Identification the early components of metabolic syndrome and some hematological test alteration related to cigarette, water pipe and dual smoking among young healthy adults: cross-sectional study

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ABSTRACT

Introduction: Tobacco epidemics permitted premature death and disability due to pathophysiological alterations related to distinct smoking patterns through cigarettes or waterpipes; the latter became as prominent as cigarettes. The preliminary intentions of this study were to explore the mutual correlation of metabolic syndrome (MetS) elements with alterations in some hematological, renal, and hepatic function biomarkers due to different tobacco smoking patterns, including cigarette smokers, waterpipe smokers, and dual smokers.

Methods: A total of 100 participants were evenly divided into non-smokers, exclusive cigarette or water pipe smokers, and dual smokers for this cross-sectional study conducted in Raparin district from September 1 to December 20, 2022. All participants were healthy, non-diabetic, normotensive, non-alcoholic, and non-coffee drinkers. Measurements included complete blood count (CBC), body mass index (BMI), lipid profile, blood pressure, glucose levels, liver enzymes (AST, ALT), and renal markers (creatinine, urea). Tests were performed using the Cobas C111 and Cobas e411 analyzers (Roche Diagnostics, Switzerland). Fasting blood glucose (FBG) was measured using glucose reagent strips and a Glucometer II, providing reliable quantitative results.

Results: Some Hematological parameters including hematocrit (HCT) and red blood cells (RBCs) had a tendency to be lower in smokers' samples compared to non-smokers, However, White blood cells (WBCs) were higher in smokers compared to non-smoker samples. Lipid profile makers including cholesterol and triglyceride including Triglyceride (TG) and total cholesterol (TC) low-density lipoprotein (LDL) were higher in smokers compared to non-smokers. Fasting glucose and liver function tests including AST, ALT was higher in smokers in comparison with non-smokers.

Conclusion: Our findings demonstrate that tobacco smoking directly modulates hemostasis and increases the risk of the development of metabolic syndrome components. Noteworthy, the tendency to develop MetS was more prevalent among dual smokers.

INTRODUCTION

Chronic tobacco consumption has initiated pathophysiological alterations, predisposing individuals to a high risk for cardiopulmonary illness, cerebrovascular lesions, and malignant tumors, eventually leading to disability and premature death. Together, a decline in fertility rate and fetal growth restriction may also be inevitable (Banks et al., 2019; General, 2006). A global tobacco curtailment effort by the World Health Organization (WHO) has been devoted while tobacco epidemics have raged. Since tobacco consumption is estimated to be responsible for up to 8 million deaths per year, with 80% of smokers residing in low- and middle-income countries (LMICs) (Perez-Warnisher et al., 2018).

Waterpipe smoking is an old form of tobacco smoking. The use of water pipe tobacco has evolved into cigarettes since the last decade, particularly among the young adult population who smoke cigarettes in combination with water pipe (Ma et al., 2022). Acquiring a cultural habitat of relaxation, enjoyment, and entertainment is supposed to be one of the major motives and attitudes towards smoking water pipes that have a strong social standing (Akl et al., 2013) There is a misconception that substances contained in water pipe tobacco smoking (WTS) are less toxic than cigarettes, but a tremendous amount of published evidence has disproved this perception (Abdulrashid et al., 2018). A comprehensive study has demonstrated 5000 to 7000 analyzed chemicals contained in tobacco products, at least 69 of which are known carcinogens (Mendel et al., 2018; Xue et al., 2014). Hence, toxicants contained in tobacco products significantly exert pathophysiological changes involving multiple systems and organs, triggering mutations, deregulating host immune responses, destructing endothelial cells, and disrupting metabolic pathways (Caliri et al., 2021; Feltes et al., 2013).

Metabolic pathway dysfunction in heavy smokers raises the risk of metabolic syndrome (MetS) (Sun et al., 2012). MetS isn't diagnosed unless three subsets of its diagnostic criteria are seen: increased abdominal obesity, hyperglycemia, hypertension, elevated TC, and decreased HDL-C (Costa et al., 2012). The existence of one of the MetS components raises the risk of delayed-onset MetS, implying a significant lifetime burden of cardiovascular disease risk (CVD), type 2 diabetes mellitus (T2D), stroke nephropathy, and hepatic complications. It was extensively described how MetS can cause a complex pathogenesis that leads to a chronic inflammatory response (Kendall & Harmel, 2002; Tan et al., 2014). New clinical data has also shown that the hematopoietic system's cellular and non-cellular parts play a role in changing the inflammatory response that isn't working properly and is at the root of atherosclerosis (Tall & Fuster, 2022; Wang et al., 2022). For instance, smoking causes an increase in total white blood cells, a well-known indicator of an inflammatory response, and there is debatable evidence linking RBC and platelet-related indices to smoking (Higuchi et al., 2016). Even though limited or compelling prospective clinical findings in other populations have partially collected evidence about the exclusive cigarette, waterpipe smoking, or dual smoking status correlation with the clinically validated MetSyn biomarkers, which might reflect greater hematological fluctuations (Shafique et al., 2012) Therefore, we hypothesized a mutual link between smoking status and some MetS criteria's, including SysBP, DisBP, MAP, HR, BG, BMI, TC, TG, HDL-C and LDL-C, complete blood count (CBC), creatinine, and urea for renal function, while AST and ALT as hepatic indices in a young, healthy Iraqi Kurdish population residing at Raparin Governorate were extensively analyzed, which has been missing before and warranted our investigation.

MATERIALS AND METHODS

Study design and ethics

This study included 100 healthy male participants, aged 18 and older, from the Raparin area of Sulaymaniyah, Iraqi Kurdistan, between 01-09-2022 and 20-12-2022. Participants provided written informed consent and were randomly assigned to one of four groups: non-smokers (NS), cigarette smokers (CS), waterpipe smokers (WPS), and dual smokers (DS). Exclusion criteria involved individuals with chronic conditions or those on medications containing caffeine or alcohol. Female smokers were excluded for cultural reasons. The study adhered to national clinical laboratory guidelines, with randomization facilitated by private labs in Ranya and Qaladiza using an online program (https://www.randomizer.org).

Self-administrated Questioner

A self-administered Kurdish questionnaire was used to collect sociodemographic information, including age, marital status, education, economic status, comorbidities, medication use, physical activity, and coffee and alcohol consumption. Participants' mental health was categorized as calm, energetic, enthusiastic, anxious, or depressed, following Richards & Smith (2015). The questionnaire also explored smoking habits, linking them to psychological factors such as loneliness, addiction, social enjoyment, relaxation, depression relief, and self-esteem, with unemployment identified as a key smoking trigger. A brief food frequency questionnaire (FFQ) assessed participants' diets, focusing on grains, dairy, meats, eggs, fish, bread, sweets, and fast foods, with responses recorded as "yes" or "no." To evaluate sleep quality, habitual sleep efficiency (HSE%) was calculated using the following formula (Hosseinbor et al., 2014; Rothenberg et al., 2021):

HSE% = *(number of hours slept − number of hours spent in bed) × 100*
For current smokers, cigarette consumption was quantified using the pack-year method (below

Equation):

Pack year = (Cigarettes smoked per day × Smoking years) ÷ 20

Since no standard definition of waterpipe smoking was available, a cumulative waterpipe smoking (AWS) equation (Equation 3) was employed to estimate the weekly smoking rate for waterpipe users. This equation was adapted from Labib et al. (2007):

AWS = *(Number of waterpipe sessions per week × Number of years smoking waterpipes)*

Anthropometric Measurement

Height and weight were measured using a tape measure and digital weighing scale (Mettler Toledo, Switzerland), with BMI calculated as weight divided by the square of height. Blood pressure was measured twice from the upper arm in a seated position, using a mercury sphygmomanometer and stethoscope (MDF Instruments, USA), with readings taken 1-2 minutes apart. The first reading was at baseline (pre-exposure), and the second after 45 minutes of waterpipe smoking (post-exposure). Mean arterial pressure (MAP) was calculated using the standard formula.:

$$MAP = [\,(2 \times diastolic\ blood\ pressure) + systolic\ blood\ pressure\,] \div 3$$

Blood Sample Collection and Laboratory Analysis

A 5 mL blood sample was collected from the antecubital vein after an overnight fast for immediate analysis. The blood was tested using the Swelab™ Alfa Plus 3-part hematology analyzer (Sweden) to measure the complete blood count. This included categorizing white blood cells (WBC) into different types such as lymphocytes, mid-sized monocytes, and granulocytes (neutrophils, eosinophils, and basophils). Red blood cell (RBC) indices like hemoglobin, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), hematocrit (HCT), and red cell distribution width (RDW) were also measured. Platelet indices, including platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet large cell ratio (P-LCR), were assessed as well.

The biochemical tests included a lipid profile (total cholesterol, triglycerides, HDL, and LDL), liver enzymes (AST and ALT), and kidney function markers (creatinine and urea), which were analyzed using Cobas C111 and e411 analyzers (Roche Diagnostics, Switzerland). Fasting blood glucose (FBG) levels were checked using glucose reagent strips and a Glucometer II (Miles Inc., Diagnostics Division, Elkhart, IN, USA), providing results that align with laboratory standards.

Definitions

Hyperglycemia was classified as diabetes when fasting blood glucose (FBG) levels were ≥126 mg/dL and as prediabetes when FBG ranged from 100–125 mg/dL. Body mass index (BMI) was categorized based on CDC and WHO standards: underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9), and obese (≥30.0). Blood pressure was classified as normotensive at SysBP/DisBP = 120/80 mmHg, while values between 120–139/80–89 mmHg indicated a prehypertensive state (Elliot).

Statistical Analysis

Data were analyzed using IBM® SPSS® software (version 25), with statistical significance defined as $p < 0.05$. Bivariate analysis via the Pearson correlation coefficient assessed relationships between quantitative variables. Mean comparisons of continuous variables were conducted using ANOVA F and Student's t-tests, while categorical variables were analyzed with chi-square tests at a 95% confidence interval.

Ethical considerations

This study adhered to the ethical principles outlined in the Declaration of Helsinki (2013). Approval for the longitudinal study was granted by the scientific and ethics committee of the College of Science, University of Raparin (Approval No. 22, dated August 7, 2022). All participants provided written informed consent before participation.

RESULTS

This study included 100 healthy male participants categorized as non-smokers (NS, n = 25), cigarette smokers (CS, n = 25), waterpipe smokers (WPS, n = 25), and dual smokers (DS, n = 25). Individuals with underlying health conditions or ongoing medication use were excluded. Dietary intake and economic status data were excluded due to incomplete responses. After adjusting for age and sociodemographic factors, the relationship between smoking, metabolic syndrome (MetS) components, and hematological indices was assessed. Non-smokers exhibited significantly better habitual sleep efficiency (HSE%) at 95.27% ($p = 0.044$) and mental state ($p = 0.039$) and were more

likely to hold higher educational degrees than smokers ($p < 0.001$), as outlined in Table 1. Notably, socialization emerged as a primary driver for smoking behavior ($p = 0.003$).

Table 1: Sociodemographic characteristics of participants.

Factor	Non-Smokers	Cigarette smokers	Waterpipe smokers	Dual smokers	P-value
Age	29.96[a]	29.66[a]	28.34[a]	24.50[b]	0.362
HSE%	95.270[b]	84.91[a]	85.49[a]	88.53[ab]	**0.044**
BMI	24.8 [b]	24.1[b]	26.5[a]	23.12[b]	0.23
I. Defining cigarette smoking habitat (Mean ± SD)					
Cumulative amount of smoking (Pack year)	0	19.32 ± 25.74	0	5.89 ± 6.24	0.126
Duration of smoking (years)	0	14.72 ± 8.84	0	6.72 ± 5.26	0.256
Number of cigarettes smoked per day	0	24.12 ± 11.07	0	16.76 ± 9.64	0.812
II. Defining water pipe smoking habitat (Mean ± SD)					
A cumulus waterpipe smoking (AWS)	0	0	31.36 ± 20.2	23.45 ± 22.01	0.75
Duration of smoking (years)	0	0	5.92 ± 2.54	4.69 ± 3.55	**0.094**
One smoking session per minute	0	0	113.20 ± 71.04	70 ± 40.49	**0.004**
Education NO. (%)					
Illiterate	1 (4)	2 (8)	3 (12)	1 (4)	**<0.001**
Basic education	7 (29)	3 (12)	9 (36)	6 (24)	
High school	2 (8)	7 (28)	7 (28)	9 (36)	
Diploma	0 (0)	2 (8)	3 (12)	9 (36)	
University	14 (59)	11 (44)	3 (12)	0 (0)	
Marital status NO. (%)					
Married	10 (40)	16 (64)	9 (36)	10 (40)	0.174
Single	15 (60)	9 (36)	16 (64)	15 (60)	
Motives for smoking NO. (%)					
Loneliness	0 (0)	3 (12)	2 (8)	2 (8)	**0.003**
Addiction	0 (0)	4 (16)	0 (0)	0 (0)	
Pleasurable, entertaining and relaxing social experience	0 (0)	15 (60)	11 (44)	13 (52)	
Relieving depression and increase self confidence	0 (0)	3 (12)	0 (0)	2 (8)	
Unemployment	0 (0)	0 (0)	12 (48)	8 (32)	
State of mind NO. (%)					
Calm	21 (88)	19 (76)	15 (60)	17 (68)	**0.039**
Energetic	1 (4)	0 (0)	5 (20)	1 (4)	
Enthusiastic	0 (0)	0 (0)	0 (0)	1 (4)	
Anxious	2 (8)	0 (0)	3 (12)	2 (8)	
Depressed	0 (0)	6 (24)	2 (8)	4 (16)	
Regular sport NO. (%)					
Non-exist	15 (60)	21(84)	16 (67)	16 (84)	0.294
Exist	10 (48)	4 (60)	8 (72)	8 (76)	

Note: Boldface indicates statistical significance ($p<0.05$).
Non-smokers (N = 25), cigarette smokers (N = 25), waterpipe smokers (N = 25), and dual smokers (N - 25).

Compared to dual smokers, exclusive cigarette smokers had higher daily consumption, longer smoking history, and over 19 pack years (PY) (Table 1). Table 2 shows Pearson correlation analysis revealing positive correlations between MID (r = 0.436), PDWa (r = 0.814), and total cholesterol (TC) (r = 0.44) with PY. Higher MID (r = 0.712), MID% (r = 0.504), RDW% (r = 0.738), PDWa (r = 0.738), and TC (r = 0.56) were linked to smoking history, with PDWa (r = 0.533) associated with higher daily cigarette consumption.

Table 2: Bivariate analysis of correlations between variables in cigarette smokers

Cigarette smokers		
Parameters	**Correlation factor**	**p-value**
WBC vs. TC	0.453	0.023
Cumulative amount of smoking (Pack year) association with:		
MID	0.436	0.024
PDWa	0.814	<0.001
Cholesterol	0.44	0.024
Smoking history (duration) in years association with		
WBC	0.462	0.02
MID	0.625	0.01
PDWa	0.609	0.01
Cholesterol	0.676	0.01
Cigarette number vs. PDWa	0.533	0.06

Note: The correlations between variables are considered significant if the p-value is <0.05.

The white blood cell count (WBC) positively correlated with total cholesterol (TC) (r = 0.453), indicating that prolonged smoking is linked to elevated hematological markers related to MetS. Longer waterpipe smoking sessions (AWS) (p = 0.004) were associated with decreased fasting blood glucose (FBG) (r = -0.339) and aspartate aminotransferase (AST) (r = -0.439). Exclusive waterpipe smokers, generally overweight (BMI = 26.5 kg/m²), showed higher triglycerides (TG) (r = 0.533), diastolic blood pressure (DisBP) pre/post (r = 0.425/0.562), and mean arterial pressure (MAP) pre/post (r = 0.443/0.525). Conversely, WBC (r = -0.411), granulocytes (GRA) (r = -0.433), and red blood cell count (RBC) (r = -0.472) showed inverse correlations with low-density lipoprotein (LDL) and TC, as shown in Table 3.

Table 3. Bivariate analysis comparing the relationship between two categorical variables in water pipe smokers. Data represent correlation factors.

Water pipe smokers		
Parameters	**Correlation factor**	**p-value**
WBC vs. LDL	-0.411	0.041
GRA vs. LDL	-0.433	0.031
GRA% vs. LDL	-0.408	0.043
RBC vs. TC	-0.472	0.017
AST vs. AWS	-0.439	0.028
BG vs. Smoking session	-0.339	0.048
BMI association with:		
TG	0.533	0.006
DisBP. pre	0.425	0.034
DisBP. post	0.562	0.003
MAP. pre	0.443	0.027
MAP. post	0.525	0.007

Note: The correlations between variables are considered significant if the p-value is <0.05.

The second aim of this study was to examine the early components of Metabolic Syndrome (MetSyn) and hematological changes in smokers. As presented in Table 4, smoking significantly impacted systolic blood pressure (SysBP), diastolic blood pressure (DisBP), mean arterial pressure (MAP), heart rate (HR), and fasting blood glucose (FBG) among smokers. However, no significant increase was observed in these measures either at baseline or following waterpipe smoking.

Table 4: Statistical for systolic blood pressure, diastolic blood pressure, mean atrial pressure, heart rate, and fasting blood glucose among all type smokers and non-smokers

Parameters	Mean				P value	Reference value
	Non-Smokers (n=25)	Cigarette smokers (n=25)	Water pipe smokers (n=25)	Dual smokers (n=25)		
SysBP.pre	106.04^{c}	120.96^{b}	130.65^{a}	123.70^{ab}	**<0.001**	< 120 mm Hg
SysBP.post	106.04^{c}	120.96^{b}	129.65^{a}	120.66^{ab}	**<0.001**	
DisBP.pre	76.84^{a}	78.90^{a}	79.8^{a}	78.16^{a}	0.793	< 80 mmHg
DisBP.post	76.84^{a}	78.90^{a}	78.28^{a}	77.37^{a}	0.895	
MAP.pre	86.11^{b}	92.92^{a}	96.74^{a}	93.33^{a}	**0.001**	70-100 mm Hg
MAP.post	86.11^{b}	92.922^{a}	95.40^{a}	91.80^{a}	**0.007**	
HR.pre	76.24^{c}	79.44b^{c}	89.02^{a}	82.91^{b}	**<0.001**	60-100 Beats/min
HR.post	76.24^{c}	79.44bc	94.77a	83.37b	**<0.001**	
FBG	75.28^{c}	112.40^{a}	96.74^{b}	117.12^{a}	**<0.001**	<100mg/dl

Note: If the p-value is <0.05 are considered significant. For post hoc analysis, similar letters mean insignificant, different letters means significant. Pre-exposed (pre): before exposure to water pipe, post-exposed (post) to water pipe smoking. SysBP, Systolic blood pressure; DisBP, diastolic blood pressure; MAP, mean atrial pressure; HR, heart rate; FPG, fasting blood glucose.

Individuals who have known to be exclusive cigarettes or dual smokers or reportedly have an aberrant BG level (p-value <0.001) compared with exclusive water pipes or non-smokers (Table 4). Also, the CSs, WPS, and DSs groups all had serum triglyceride (TG) levels that were too high. These levels were 263.680 mg/dl, 280.160 mg/dl, and 294.120 mg/dl, respectively (Table 5).

Table 5. Lipid profile index among study participants

Parameters	Mean value for all groups				P-value	Reference value
	Non-Smokers (n=25)	Cigarette smokers (n=25)	Water pipe smokers (n=25)	Dual smokers (n=25)		
TC	147.440^{b}	187.00^{a}	184.400^{a}	200.600^{a}	**<0.001**	<200mg/dl
TG	132.08^{b}	263.680^{a}	280.160$_{a}$	294.120^{a}	**0.002**	<180mg/dl
HDL-C	39.292^{b}	41.680^{b}	52.560^{a}	40.636^{b}	**0.001**	40-60mg/dl
LDL-C	82.404^{b}	104.0400^{a}	76.400^{b}	105.200^{a}	**<0.001**	<120mg/dl

Note: If the p-value is <0.05 are considered significant. For post hoc analysis, similar letters mean non-significant,

and different letters mean significant.

Cholesterol levels were significantly higher in CSs = 187 (mg/dl), WPS = 184.4 (mg/dl), and DSs = 200.60 (mg/dl) compared to NS = 132.080 (mg/dl), as described in Table 5. Controversial results were obtained regarding HDL or LDL concentrations in WPSs.

As shown in Table 6, according to laboratory standards, all white blood cell (WBC) parameters were within the normal range. However, smoking may have had a big effect on the rise in WBC cells, lymph, and lymph%, MID, MID%, GRA, and GRA% levels.

Table 6. Statistical comparison between non-smokers, cigarette smokers, water-pipe smokers, and dual smokers for complete blood cell account parameters.

Parameters	Non-Smokers (n=25)	cigarette smokers (n=25)	Water pipe smokers (n=25)	Dual smokers (n=25)	P value	Reference value (mg/dl)
WBC indices						
WBC	6.184^{b}	7.780^{a}	7.512^{a}	7.524^{a}	**0.001**	3.5- 10
Lymph	2.208^{b}	2.720^{a}	2.392^{b}	2.888^{a}	**<0.001**	0.5- 5
Lymph%	36.520^{ab}	35.508^{ab}	32.904^{b}	39.208^{a}	**0.012**	15 – 50
MID	0.292^{b}	0.365^{b}	0.552^{a}	0.356^{b}	**<0.001**	0.1-1.5
MID%	4.340^{b}	5.140^{b}	6.660^{a}	5.096^{b}	**<0.001**	(2- 15)
GRA	3.724^{b}	4.696^{a}	4.568^{a}	4.280^{ab}	**0.022**	1.2- 8
GRA%	58.712^{a}	57.076^{a}	57.432^{a}	53.544^{a}	0.54	35- 80
RBC indices						
HGB	15.312^{cb}	14.588^{c}	17.416^{a}	16.036^{b}	**<0.001**	11.5- 16.30
MCH	28.024^{b}	28.232^{ab}	29.300^{a}	28.232^{ab}	**0.116**	25-35
MCHC	32.480^{a}	32.956^{a}	32.686^{a}	32.564^{a}	0.951	31-38
RBC	5.481^{b}	5.123^{c}	5.828^{a}	5.688^{ab}	**<0.001**	3.5-5.5
MCV	86.344^{a}	81.813^{a}	86.544^{a}	86.732^{a}	0.304	75-100
HCT	47.280^{a}	43.088^{b}	48.136^{a}	49.352^{a}	**0.015**	35-55
RDWa	47.940^{a}	48.628^{a}	24.916^{b}	48.216^{a}	**<0.001**	30-150
RDWa%	10.600^{b}	10.692^{ab}	11.308^{a}	10.868^{ab}	0.145	(11- 16)
Platelet indices						
PLT	199.840^{a}	218^{a}	213.360^{a}	212.720^{a}	0.667	100-400
MPV	8.792^{a}	9.112^{a}	8.540^{a}	8.760^{a}	0.235	(8- 11)
PDWa	11.772^{ab}	12.896^{a}	11.248^{b}	11.852^{ab}	0.042	0.1-9.99
PCT	0.168^{a}	0.191^{a}	0.176^{a}	0.180^{a}	0.245	0.01- 9.99
P-LCR	19.608^{a}	22.580^{a}	18.708^{a}	19.344^{a}	0.212	0.1-9.99

Note: If the p-value is less than (0.05) are considered significant. For post hoc analysis, similar letters mean insignificant, different letters means significant. NSs, Non-smokers; CSs, Cigarette smokers; WPSs, Waterpipe

smokers; CWPSs, Cigarette and water pipe smokers.

Waterpipe smokers (WPSs) showed significantly higher levels of MID ($p < 0.001$) and MID% (6.66 mg/dl; $p < 0.001$) compared to non-smokers (NSs), cigarette smokers (CSs), and dual smokers (CWPSs), as well as increased concentrations of hemoglobin (HGB) (17.16 mg/dl), red blood cells (RBC) (5.826 mg/dl), and hematocrit (HCT) (49.35 mg/dl) (Table 6). However, exclusive waterpipe smoking resulted in a significant reduction in red cell distribution width (RDWa) (24.91 mg/dl; $p < 0.001$). No significant differences were observed in MCH, MCHC, MCV, PLT, MPV, PDWa, PCT, and P-LCR among the groups. Active smokers exhibited higher levels of hepatic enzymes such as ALT ($p = 0.152$), AST ($p = 0.083$), and blood urea ($p = 0.02$), though these remained within the normal range. Notably, exclusive waterpipe smoking led to an abnormal increase in serum creatinine ($p = 0.001$), as shown in Table 7.

Table 7: Statistical comparison for hepatic enzymes and kidney waste products among smokers and non-smokers.

Parameters	Mean				P-value	Reference value (mg/dl)
	Non-Smokers (n=25)	cigarette smokers (n=25)	Water pipe smokers (n=25)	Dual smokers (n=25)		
ALT(GPT)	22.525[a]	30.404[a]	34.960[a]	36.768[a]	0.152	7-53
AST (GOT)	22.592[b]	29.300[a, b]	29.000[a, b]	31.284[a]	**0.083**	11-47
S-Creatinine	0.984[b]	0.967[b]	1.30[a]	1.052[b]	**0.001**	0.2 - 1.2
Blood urea	29.400[b]	31.800[b]	38.160[a]	31.520[b]	**0.002**	16.6-48.5

Note: Boldface indicates statistical significance ($p<0.05$). For post hoc analysis, similar letters mean insignificant, and different letters mean significant.

DISCUSSION

The recognition of tobacco-related health burdens by the World Health Organization (WHO) has catalyzed a global initiative aimed at mitigating the tobacco epidemic (Flor et al., 2021). To the best of our knowledge, the present study represents the first large-scale effort in the Raparin district to investigate early indicators of dyslipidemia, diabetes, hypertension, and obesity, which are key components of metabolic syndrome (MetS), along with associated hematological alterations and hepatic and renal dysfunction. This analysis focused on the effects of cigarette and water pipe smoking, both independently and in combination, among young and otherwise healthy adults.

Although smoking often begins as a recreational activity or a pleasurable social experience, it frequently escalates into dependence, as reflected in the data presented in Table 1. Interestingly, while cigarette smokers readily acknowledged addiction, participants who smoked water pipes consistently denied such dependency. This finding aligns with a previous study by Hessami et al. (2020), in which participants similarly rejected the notion of addiction but instead reported experiencing a form of social reliance or behavioral attachment associated with water pipe smoking. These nuanced differences underscore the complex social and psychological dimensions of smoking behaviors, particularly among young adults.The positive linear correlation of heavy

exclusive cigarette smoking status with hematological analysis and MetS components including WBC, MID, PDWa, and TC (Tables 1 and 2) reinforces the fact that chronic hyper acclimatized acute smoke-induced deregulated proinflammatory response might contribute toward a detrimental outcome (Shahabinejad et al., 2016). However, an indirect or U-shaped relationship between water pipe smoking status, BMI, and hematological indices might have provided a partial explanation for deregulated hematological, blood pressure, and lipid profile indices that is well documented in Table 3. Even though LDL-C is inversely correlated with a higher WBC and GRA numbers align with Lai et al (Liu et al., 2023), defying the U-shaped assumption.

Late-onset noncommunicable diseases like CVD, T2D, and injuries to the vascular system, kidneys, or liver may be linked to a lot of long-term metabolic risks in adulthood (Martín-Timón et al., 2014). In contrast, neither high blood pressure nor diabetes were found in smokers in Table 4, which is in line with (Mehboudi et al., 2017; Sohn, 2018). However, it appears that smoking cigarettes alone or with waterpipe smokers has made people more likely to be in a state of prediabetes (Table 4). Even though heterogeneous screening criteria for prediabetes have been proposed (Kaur et al., 2020), Further HbA1c, glucose intolerance, and FBG testing in combination with other metabolic syndrome risk factors will confirm the stratification of high-risk individuals for delaying the onset of DM or the allocation of better therapeutic approaches (Evron et al., 2019). Therefore, suggesting immediate smoking cessation for at least five years of duration in our young adults may spontaneously reverse prediabetes into a normoglycemia, which has been well intervened by prospective studies (Durlach et al., 2022).

According to studies (Hallit et al., 2019; Hallit et al., 2017), smoking has been linked to higher SysBP and HR in tobacco users, especially those who smoked water pipes alone (Table 4). This is also a strong indicator of a state of prehypertension. While interacting with other MetS risk factors such as obesity (Table 3), prehypertension conditions have a higher tendency to progress into hypertension or serious health issues such as cardiovascular injuries (Egan & Stevens-Fabry, 2015). Immediate rises in heart rate causing higher cardiac output and peripheral vascular resistance were suggested as possible causes of smoke-induced hypertension (Hallit et al., 2019). This suggests that both long-term and short-term smoking may turn prehypertension into hypertension. This effect might go away once the smoking effect is gone, but the body can keep blood pressure in check in response to compounds found in tobacco products (Choi et al., 2021). This could also explain why there were no clear changes in blood pressure or heart rate on the day of the water pipe smoking test, either before or after exposure (Felber Dietrich et al., 2007). This situation is comparable to the results of this research. In addition, chronic nicotine exposure leads to the phenomenon of masked hypertension, which prevents manifestations of hypertension symptoms for a while, especially among young adults. However, these symptoms will be inevitable later in life unless acute injuries happen to the arterial wall (Cierpka-Kmieć & Hering, 2020; Leone, 2011).

The interaction of the prehypertension state with other metabolic risks, such as obesity, has been shown to be responsible for late-onset burdens (Egan & Stevens-Fabry, 2015). Even though none of the people in the study were obese, those who only smoked water pipes were more likely to be overweight (Table 1), showing how the MetS components interact (Table 3). This is why we said that their BMI has affected their blood pressure, which is in line with a recent study (Yao et al., 2020). But cigarette consumption was predominant among American young adults (Hu et al., 2018; Sidani et al., 2016) as an attempt to suppress appetite and maintain a healthy weight, which is similar to our finding (Table 1), but Pan et al. (2020) discovered that middle-aged and elderly Chinese rural residents who were heavy cigarette smokers tend to have a low BMI (Pan et al., 2020). Proposing

that recruitment of different age and gender groups, assessment of dietary intake, scoring distress level, predicting physical activity, calculating smoking dose, and history within a longitudinal future study ensure a comprehensive analysis due to such contradictive outcomes.

In an approximate manner, our discovery in Table. 5 coincides with conflicting previous trends in terms of smoking correlation with dyslipidemia (Jeong, 2022; Kumar et al., 2022; Mouhamed et al., 2013), as the whole smokers experienced an aberrant rise in TG, with the exception that dyslipidemia was more evident among dual smokers since their TC concentration reached a high borderline reference value. In contrast to the widely accepted view that smoking induces an increase in LDL-C with a decrease in HDL-C (Slagter et al., 2013), no change has occurred in our finding, but unexpectedly high or low LDL-C concentrations in smokers, particularly within the exclusive water pipe group, might raise awareness. Since individuals with such outcomes might be at an increasing risk of CVD injuries due to the presence of other components of MetS, As suggested, monitoring the lipid particle size of LDL-C will be of significant importance because the effect of smoking on LDL might be both qualitative and quantitative (Slagter et al., 2013).

Chronic tobacco use raises hematological markers much more than MetS elements alone, which may mean more inflammation even when MetS elements are not present (Aldaham et al., 2015; Lakshmanan & Saravanan, 2014; Shakiba et al., 2023). Both of these changes affect the immune system, affecting both systemic and local inflammatory processes. Measuring clinically validated inflammatory biomarkers, such as white blood cells (WBC), would critically diagnose the most vulnerable individuals to cardiovascular and pulmonary illness (Alzurfi et al., 2019; Elisia et al., 2020; Lassale et al., 2018). A remarkable increase in WBC numbers in smokers is observed in Table 6, which agrees with the previous studies conducted in Canada, Saudi Arabia, and Iraq (Aldosari et al., 2020; Alzurfi et al., 2019; Elisia et al., 2020). However, the fact that the number of lymphocytes in waterpipe smokers in this study (Table 6) did not rise was different from other studies (Elisia et al., 2020).

We found that a drop in the number of lymphocytes in the blood was a sign of a bad outlook for middle-aged smokers with or without COPD. This suggests the need for a longitudinal study to confirm this effect on our participants as they get older. The buildup of GRAs like neutrophils in the bronchial airways has been shown to cause persistent inflammatory responses within a tumor microenvironment, which leads to bad outcomes. As a result, this could be a sign that smokers will have a higher risk of lung cancer in the future (Goto, 2020; Lerman & Hammes, 2018; Stämpfli & Anderson, 2009; Strzelak et al., 2018). In this way, the higher numbers of MID monocytes and GRAs like neutrophils, basophils, and eosinophils in people who only smoke cigarettes and the higher numbers of MID neutrophils and basophils in people who only smoke water pipes (Table 6) show the part that granulocyte-stimulating growth factor G-CSF plays in protecting bronchial epithelial cells from damage caused by smoke (Tsantikos et al., 2018). For further verification, we recommend manual automation with sophisticated homological analyzers, through which further leukocyte subpopulations will be accurately measured. You can figure out the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) ahead of time. Both of these ratios are useful for predicting how well someone will do in treating a wide range of illnesses, from infections to lung and heart problems (Swaminathan et al., 2015; Tulgar et al., 2016).

Smokers also tend to have a higher HB and RBC level, ensuring sufficient oxygen delivery to their target tissue (Elisia et al., 2020; Malenica et al., 2017). Here in Table 4, exclusive water pipe smoking might have exerted the same effect as compensation for a shift toward increased carboxyhemoglobin, which has a limited oxygen-carrying capacity but not oxyhemoglobin (Kahar

et al., 2022; McDonough & Moffatt, 1999). The heterogeneity of erythrocyte volume, collectively referred to as RDW, also affects the blood's oxygen-carrying capacity in smokers (Elisia et al., 2020), and a high RDW is associated with inflammation, predisposing individuals to MetSyn and CVD development (Yan et al., 2019). However, a notable drop in RDW concentration among people who only smoked waterpipes (Table 4) has not been explained. However, suggested that using hematological analyzers at two different labs might have made these problems easier to spot (Aldosari et al., 2020). Correspondingly, exclusive cigarette smokers have a lower HCT level. The other RBC indices, such as MCH, MCHC, MCV, and RDWa% concentration, did not change in a way that was not statistically significant. This is in line with what has been found before (Malenica et al., 2017).

When people smoke a lot of cigarettes, atherothrombs form, which damages the endothelium (Messner & Bernhard, 2014) and leads to higher platelet levels like PLT, MPV, PDWa, and PCT (Elisia et al., 2020; Lassale et al., 2018). These findings contradict the results of this study, since no significant changes were observed in platelet indices among study participants in Table 6, which was comparable to studies conducted previously (Dewi et al., 2020; Mohammed et al., 2016; Suwansaksri et al., 2004). There is not a firm consensus explanation for this inconsistency, although previous research yielded varied results (Nadia et al., 2015; Tell et al., 1985).

We showed in Table 7 that the levels of AST and ALT in the blood have not changed significantly among the study participants. This is because smoking cigarettes does not directly harm hepatocytes, but it can change how drinking alcohol affects AST, ALT, and GGT activities by affecting many factors that change the functions of liver enzymes (Jang et al., 2012; Wannamethee & Shaper, 2010). Thus, we have evaluated the exclusive effect of smoking on liver damage independent of alcohol use since our tobacco consumers were not alcohol drinkers, and therefore, future studies should consider the interaction of alcohol and smoking dependent on each other in a Kurdish population.

The kidney is a major target organ for smoking-related harm, whether direct or indirect (Munzir & Ahmed, 2015; Van Laecke & Van Biesen, 2017). Table 7 shows a modest rise in serum creatinine and urea in water pipe smokers but not in cigarette or dual smokers, which is consistent with the findings of (Yamada et al., 2015) but not with (Yoon et al., 2009), who found renal function changes in patients with hypertension at high levels, but our participants were normotensive except for water pipe smokers that were in a prehypertensive state, and therefore, a slight increase in creatinine and urea was observed among them. For that reason, future research should consider renal function tests in relation to hypertensive patients who are current cigarette or water pipe smokers.

CONCLUSION

In contrast with the public belief that water pipes eliminate the toxicity of tobacco in comparison with cigarettes, we found that the adverse effects of exclusive water pipe smoking could be even greater than those of cigarettes, even with dual smokers. The prevalence of components of MetS and alteration in hematological parameters was significantly higher in smokers, especially among exclusive water pipe smokers, in comparison with non-smokers and even cigarette smokers. However, dyslipidemia was more prevalent among dual smokers. Therefore, our findings add to the existing body of knowledge, and there is no firm consensus on the relationship between various

forms of tobacco smoking and hematological indices and components of MetS. Controversy on this issue is expected to persist in the near future due to multiple confounding factors.

Further studies are required on the relationship between tobacco smoking and smoking to clarify the finding. However, in the current study, immediate identification of the indicators of long-term metabolic risks and some biochemical and hematological profiles in adulthood might raise public awareness and reduce risks later in life.

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AUTHORS' CONTRIBUTION

BK and ShM collected data, while RK, ShM, and RI analyzed it. MA verified the analysis, and BK, SHM, RI, and RK participated in the final interpretation. MA conceptualized the manuscript scope and provided senior author mentorship. All authors provided critical input and read and approved the final version, agreeing to be accountable for all aspects of the work.

AVAILABILITY OF DATA AND MATERIALS

If requested, authors will provide the data required for review by publishers.

CONFLICT OF INTEREST

Not applicable.

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