	88 (63.8%)	
Punjabi		55 (18.0%)	56 (18.3%)		29 (17.3%)	18 (10.7%)		26 (18.8%)	38 (27.5%)	
Sindhi		23 (7.5%)	24 (7.8%)		13 (7.7%)	21 (12.5%)		10 (7.2%)	3 (2.2%)	
Pashtun		34 (11.1%)	30 (9.8%)	-	20 (11.9%)	26 (15.5%)	-	14 (10.1%)	4 (2.9%)	-
Balochi		8 (2.6%)	5 (1.6%)		3 (1.8%)	4 (2.4%)		5 (3.6%)	1 (0.7%)	
Other		14 (4.6%)	22 (7.2%)		9 (5.4%)	18 (10.7%)		5 (3.6%)	4 (2.9%)	

Categorical variables are represented as counts with percentages in parenthesis. Demographic characteristics and parameters of eating behavior are compared between cases and controls by Fisher's exact test. [a] Parental consanguinity was taken as marriage with a first cousin. [b] Family history of obesity was taken as presence or absence of obesity in parents and siblings. Abbreviations; OW+OB: overweight and obese cases, TFDF, tendency toward fat dense food. *A P-value <0.05 was considered significant

Table 3 Comparison of continuous variables between obese cases (BMI $\geq$ 30 kg/m^2) and normal weight controls

Continuous study variables	All (males and females) N = 388			Males N = 214			Females N = 174		
	Obese N = 194	Controls N = 194	*P*-value	Obese N = 107	Controls N = 107	*P*-value	Obese N = 87	Controls N = 87	*P*-value
Anthropometric parameters									
Weight (kg)	289.47	99.53	**<0.001***	159.81	55.19	**<0.001***	130.97	44.03	**<0.001***
Height (cm)	187.90	201.10	0.246	103.50	111.50	0.346	81.13	93.87	0.095
BMI (kg/m^2)	291.50	97.50	**<0.001***	161.00	54.00	**<0.001***	131.00	44.00	**<0.001***
WC (cm)	290.48	98.52	**<0.001***	160.32	54.68	**<0.001***	130.74	44.26	**<0.001***
HC (cm)	289.55	99.45	**<0.001***	159.63	55.37	**<0.001***	130.59	44.41	**<0.001***
WHR	263.97	125.03	**<0.001***	144.01	70.99	**<0.001***	121.29	53.71	**<0.001***
Biceps SFT (mm)	270.25	118.75	**<0.001***	151.46	63.64	**<0.001***	125.05	49.95	**<0.001***
Triceps SFT (mm)	283.99	105.01	**<0.001***	158.45	56.55	**<0.001***	126.32	49.95	**<0.001***
Abdominal SFT (mm)	281.90	107.10	**<0.001***	155.86	55.14	**<0.001***	127.02	47.98	**<0.001***
Supra-iliac SFT (mm)	277.33	111.67	**<0.001***	157.73	57.27	**<0.001***	122.57	52.83	**<0.001***
Thigh SFT (mm)	287.16	101.84	**<0.001***	159.88	55.12	**<0.001***	126.76	48.24	**<0.001***
Sub-scapular SFT (mm)	279.64	107.91	**<0.001***	155.33	60.20	**<0.001***	127.52	47.48	**<0.001***
% Body fat	288.09	100.91	**<0.001***	159.66	55.34	**<0.001***	129.53	45.47	**<0.001***
Metabolic parameters									
Systolic BP (mmHg)	227.54	161.46	**<0.001***	117.30	97.70	**0.016***	110.64	64.54	**<0.001***
Diastolic BP (mmHg)	223.47	155.53	**<0.001***	121.20	93.80	**0.001***	102.77	72.23	**<0.001***
VAI (mmol L-1)	225.97	163.03	**<0.001***	124.03	90.97	**<0.001***	103.26	71.74	**<0.001***
LAP (mmol L-1)	278.04	110.96	**<0.001***	153.83	61.17	**<0.001***	124.68	50.32	**<0.001***
TyG index	232.18	156.82	**<0.001***	129.08	85.92	**<0.001***	103.65	71.35	**<0.001***
FBG (mg/dl)	216.07	172.93	**0.003***	116.98	98.11	**0.026***	100.30	74.70	**0.001***
Insulin (μl U/ml)	243.75	145.25	**<0.001***	140.77	74.23	**<0.001***	103.89	71.11	**<0.001***
HOMA-IR	245.91	143.09	**<0.001***	141.45	73.55	**<0.001***	109.01	70.85	**<0.001***
HOMA-IS	143.09	245.91	**<0.001***	73.55	141.45	**<0.001***	69.34	105.66	**<0.001***
Cholesterol (mg/dL)	211.32	177.68	**0.003***	120.72	94.28	**0.002***	90.26	88.77	0.368
Triglycerides (mg/dL)	227.07	161.93	**<0.001***	127.76	87.24	**<0.001***	100.22	74.48	**0.001***
HDL-C (mg/dL)	193.34	195.66	0.839	111.72	103.28	0.319	81.96	93.04	0.147
LDL-C (mg/dL)	234.43	154.57	**<0.001***	134.49	80.51	**<0.001***	100.38	74.62	**0.001***
VLDL-C (mg/dL)	224.78	164.22	**<0.001***	126.18	88.82	**<0.001***	99.19	75.81	**<0.001***
CHR	210.83	178.17	**0.004***	115.56	99.44	0.057	95.74	79.26	**0.031***

CRI	210.77	178.23	**0.004***	115.01	99.99	0.076	96.07	78.93	**0.025***
AI	232.70	156.30	**<0.001***	130.06	84.94	**<0.001***	103.67	71.33	**<0.001***
TG/HDL-C	223.23	165.77	**<0.001***	122.66	92.34	**<0.001***	101.25	73.75	**<0.001***

Continuous study variables are expressed in mean ranks and compared by Mann–Whitney U test between cases and controls. Abbreviations; OW+OB: overweight and obese, BMI: body mass index, WC: waist circumference, HC: hip circumference, WHR: waist-to-hip ratio, SFT: skin fold thickness, BP: blood pressure, VAI: visceral adiposity index, LAP: lipid accumulation product, TyG: product of triglyceride and glucose, FBG: fasting blood glucose, HOMA-IR: homeostasis model assessment of insulin resistance, HDL: high density lipoprotein, LDL: low density lipoprotein, VLDL: very low density lipoprotein, CHR: cholesterol HDL ratio, CRI: Coronary Risk Index, AI: Atherogenic Index, TG/HDL-C: triglyceride-to-HDL-C ratio.*A P-value <0.05 was considered significant.

Table 4 Comparison of categorical study variables between obese cases (BMI ≥ 30 kg/m^2) and normal weight controls

Categorical study variables	Response	All (males & females) $N = 388$			Males $N = 214$			Females $N = 174$		
		Obese $N = 194$	Controls $N = 194$	*P*-value	Obese $N = 107$	Controls $N = 107$	*P*-value	Obese $N = 87$	Controls $N = 87$	*P*-value
Demographic characteristics										
Parental consanguinity [a]	Yes	46 (23.7%)	41 (21.1%)	0.626	27 (25.2%)	26 (24.3%)	1.000	19 (21.8%)	15 (17.2%)	0.567
	No	148 (76.3%)	153 (78.9%)		80 (74.8%)	81 (75.7%)		68 (78.2%)	72 (82.8%)	
Family history of obesity [b]	Yes	100 (55.5%)	75 (39.3)	**0.014***	54 (50.5%)	41 (38.3%)	0.098	46 (52.9%)	34 (39.1%)	0.094
	No	94 (48.5%)	119 (60.7%)		53 (49.5%)	66 (61.7%)		41 (47.1%)	53 (60.9%)	
Eating behavior										
Eating timings	Random	131 (67.4%)	96 (49.5%)	**<0.001***	71 (66.4%)	54 (50.5%)	**0.026***	60 (69.0%)	42 (48.3%)	**0.009***
	Specific	63 (32.5%)	98 (50.5%)		36 (33.6%)	53 (49.5%)		27 (31.0%)	45 (51.7%)	
Diet unconsciousness	Yes	148 (76.3%)	133 (68.6%)	0.112	88 (82.2%)	75 (70.1%)	0.054	60 (69.0%)	58 (66.7%)	0.871
	No	46 (23.7%)	61 (31.4%)		19 (17.8%)	32 (29.9%)		27 (31.0%)	29 (33.3%)	
TFDF [c]	High	77 (39.7%)	38 (19.6%)	**<0.001***	49 (45.8%)	27 (25.2%)	**0.003***	28 (32.2%)	11 (12.6%)	**0.003***
	Moderate-low	117 (60.3%)	156 (80.4%)		58 (54.2%)	80 (74.8%)		59 (67.8%)	76 (87.4%)	
Ethnicity										
Urdu speaking		112 (57.7%)	106 (54.6%)		65 (60.7%)	54 (50.5%)		47 (54.0%)	52 (59.8%)	
Punjabi		35 (18.0%)	37 (19.1%)		17 (15.9%)	11 (10.3%)		18 (20.7%)	26 (29.9%)	
Sindhi		10 (5.2%)	16 (8.2%)		5 (4.7%)	14 (13.1%)		5 (5.7%)	2 (2.3%)	
Pakhtun		23 (11.9%)	20 (10.3%)	-	14 (13.1%)	17 (15.9%)	-	9 (10.3%)	3 (3.4%)	-
Balochi		7 (3.6%)	3 (1.5%)		3 (2.8%)	2 (1.9%)		4 (4.6%)	1 (1.1%)	
Other		7 (3.6%)	12 (6.2%)		3 (2.8%)	9 (8.4%)		4 (4.6%)	3 (3.4%)	

Categorical variables are represented as counts with percentages in parenthesis. Demographic characteristics and parameters of eating behavior are compared between cases and controls by Fisher's exact test. [a] Parental consanguinity was taken as history of marriage with a first cousin. [b] Family history of obesity was taken as presence or absence of obesity in parents and siblings. [c]Tendency towards fat dense food. *A *P*-value <0.05 was considered significant.

Table 5 Genotypic frequencies of the *NEGR1* rs2815752 variant among cases (overweight and obese) and controls and assessment of the rs2815752 association with overweight/obesity

Genetic Model	Genotype	Cases Count (%)	Controls Count (%)	Adjusted OR[a] (95% CI)	Adjusted *P*-value[a]
Co-dominant	GG	35 (11.44)	42 (13.73)	-	-
	GA	133(43.46)	132 (43.14)		
	AA	138 (45.10)	132 (43.14)		
Pair-wise comparison	GG vs. GA	-	-	1.207 (0.724-2.012)	0.470
	GG vs. AA			1.278 (0.767-2.128)	0.347
Dominant	(GA+AA)	271(88.56)	264 (86.27)	1.242 (0.768-2.009)	0.378
	GG	35 (11.44)	42 (13.73)		
Recessive	AA	138 (45.10)	131 (42.81)	1.104 (0.801-1.521)	0.546
	(GG+GA)	168 (54.90)	175 (57.19)		
Over-dominant	GA	133 (43.46)	133 (43.46)	0.998 (0.724-1.376)	0.990
	(GG+AA)	173 (56.54)	173 (56.54)		
Hardy–Weinberg Equilibrium (HWE):					
Cases					0.729
Controls					0.333

Data represents genotype counts and percentages in parenthesis in cases and controls. Data also indicate genotypic frequencies in HWE. Associations were tested using chi-square and multinomial regression for co-dominant model and binary logistic regression for other models. [a]Analysis was also performed with adjustment for age and gender. An adjusted *P*-value <0.05 was considered significant. Abbreviations: GG: wild-type homozygous genotype; GA: heterozygous genotype; AA: mutant homozygous genotype; OR: odds ratio; CI: confidence interval.