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Evaluation of prediabetes patients in terms of metabolic syndrome

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Abstract. – OBJECTIVE: Prediabetes accompanied by metabolic syndrome accelerates the process leading to diabetes and causes an increase in complications. The current study aimed to investigate the clinical conditions accompanying prediabetes and the effect of the association of metabolic syndrome on clinical outcomes in prediabetics.

SUBJECTS AND METHODS: This cross-sectional study was conducted with 88 prediabetic individuals between November 2022 and January 2023. Prediabetes was diagnosed using the American Diabetes Association (ADA) criteria, and metabolic syndrome was diagnosed using the International Diabetes Federation criteria. Clinical history, physical examination and laboratory tests of the participants were recorded.

RESULTS: Metabolic syndrome (MetS) was present in 69 of 88 prediabetic patients included in the study (78.4%). Hypertension (p=0.019), abdominal obesity (p<0.001), low-density lipoprotein (LDL) elevation (p=0.006), and dyslipidemia (p=0.020) were detected more frequently in prediabetic individuals accompanied by MetS. Median values of waist circumference (p=0.020), systolic blood pressure (p=0.021), triglyceride (p<0.001), LDL (p=0.003) and postprandial blood sugar (p=0.049) in prediabetics accompanied by MetS were statistically significant. It was higher than those without MetS. The median Vit-D level of prediabetics without MetS was higher than those with MetS (p=0.049). The median creatinine value of prediabetics without MetS was higher than that of prediabetics with MetS (p=0.049).

CONCLUSIONS: Hypertension, dyslipidemia, abdominal obesity, and metabolic obesity increased in the coexistence of prediabetes and MetS. At the same time, the coexistence of prediabetes and MetS was associated with higher systolic blood pressure, postprandial blood sugar, and LDL levels. Prediabetic individuals accompanied by MetS are at greater metabolic risk.

Key Words:
Prediabetes, Metabolic Syndrome, Abdominal obesity, Dyslipidemias, Blood pressure.

Introduction

Prediabetes is the clinical condition in which blood sugar levels are higher than normal but lower than the diagnostic criteria for type II diabetes, with abnormal glucose hemostasis a precursor to type II diabetes. The increase in insulin resistance and the decrease in β-cell function make blood glucose levels irregular and first pre-diabetes then turns into diabetes[1]. It is estimated that there are over 470 million prediabetic cases worldwide today, and this number is on an alarmingly increasing trend[2]. The Center for Disease Control and Prevention (CDC) reported that nearly half (48.3%) of the adult population aged 65 and older had prediabetic conditions in 2015, and approximately 84.1 million people in the United States were already prediabetic. Previous scholars[2] have reported that 37% of untreated prediabetes develop diabetes within 4 years. Additionally, long-term studies have shown that with lifestyle changes and medical treatment, the risk of this progression from prediabetes to diabetes can be reduced over a longer period of 10 years[3].

Current data have reported that diabetes mellitus-related disorders can also be seen in prediabetics. Diseases such as diabetes-related cardiovascular disease (CVD), periodontal disease, cognitive dysfunction, microvascular disease, blood pressure abnormalities, obstructive sleep apnea (OSA), low testosterone, metabolic syndrome, fatty liver disease, and cancer are also associated with prediabetes[4]. Prediabetes is often referred to as "benign" in the absence of comorbidities. Early intervention in prediabetic individuals is vital to prevent related conditions[4]. Metabolic syndrome is the most important clinical condition accompanying prediabetes. A previous study[5] reported that approximately 2/3 of prediabetic individuals had metabolic syndrome. Another study[6] showed

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that one-third of patients with metabolic syndrome had prediabetes, but more than half of prediabetics had metabolic syndrome. Prediabetes, accompanied by metabolic syndrome, accelerates the process leading to diabetes and causes an increase in complications. It is known that the risk of cardiovascular disease increases in the presence of prediabetes and metabolic syndrome (MetS). Chen et al[7] reported 1.5 times more cardiovascular events in prediabetics with MetS than in those without MetS. Previous studies[8,9] have also shown that the risk of neuropathy and non-alcoholic liver disease increases in prediabetes accompanied by MetS. In addition to these conditions, many pathologies, such as nephropathy, cognitive dysfunction, obstructive sleep apnea, and sexual dysfunction, have been associated with the coexistence of prediabetes and MetS[10]. Studies examining the effect of metabolic syndrome accompanying prediabetes on these diseases are limited.

The current study aimed to investigate the clinical conditions accompanying prediabetes and the effect of the association of metabolic syndrome on clinical outcomes in prediabetics.

Subjects and Methods

Study Design and Population

This cross-sectional study was conducted between November 2022 and January 2023 in the diabetes clinic of a tertiary care center in the Eastern Anatolia Region of Turkey. The study population consisted of all individuals over the age of 18 who were newly diagnosed with prediabetes in our clinic. The sample size calculation was performed using the open-access statistical program available at http://biostatapps.inonu.edu.tr/WSSPAS/. The type error (alpha) was 0.05, the power of the test (1-beta) was 0.8, the effect size was 0.20, and the minimum sample size required for a significant difference for a single sample proportion test was 37[5]. A total of 88 prediabetic individuals were included in the study. All 88 prediabetic individuals included in the study were newly diagnosed patients. Patients who did not receive any treatment for prediabetes were included in the study. While selecting the study patients, patients with normal levels of vitamin B12 and folic acid were included. Pregnancy, lactation, known neurological and renal disease, receiving treatment for chemotherapy, radiotherapy or rheumatological disease, organ transplant, acute infection (urinary system, etc.), hematuria, gout, chronic liver disease, alcohol use, HAV, HBV, HCV, HIV-infected patients were excluded from the study.

The current study was approved by the ethics committee of İnonu University in accordance with the Declaration of Helsinki, and written informed consent was obtained from each participant (Date: 2022; number: 114).

Diagnostic Criteria for Prediabetes and MetS

Prediabetes was diagnosed by one of the following three principles According to the American Diabetes Association (ADA) criteria: (1) HbA1c: 5.7%-6.4%; (2) fasting plasma glucose: 100 mg/dl (5.6 mmol/l)-125 mg/dl (7.0 mmol/L); (3) oral glucose tolerance test: 140 mg/dl (7.8 mmol/l)-199 mg/dl (11.0 mmol/L)[11].

Patients with a body mass index (BMI) of 25-30 kg/m^2 were diagnosed as overweight, and those with BMI ≥30 kg/m^2 were diagnosed as obese. For some comparisons, we categorized BMI ≥27 kg/m^2 as metabolically obese[12]. Participants' waist circumference was measured to diagnose central obesity. Waist circumference (in centimeters) was collected with non-extendable tape from the midpoint between the iliac crest and the last rib. The measurement was made twice to avoid inconsistency, and the average was recorded. The waist circumference cut-off value for central obesity was ≥90 cm for women and obese ≥100 cm for men[13,14].

Dyslipidemia (DL) was classified as follows: triglyceride (TG) ≥150 mg/dl, low-density lipoprotein cholesterol (LDL-C) ≥100 mg/dl, high-density lipoprotein cholesterol (HDL-C) <60 mg/dl. Arterial blood pressure (ABP) was classified as follows: normal (<120/80 mmHg), elevated blood pressure (120-139/80-89 mmHg); hypertension (≥140/90 mmHg). For some comparisons, we categorized blood pressure (BP) ≥130/85 mmHg as high normal BP[15].

Metabolic syndrome was diagnosed by three of the following five criteria: i) elevated waist circumference [the waist circumference (WC) cutoff levels of 100 cm define obese males while the levels of 90 cm define obese females for Turkey]; ii) elevated triglycerides ≥150 mg/dL (1.7 mmol/L); iii) reduced HDL-C <40 mg/dL (1.0 mmol/L) in males and <50 mg/dL (1.3 mmol/L) in females; iv) elevated blood pressure systolic ≥130 and/or diastolic ≥85 mm Hg; v) elevated fasting glucose ≥100 mg/dL[13,14].

Non-invasive scoring systems were used to calculate patients' liver fibrosis risk. Participants' fibrosis risk was classified according to Fibrosis-4 (FIB-4) score (FIB-4 = age [years] × AST [U/L])/([platelets (10^9/L)] × ALT/2 [U/L]). While a FIB-4 score <1.3 rejects the risk of fibrosis at a 90% level, a FIB-4 score of 1.3-2.67 indicates a moderate risk, and a FIB-4 score >2.67 indicates a high risk[16].

Insulin resistance of the participants was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR) formula: fasting plasma glucose (mmol/L) × fasting plasma insulin (mIU/L)/22.5; a cut-off value of ≥2.5 was considered to ascertain insulin resistance[11]. A positive history of coronary artery disease (CAD) was noted. In addition, the electrocardiography (ECG) results of all participants were examined for vascular complications according to the Minnesota Code Classification[11].

Vitamin D deficiency was defined as a 25(OH)D below 20 ng/ml (50 nmol/liter), and vitamin D insufficiency as a 25(OH)D of 21-29 ng/ml (525-725 nmol/liter)[17]. The C-reactive protein (CRP) level of patients was categorized as <3.5 mg/L normal and >3.5 mg/L high. CRP level between 3.5-10 mg/L is minor inflammation, and CRP level >10 mg/L is significant inflammation[18].

Prediabetes and MetS diagnosis and all the above classifications were confirmed by expert endocrinologists, taking into account the diagnostic criteria[11].

Statistical Analysis

Statistical analysis of the study data was performed with the IBM SPSS 23 package program (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was analyzed with the Shapiro-Wilk test. Categorical variables were presented as frequency (n) and percentage (%), and continuous variables were presented as mean (standard deviation) or median (min-max), considering their distribution. Pearson Chi-square test or Fisher's Exact test was used to analyze categorical data. Data that conformed to normal distribution between two independent groups were compared with the student *t*-test, and data that did not conform to normal distribution were compared with the Mann-Whitney U test. $p<0.05$ was considered statistically significant.

Results

A total of 88 prediabetic patients, 44 (50.0%) women, and 44 (50.0%) men, were included in the study. The mean age was 47.6 years (SD ± 9.2). Prediabetes was accompanied by MetS in 37 (84.1%) of the women and 32 (72.7%) of the men. Obesity (BMI>30) ($p=0.005$) and abdominal obesity ($p=0.002$) were statistically significantly higher in women than in men. There was no significant difference between genders in terms of the presence of MetS risk factors (Table I).

The median BMI of women was higher than men ($p=0.005$). Both AST ($p=0.003$) and ALT ($p<0.001$) median values of men were higher than women. The biochemical and hematological parameters of the participants are presented in Table II.

The frequency and components of MetS in our prediabetic patient population are presented in Table III. MetS was present in 69 of 88 prediabetic patients included in the study (78.4%). Hypertension ($p=0.019$), abdominal obesity ($p<0.001$), LDL elevation ($p=0.006$), and dyslipidemia ($p=0.020$) were detected more frequently in prediabetic individuals accompanied by MetS (Table III).

Some demographic, biochemical and hematological characteristics of the study population, divided by MetS, are presented in Table IV. Median values of waist circumference ($p=0.020$), systolic blood pressure ($p=0.021$), triglyceride ($p<0.001$), LDL ($p=0.003$) and postprandial blood sugar ($p=0.049$) in prediabetics accompanied by MetS were statistically significant. It was higher than those without MetS. The median Vit-D level of prediabetics without MetS was higher than those with MetS ($p=0.049$). The creatinine ratio of prediabetics without Mets was higher than that of prediabetics with Mets ($p=0.049$) (Table IV).

Discussion

The prevalence of MetS in the prediabetic study population was 78.4%. Although the prevalence of MetS is difficult to assess, its prevalence has been reported to be approximately 30% in the adult population in the United States[19]. Duarte et al[20] reported the prevalence of adult MetS as 45% in their study in the urban population. It is expected that the prevalence of MetS will be higher in the prediabetic population. Previous studies reported the prevalence of MetS in prediabetic

Table I. Baseline characteristics of study populations by gender.

Variables		Male (n=44) n (%)	Female (n=44) n (%)	*p*-value
MetS	Have not	12 (27.3)	7 (15.9)	0.195[a]
	Have	32 (72.7)	37 (84.1)	
Age (year)	<40	11 (25.0)	5 (18.2)	0.097[a]
	≥40	33 (75.0)	39 (81.8)	
HBA1C (%)	< 6%	29 (65.9)	20 (45.5)	0.053[a]
	≥ 6%	15 (34.1)	24 (54.5)	
Prediabetes type	IFG	17 (38.6)	10 (22.7)	0.248[a]
	IGT	3 (6.8)	5 (11.4)	
	CGI	24 (54.5)	29 (65.9)	
Prediabetes type (according to CGI)	IFG or IGT	20 (45.5)	15 (34.1)	0.276[a]
	CGI	24 (54.5)	29 (65.9)	
MetS (WC ≥102/88 cm)	Have	12 (27.3)	7 (15.9)	0.195[a]
	Have not	32 (72.7	37 (84.1)	
MetS (WC ≥100/90 cm)	Have	12 (27.3)	7 (15.9)	0.195[a]
	Have not	32 (72.7)	37 (84.1)	
Blood pressure (mmHg)	Normal (<120/80)	10 (22.7)	9 (20.5)	0.796[a]
	Increased (≥120/80)	34 (72.8)	35 (79.5)	
HOMA-IR (≥2.5)	No	17 (38.6)	14 (31.8)	0.503[a]
	Yes	27 (61.4)	30 (68.2)	
BMI (kg/m^2)	Normal <25	5 (11.4)	0 (0.0)	**0.005[b]**
	Overweight=25-29.9	20 (45.5)	14 (31.8)	
	Obese ≥30	19 (43.2)	30 (68.2)	
BMI (kg/m^2)	<27	10 (22.7)	3 (6.8)	**0.035[a]**
	≥27	34 (77.3)	41 (93.2)	
Abdominal obesity (WC≥100/90 cm)	No	11 (25.0)	1 (2.3)	**0.002[a]**
	Yes	33 (75.0)	43 (97.7)	
Abdominal obesity (WC≥102/88 cm)	No	15 (34.1)	2 (4.5)	**<0.001[a]**
	Yes	29 (65.9)	42 (95.5)	
Abdominal fat (WC≥90/80 cm)	No	3 (6.8)	0 (0.0)	0.241[b]
	Yes	41 (93.2)	44 (100.0)	
Triglyceride (mg/dL)	<150	23 (52.3)	25 (56.8)	0.669[a]
	≥150	21 (47.7)	19 (43.2)	
LDL (mg/dL)	LDL <100	13 (29.5)	10 (22.7)	0.467[a]
	LDL ≥100	31 (70.5)	34 (77.3)	
HDL (mg/dL)	HDL ≥60	6 (13.6)	15 (34.1)	**0.024[a]**
	HDL <60	38 (86.4)	29 (65.9)	
Dyslipidemia	No	35 (79.5)	35 (79.5)	>0.999[a]
	Yes	9 (20.5)	9 (20.5)	
Smoking	No	23 (52.3)	35 (79.5)	**0.007[a]**
	Yes	21 (47.7)	9 (20.5)	
HTN	No	37 (84.1)	28 (63.6)	**0.029[a]**
	Yes	7 (15.9)	16 (36.4)	
History of dyslipidemia	No	38 (86.4)	42 (95.5)	0.266[b]
	Yes	6 (13.6)	2 (4.5)	
Family history-DM	No	16 (36.4)	18 (40.9)	0.661[a]
	Yes	28 (63.6)	26 (59.1)	
MetS risk factor	No	2 (4.7)	0 (0.0)	0.241[b]
	Yes	42 (95.3)	44 (100.0)	
Vit-D (ng/ml)	≤20	23 (52.3)	33 (75.0)	**0.027[a]**
	>20	21 (47.7)	11 (25.0)	
FIB-4 (fibrosis-4) score	Low <1.3	35 (79.5)	42 (95.5)	**0.049[b]**
	Moderate risk 1.3-2.67	8 (18.2)	2 (4.5)	
	High ≥2.67	1 (2.3)	0 (0.0)	
CAD	No	37 (84.1)	42 (95.5)	0.151[b]
	Yes	7 (15.9)	2 (4.5)	
History of CAD	No	34 (77.3)	36 (81.8)	0.597[a]
	Yes	10 (22.7)	8 (18.2)	
Ischemia on ECG	No	41 (93.2)	38 (86.4)	0.484[b]
	Yes	3 (6.8)	6 (13.6)	

[a]Pearson Chi-square test; [b]Fischer's Exact test; HTN: Hypertension; MetS: metabolic syndrome; BMI: body mass index; WC: waist circumference; LDL: low density lipoprotein; HDL: high density lipoprotein; DM: diabetes mellitus; CAD: coronary artery disease; ECG: electrocardiography.

Table II. Descriptive statistics of numerically structured features.

Variables	Male	Female	p	Variables	Male	Female	p
Age (year)	47.3±10.1	48.0±8.3	0.705	Creatinine	0.9 (0.7-1.3)	0.7 (0.6-1.0)	**<0.001**
Weight (kg)	88.3 (56.4-151.0)	78.3 (54.1-128.0)	**0.028**	Uric acid	5.5±1.4	4.6±0.9	**0.003**
Height (cm)	171.0 (162.0-183.0)	159.5 (143.0-168.0)	**<0.001**	PCR (MG/G)	80.0 (29.0-315.0)	84.0 (25.0-188.0)	0.383
BMI	29.4 (19.5-54.8)	31.8 (26.5-58.4)	**0.005**	GFR-MDRD	93.3±15.7	90.7±13.3	0.406
WC (cm)	103.0 (76.0-140.0)	106.0 (85.0-140.0)	0.312	Albumin	4.5±0.3	4.5±0.3	0.822
SBP (mmHg)	125.7±12.3	123.6±18.3	0.527	AST	25.0 (13.0-98.0)	20.0 (15.0-51.0)	**0.003**
DBP (mmHg)	79.6±7.6	82.6±9.6	0.114	ALT	27.5 (12.0-136.0)	19.5 (10.0-101.0)	**<0.001**
TG	145.5 (64.0-331.0)	129.5 (20.0-380.0)	0.704	WBC	7.6 (5.7-27.9)	7.7 (84.4-16.6)	0.502
LDL	117.1 (53.8-204.0)	124.5 (54.8-261.2)	0.274	Hb	14.5 (12.2-17.5)	13.6 (9.2-15.0)	**<0.001**
HDL	45.2±9.5	54.3±12.7	**<0.001**	Platelet	252.5 (136.0-594.0)	287.0 (212.0-549.0)	**0.006**
HBA1C	5.9±0.2	5.9±0.2	0.259	Vit-D	19.3 (4.9-43.7)	12.4 (3.3-50.9)	**0.003**
FBG	108.2±7.5	106.2±8.8	0.264	Vit-B12	174.0 (105.0-479.0)	202.0 (104.0-762.0)	**0.033**
OGTT-2hr	148.2 (58.0-199.0)	163.1 (33.2-169.5)	0.080	Folic acid	7.8 (4.4-15.0)	8.6 (4.8-18.5)	**0.040**
C-peptide	2.1 (0.7-6.5)	2.0 (0.9-6.9)	0.086	Zinc	102.6±12.4	99.4±10.9	0.207
Insulin	12.3 (1.5-28.9)	11.5 (5.2-33.4)	0.877	FIB-4 score	0.8 (0.3-3.2)	0.8 (0.3-1.9)	0.278
HOMA-IR	3.3 (0.4-8.3)	3.3 (1.4-8.5)	0.894	AST/PLT ratio	0.1 (0.04-8.6)	0.1 (0.03-0.2)	**0.001**
BUN	13.8 (7.9-26.2)	12.4 (7.5-21.5)	0.096	AST/ALT ratio	0.9±0.3	1.1±0.3	**0.001**

BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: Triglyceride; LDL: low density lipoprotein; HDL: high density lipoprotein; FBG: fasting blood glucose; WBC: white blood cell; Hb: hemoglobin.

Table III. Frequency and relationship of MetS according to various factors.

Variables		MetS No (n=19) n (%)	MetS Yes (n=69) n (%)	Total (n=88) n (%)	*p*-value
Age (year)	<40	3 (15.8)	13 (18.8)	16 (18.2)	0.760[a]
	≥40	16 (84.2)	56 (81.2)	72 (81.8)	
Gender	Male	12 (63.2)	32 (46.4)	44 (50.0)	0.195[a]
	Female	7 (36.8)	37 (53.6)	44 (50.0)	
Smoking	No	15 (78.9)	43 (62.3)	58 (65.9)	0.176[a]
	Yes	4 (21.1)	26 (37.7)	30 (34.1)	
History of HT	No	18 (94.7)	47 (68.1)	65 (73.9)	**0.019[a]**
	Yes	1 (5.3)	22 (31.9)	23 (26.1)	
History of dyslipidemia	No	19 (100.0)	61 (88.4)	80 (90.9)	0.120[b]
	Yes	0 (0.0)	8 (11.6)	8 (9.1)	
MetS risk factor	No	14 (73.7)	27 (39.1)	41 (46.6)	**0.008[a]**
	Yes	5 (26.3)	42 (60.9)	47 (53.4)	
Prediabetes type	IFG or IGT	11 (57.9)	24 (34.8)	35 (39.8)	0.068[a]
	CGI	8 (42.1)	45 (65.2)	53 (60.2)	
Abdominal obesity (WC>102/88 cm)	No	19 (100.0)	0 (0.0)	19 (21.6)	**<0.001[a]**
	Yes	0 (0.0)	69 (100.0)	69 (78.4)	
Abdominal obesity (WC≥100/90 cm)	No	19 (100.0)	0 (0.0)	19 (21.6)	**<0.001[a]**
	Yes	0 (0.0)	69 (100.0)	69 (78.4)	
Abdominal fat (WC≥90/80 cm)	No	1 (5.3)	2 (2.9)	3 (3.4)	0.523[b]
	Yes	18 (94.7)	67 (78.8)	85 (96.6)	
BMI (kg/m^2)	<27	6 (31.6)	7 (10.1)	13 (14.8)	**0.020[a]**
	≥27	13 (68.4)	62 (89.9)	75 (85.2)	
BMI (kg/m^2)	<30	11 (57.9)	28 (40.6)	39 (44.3)	0.179[a]
	≥30	8 (42.1)	41 (59.4)	49 (55.7)	
HbA1c (%)	<6	12 (63.2)	37 (53.6)	49 (55.7)	0.459[a]
	≥6	7 (36.8)	32 (46.4)	39 (44.3)	
HOMA-IR (≥2.5)	No	9 (47.4)	22 (31.9)	31 (35.2)	0.211[a]
	Yes	10 (52.6)	47 (68.1)	57 (64.8)	
Dyslipidemia	Have not	11 (57.9)	59 (85.5)	70 (79.5)	**0.020[b]**
	Have	8 (44.4)	10 (14.5)	18 (20.5)	
LDL (mg/dL)	<100	10 (52.6)	13 (18.8)	23 (26.1)	**0.006[b]**
	≥100	9 (47.4)	56 (81.2)	65 (73.9)	
History of CAD	No	17 (89.5)	62 (89.9)	79 (89.8)	0.961[a]
	Yes	2 (10.5)	7 (10.1)	9 (10.2)	
FIB-4 score	Low< 1.3	17 (89.5)	60 (87.0)	77 (87.5)	0.769[a]
	≥1.3	2 (10.5)	9 (13.0)	11 (12.5)	
Hyperuricemia	No	16 (84.2)	55 (79.7)	71 (80.7)	0.660[a]
	Yes	3 (15.8)	14 (20.3)	17 (9.3)	
CRP (mg/mL)	3-10	14 (73.7)	59 (85.5)	73 (83.0)	0.225[a]
	≥ 10	5 (26.3)	10 (15.5)	15 (17.0)	
Increased CRP	No	11 (57.9)	42 (60.9)	53 (60.2)	0.815[a]
	Yes	8 (42.1)	27 (39.1)	35 (39.8)	
Vit-D (ng/ml)	≤20	9 (47.4)	47 (68.1)	19 (21.6)	0.096[a]
	>20	10 (52.6)	22 (31.9)	69 (78.4)	

[a]Pearson Chi-square test; [b]Fischer's Exact test, IFG: impaired fasting glucose; IGT: impaired glucose tolerance, BMI: body mass index; WC: waist circumference; LDL: low-density lipoprotein; CAD: coronary artery disease.

individuals as 77.8% and 63%, respectively[5,20]. The primary aim of the current study is to draw attention to the accompanying metabolic syndrome in prediabetic individuals. Study data have shown that the majority of prediabetic individuals are affected by metabolic syndrome.

Obesity, abdominal fat, and increased waist circumference were found to be significantly higher in prediabetic individuals accompanied by MetS. Duarte et al[20] examined the frequency of prediabetes and MetS; they reported increased waist circumference in 2/3 of the population. In the same study, it was reported that increased waist circumference thickness was the most common component of MetS[20]. Rajput et al[5] reported the prevalence of central obesity as 80.2% in prediabetic men and 82.2% in prediabetic women. In this study, it was emphasized that the most

Table IV. Examination of some biochemical parameters in association with prediabetes and MetS.

Variables	MetS No (n=19) n (%)	MetS Yes (n=69) n (%)	*p*-value
Age (year)	48.3 ± 9.0	47.4 ± 9.3	0.715[a]
BMI (kg/m^2)	29.8 (19.5-49.0)	30.8 (22.9-58.4)	0.200[b]
FIB-4 score	0.9 (0.6-1.7)	0.8 (0.3-3.2)	0.135[b]
WC (cm)	98.0 (76.0-140.0)	106.0 (84.0-140.0)	**0.020[b]**
SBP (mmHg)	119.3 ± 9.0	126.1 ± 16.7	**0.021[a]**
DBP (mmHg)	78.4 ± 5.8	81.8 ± 9.3	0.126[a]
TG	80.0 (20.0-124.0)	162.0 (61.0-380.0)	**<0.001[b]**
HDL	54.0 (40.0-93.0)	47.0 (27.0-86.0)	0.079[b]
LDL	102.6 ± 22.5	133.6 ± 42.7	0.003[a]
AST	23.0 (15.0-44.0)	22.0 (13.0-98.0)	0.799[b]
ALT	23.0 (11.0-64.0)	24.0 (10.0-136.0)	0.633[b]
Vitamin-D (ng/mL)	20.4 (4.9-43.7)	16.2 (3.3-50.9)	**0.049[b]**
Vit-B12	173.0 (104.0-762.0)	184.0 (106.0-479.0)	0.285[b]
Folic acid	8.6 (4.5-14.2)	7.8 (4.4-18.5)	0.804[b]
Zinc	97.4 ± 12.9	102.0 ± 11.2	0.134[a]
FBG (mg/dl)	104.0 (94.0-125.0)	108.0 (84.0-122.0)	0.208[b]
PBG (mg/dl)	152.0 (59.0-198.0)	161.0 (58.0-199.0)	**0.049[b]**
HbA1c	5.9 (5.7-6.2)	5.9 (5.7-6.4)	0.650[b]
C-peptide	2.1 (0.7-6.9)	2.0 (0.9-5.1)	0.769[b]
Insulin	10.4 (1.7-33.4)	12.6 (1.5-28.9)	0.210[b]
HOMA-IR	3.2 (0.5-8.5)	3.4 (0.4-8.3)	0.262[b]
BUN	13.1 (9.4-26.2)	13.6 (7.5-21.5)	0.549[b]
Creatinine	0.9 (0.7-1.2)	0.8 (0.6-1.3)	**0.049[b]**
GFR-MDRD	88.0 ± 11.2	93.1 ± 13.9	0.177[a]
Urinary protein	13.0 (5.0-26.0)	12.0 (4.0-47.0)	0.431[b]
Urinary creatinine	159.0 (51.0-273.0)	141.0 (30.0-434.0)	0.757[b]
AST/PLT	0.08 (0.05-8.57)	0.08 (0.03-0.60)	0.156[b]
AST/ALT	1.1 ± 0.3	1.0 ± 0.3	0.370[a]
WBC	7.6 (4.7-12.2)	7.8 (4.4-27.9)	0.619[b]
Hb	15.0 (10.5-17.1)	14.1 (9.2-17.5)	0.218[b]
CRP	0.33 (0.32-14.2)	7.8 (4.4-18.5)	0.408[b]

[a]Independent samples *t*-test; [b]Mann-Whitney U test; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: Triglyceride; LDL: low density lipoprotein; HDL: high density lipoprotein; FBG: fasting blood glucose; PBG: postprandial blood glucose; WBC: white blood cell; Hb: hemoglobin.

common component of MetS is central obesity[5]. The current study and previous literature data have again shown the threat that increased waist circumference and central obesity pose to public health. This dangerous increase in abdominal obesity has increased cardiovascular morbidity and mortality[21]. Our findings and previous literature[5,20] suggest that policies that aggressively promote abdominal circumference reduction should be encouraged in both the prediabetic and general populations.

Lifestyle changes, prevention of diabetes, and treatment of hyperglycemia are of fundamental importance in reducing cardiovascular events in prediabetic individuals. Additionally, aggressive treatment of metabolic syndrome components is recommended[4]. In the current study, the frequency of hypertension, obesity, abdominal obesity, dyslipidemia, and increased LDL was more common in prediabetics accompanied by MetS. In addition, systolic blood pressure, triglyceride, LDL, waist circumference, and postprandial blood sugar were found to be higher in prediabetics with MetS. Chen et al[7] reported that waist circumference, systolic blood pressure, diastolic blood pressure, triglyceride, fasting, and postprandial blood sugar were higher in prediabetics with MetS than in prediabetics without MetS. In the same study, it was shown that MetS accompanying prediabetes increased the total risk of cardiovascular events by 1.92 times[7]. A previous prospective cohort study[22] showed that MetS-induced increased blood pressure, hyperglycemia, and dyslipidemia were associated with increased CVD risk. Current study data have shown that the treatment of prediabetes and MetS components should be done together in prediabetic in-

dividuals accompanied by MetS. Therefore, accounting for MS should not be ignored to reduce the risk of cardiovascular events in prediabetes.

Previous literature data[23] have reported an inverse relationship between plasma vitamin D concentrations and the features that define MetS, namely high serum glucose concentrations, total cholesterol, low-density lipoproteins, triglycerides, glycosylated hemoglobin, and high body mass index. A systematic review study reported that vitamin D reduces insulin resistance, T2D severity, prediabetes, metabolic syndrome, inflammation, and autoimmunity[24]. Additionally, low vitamin D levels have been reported to worsen hyperglycemia and glycemic control in prediabetic individuals[24]. In the current study, Vit-D levels were lower in prediabetics with MetS. Considering the possible relationship between vitamin D and metabolic diseases mentioned above, we recommend that vitamin D deficiency be taken into consideration.

In the current study, no significant difference was found in FIB-4 SCORE between prediabetics with and without MetS. The global prevalence of non-alcoholic fatty liver disease (NAFLD) is approximately 25% and is associated with components of metabolic syndrome[25]. Previous studies[26,27] reported that metabolic syndrome components (increased waist circumference, blood pressure, triglyceride, LDL, hyperglycemia, and low HDL) were seen more frequently in obese patients accompanied by NAFLD. Simple fibrosis scores, such as NAFLD fibrosis score, Fibrosis-4 (FIB-4) index, and aspartate aminotransferase-platelet ratio index, include demographic, clinical, and routine laboratory parameters and are inexpensive. Although the overall accuracy of these scores is moderate, they have high negative predictive values for excluding advanced liver fibrosis, especially in community and primary care settings[25]. NAFLD is known to be associated with many metabolic conditions (prediabetes, T2DM, obesity, metabolic syndrome, hypertension, and hyperlipidemia), and NAFLD is known to cause inflammation and fibrosis[27,28]. In this context, the coexistence of prediabetes and MetS is expected to be associated with a higher FIB-4 index. The current study was insufficient to explain the effect of the association of prediabetes and MetS on FIB-4 SCORE.

Limitations

The current study has some limitations. First, the cross-sectional design limits the ability to explain the association of prediabetes and MetS on outcomes. Prospective and long-term follow-up studies are needed to explain the effects of MetS on prediabetic individuals.

The prevalence of MetS we found in prediabetic individuals may not represent the general population since the study was conducted in a single center. Another limitation is that the duration of exposure of prediabetic individuals and individuals with MetS to prediabetes and MetS before entering the study is unknown.

The main strengths of this study include the sample size calculation and prospective cohort design with an appropriate sample size. Standardized measurements of metabolic markers, including anthropometry and laboratory data of the participants, were included, and all diagnoses were determined in accordance with the guidelines' recommendations.

Conclusions

In the current prediabetic patient population, approximately 8 out of every 10 prediabetic individuals were diagnosed with concurrent MetS. Hypertension, dyslipidemia, abdominal obesity, and metabolic obesity increased in the coexistence of prediabetes and MetS. At the same time, the coexistence of prediabetes and MetS was associated with higher systolic blood pressure, postprandial blood sugar, and LDL levels. Prediabetic individuals accompanied by MetS are at greater metabolic risk. We recommend that all individuals diagnosed with prediabetes be evaluated for MetS and that MetS components be treated simultaneously.

Conflict of Interest

The authors declare that they have no conflict of interest.

Availability of Data and Materials

All data generated or analyzed during this study are included in this article.

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Ethics Approval

The current study was approved by the Ethics Committee of İnonu University in accordance with the Declaration of Helsinki, and written informed consent was obtained from each participant (Date: 2022; number: 114).

Informed Consent

Written informed consent was obtained from all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Authors' Contribution

SG, BE: data collection, design, led and conceived the project, and authored the manuscript. SG, BE, MNA: data collection, compiling, analysis data, discussion. BE, IS: supervision, writing, review, and editing.

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