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Association of cigarette and water-pipe smoking with increased visceral adiposity, glycemic intolerance and hematological derangement in Iraqi healthy smokers

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The present study aims to investigate the impacts of cigarette smoking (CS) and water-pipe smoking (WPS) on the visceral adiposity index (VAI), hematological characteristics, and glycemic tolerance in Iraqi healthy smokers. A total of 528 healthy males from different locations of Baghdad city were allocated to three groups; nonsmokers (176), cigarette smokers (178), and WP smokers (174). Baseline characteristics, anthropometric and hematological markers and were reported. Glycemic control was evaluated using the glucose tolerance test. The evidence of elevated VAI, disrupted hematological markers, and impaired glucose tolerance was significantly ($P<0.001$) different compared with non-smokers and related to the duration of smoking. The impacts of WPS seem to be significantly greater than CS in certain parameters (hemoglobin, hematocrit, methemoglobin, and 2-hour glucose tolerance values). In conclusion, CS and WPS negatively impacted body fat distribution, glucose tolerance, and hematological markers. There is a positive association between the rate of smoking and obesity, glycemic intolerance in both groups.

Keywords: Cigarette smoking. Water-pipe smoking. Visceral adiposity. Glycemic tolerance. Hematologic markers.

INTRODUCTION

Although many global efforts halted tobacco smoking habits, significant amounts of the world population still practiced various forms of tobacco smoking (Reitsma *et al*., 2017); meanwhile, smoking is ranked among the top risk factors behind disability-adjusted loss of life years worldwide (Hamadeh *et al*., 2018). In contrast to the global reports of cigarette smoking prevalence, the World Health Organization (WHO) addressed in 2015 an 18% decrease in the prevalence of cigarette smoking within the Eastern Mediterranean Region (EMR) (Jawad, Roderick, 2017) compared with other parts of the world. However, this was associated with the increased use of water-pipe smoking among EMR people as regular or occasional use (Jawad *et al*., 2018). Water-pipe smoking (*shisha or narghile*) is a form of tobacco use widely practiced by young people in the Middle East and many other countries as an alternative to cigarette smoking. This was probably based on a misconception that this approach is less harmful than cigarette smoking because passing through water may filter the smoke before it is inhaled (Al Ghobain *et al*, 2018). The World Health Organization (WHO) study group on "Tobacco Product Regulation" had reported advisory notes on the expected health problems of water-pipe smoking, and addressed the similarity between cigarette and water-pipe smoking (Chaouachi, 2006; Kim, Kabir, Jahan, 2016). In this regard, many carcinogens from cigarette smoking like polycyclic aromatic hydrocarbons, volatile aldehydes, phenols, and heavy metals are also part

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of water-pipe smoking (Primack *et al*, 2016; Primack *et al*, 2018). The present study aimed to evaluate the impacts of cigarette water pipe smoking on the visceral adiposity index, glucose tolerance, and hematological markers of the Iraqi healthy smokers.

MATERIAL AND METHODS

Study design and participants

The current study was performed to evaluate the relationship effects of the duration and rate of the cigarette and water-pipe smoking on the hematological, body weight, fatty tissue distribution, and glycemic control markers of clinically healthy volunteers. A total of 528 healthy subjects were enrolled in the present cross-sectional study, 178 cigarette smokers, 174 water-pipe smokers, and 176 non-smokers in the age range of 18-30 years. The subjects were recruited from different locations within Baghdad City and Sulaimani City including the university campus and other facilities. The cigarette smokers were regularly consuming a minimum of 10 cigarettes/day for at least 1 year; meanwhile, the water-pipe smokers were practicing a minimum of 1 session/day for at least 1 year.

All the enrolled subjects were informed about the nature of the study and asked to give informed consent before inclusion. The study protocol was approved by the Ethical Review Committees of the College of Medicine, the University of Sulaimani, and the faculty of Pharmacy, Al-Rafidain University College. The required data on cigarette and water-pipe smoking habits including duration and rate of smoking were collected obtained by a self-administered questionnaire to be filled in by the participants. The inclusion criteria include that the subjects should have no clinical or biochemical evidence of kidney and liver diseases, chronic pancreatitis, gastrointestinal and inflammatory bowel diseases, history of ischemic heart disease, endocrine disorders, infection, regular consumption of supplements, and hormonal replacement therapy.

Anthropometric and biochemical markers

In all the subjects, systolic and diastolic blood pressure and anthropometric parameters (body weight, height, and waist circumference) were measured. Waist circumference was measured at the midpoint between the lowest rib and the iliac crest. BMI was calculated according to the formula body weight (kg)/ squared height (m^2). Systolic and diastolic blood pressure was measured using a mercury sphygmomanometer and a standard stethoscope. After overnight fasting, 1 ml of blood samples were obtained from each subject. Two milliliters were utilized for the evaluation of Hb, Hct, WBC count using an automated hematological analyzer (CELL-DYN 3700, Bellport, USA). A spectrophotometric method for measuring MetHb in small blood samples utilized based on Evelyn-Malloy and Drabkin's method (Arnaud *et al*., 2017). The other part of the blood was left to clot and the resulted serum was utilized for the spectroscopic determination of TG and HDL-c using a ready-made kit for this purpose (Hoffman-La Roche Ltd., Basel, Switzerland).

Measurement of the visceral adiposity index (VAI)

The VAI was calculated utilizing a standardized formula (Amato *et al*., 2010). The distribution pattern of adipose tissue was corrected for TG and HDL-C levels to determine the VAI as follows:

Male VAI = (WC/39.68+(1.88×BMI))×(TG/1.03)×(1.31/HDL-c),

Where waist circumference (WC is) expressed in cm, BMI in kg/m^2, TG and HDL-c in mg/dl.

Measurement of the 2-hour glucose tolerance (2-hr GT)

The 2-hr glucose tolerance test was performed to all subjects and the change in blood glucose level was evaluated during 2 hr after oral ingestion of 200 g of glucose.

Statistical analysis

Statistical analysis was performed utilizing GraphPad Prism software version 5.1 (GraphPad Software, San Diego, USA). Comparison between groups was performed using Student's unpaired *t*-test. Correlation studies were performed using the Pearson R test for variables with a normal distribution. Data were expressed as mean ± standard deviation (SD). $P<0.05$ was considered significant.

RESULTS

Table I shows the baseline characteristics and the influence of cigarette and water-pipe smoking on the studied variables of the enrolled 352 cigarette and water-pipe smokers, compared with 176 non-smokers. The mean age of non-smokers, cigarette smokers, and water-pipe users was 24.8±3.2, 25.6±3.7, and 25.5±3.0 years, respectively, and they were not significantly different. Subjects of CS and WPS groups demonstrated significantly higher body weight, BMI, and WC values compared with the NS group; meanwhile, the cigarette smokers appeared with significantly higher values of body weight (2.4%), BMI (4.6%), and WC (7%), respectively, compared with WPS group ($P<0.005$). Table I also showed that most of the participants in the CS and WPS groups have secondary school level of education (52% and 36%, respectively), while most of the non-smokers (control group) are college graduates (64%). Smoking duration in the CS group was found to be significantly higher than that in the WPS group (4.5±2.1 *vs*. 3.7±1.7 years). Moreover, the influence of smoking on BP revealed a significant elevation of both systolic and diastolic BP of both CS and WPS groups compared with non-smokers, with the significantly higher influence of WP smoking compared with cigarette smoking in this regard. In table I, both cigarette and water-pipe smoking significantly elevated Hb, Hct, WBC, and MetHb compared with non-smokers ($P<0.05$); meanwhile, WP smokers demonstrated significantly higher values of Hb, Hct, and MetHb (1.2%, 4.5%, and 18%, respectively) compared with the subjects of CS group. Additionally, TG, VAI, and 2-hr GT values were significantly elevated in CS and WPS groups compared with the NS group, while HDL-c was significantly decreased in both smoking groups. In this regard, WP smokers demonstrated significantly higher values of VAI and 2-hr GT (3.0% and 6.4%, respectively) compared with the subjects of the CS group, while the HDL-c value was significantly lower in the WPS group (5.4%) compared with the CS group. In the Cs group, correlation studies (Table II) indicated that duration of cigarette smoking was highly and significantly associated with MetHb (r= 0.958, $P<0.001$), VAI (r= 0.501, $P<0.001$) and the 2-hr GT (r= 0.906, $P<0.001$) values. Meanwhile, the oxidative change marker of hemoglobin (MetHb) was highly and significantly associated with VAI (r= 0.441, $P<0.001$) and 2-hr GT (r= 0.837, $P<0.001$) values. Moreover, the correlation studies between the rate of cigarette smoking/day (Table III) revealed significant association with Hb (r= 0.329, $P<0.001$) and Hct (r= 0.501, $P<0.001$) values. In the WPS group, correlation studies between duration of WP smoking and the studied markers demonstrated significant and high association with Hb (r= 0.613, $P<0.001$), Hct (r= 0.423, $P<0.001$), MetHb (r= 0.806, $P<0.001$), VAI (r= 0.282, $P<0.001$) and 2-hr GT (r= 0.539, $P<0.001$) values (Table IV); meanwhile, hemoglobin oxidation (metHb) was significantly associated with Hb (r= 0.415, $P<0.005$), VAI (r= 0.176, P= 0.02) and 2-hr GT (r= 0.64, $P<0.001$) values. Additionally, Table V indicated that the rate of WP smoking (session/day) was significantly associated with Hb (r= 0.574, $P<0.001$), Hct (r= 0.287, $P<0.001$), MetHb (r= 0.598, $P<0.001$), WBC (r= 0.171, P= 0.02) and 2-hr GT (r= 0.162, P= 0.03) values.

TABLE I - Demographic, anthropometric and metabolic characteristics of the surveyed subjects

Variable	**NS *n*=176**	**CS *n*=178**	**WPS *n*=174**
Age (year)	24.8±3.2	25.6±3.7	25.5±3.0
Bodyweight (kg)	79.7±9.2	82.7±6.7*[a]	80.7±9.8[b]
BMI (kg/m^2)	26.20±3.2	28.3±2.5*[a]	27.0±3.5*[b]
Waist Circumference (cm)	89.2±10.9	101.4±19.3*[a]	94.8±9.2*[b]
Education status n (%)			
None	0 (0)	14 (8)	14 (8)
Primary	28 (16)	7 (4)	49 (28)
Secondary	35 (20)	93 (52)	62 (36)
College	113 (64)	64 (36)	49 (28)
Smoking duration (Year)	0	4.5±2.1[a]	3.7±1.7[b]
Smoking rate		*Cigarette/day*	*Session/day*
	0	19.3±5.6	1.9±0.93
SBP (mmHg)	120.2±5.9	128.6±7.6*[a]	131.1±7.5*[b]
DBP (mmHg)	79.1±5.2	84.5±5.7*[a]	87.6±7.1*[b]
Hemoglobin (g/dl)	14.2±1.1	15.4±0.9*[a]	15.6±0.8*[b]
Hematocrit (%)	42.6±2.6	46.5±3.0*[a]	48.6±2.8*[b]
WBC (cell x 10^9/L)	6.8±0.9	9.4±1.5*[a]	9.3±1.1*[a]
MetHb (%)	0.61±0.6	3.03±1.4*[a]	3.57±0.95*[b]
Triglycerides (mg/dl)	155.4±10.2	192.1±19.5*[a]	192.1±13.7*[a]
HDL-c (mg/dl)	52.7±6.4	38.8±4.1*[a]	36.7±3.3*[b]
VAI	3.8±0.7	6.9±1.7*[a]	7.1±1.3*[a]
2-hr GT (mg/dl)	93.0±9.3	107.7±17.5*[a]	114.6±15.0*[b]

Values are expressed as a percentage or mean±SD; * significant difference (P<0.05) compared with non-smokers; values with different superscripts (a,b) between smokers groups are significantly different (P<0.05); *n*: number of subjects; BMI: body mass index; SBP: systolic blood pressure; DBP: Diastolic blood pressure; WBC: white blood cells; MetHb: methemoglobin; HDL-c: high-density lipoprotein cholesterol; VAI: visceral adiposity index; GT: glucose tolerance.

TABLE II - Correlation (*r* values) between the duration of cigarette smoking and some of the studied markers in cigarette smokers

	Duration (year)	**Hb (g/dl)**	**Hct (%)**	**WBC (x10^9/L)**	**MetHb (%)**	**VAI**	**2-hr GT (mg/dl)**
Duration (year)		-0.181*	-0.154	-0.153	0.958*	0.501*	0.906*
Hb (g/dl)	-0.181*		0.576*	0.075	-0.178*	-0.187*	-0.146
Hct (%)	-0.154	0.576*		0.174*	-0.131	-0.075	-0.074

TABLE II - Correlation (*r* values) between the duration of cigarette smoking and some of the studied markers in cigarette smokers

	Duration (year)	Hb (g/dl)	Hct (%)	WBC ($x10^9$/L)	MetHb (%)	VAI	2-hr GT (mg/dl)
WBC ($x10^9$/L)	-0.153	0.075	0.174*		-0.133	-0.036	-0.186*
MetHb (%)	0.958*	-0.178*	-0.131	-0.133		0.441*	0.837*
VAI	0.507*	-0.187*	-0.075	-0.036	0.441*		0.461*
2-hr GT (mg/dl)	0.906*	-0.146	-0.074	-0.186*	0.837*	0.461*	

* significant difference (P<0.05); BMI: body mass index; Hb: hemoglobin; Hct: hematocrit; WBC: white blood cells; MetHb: methemoglobin; VAI: visceral adiposity index; GT: glucose tolerance.

TABLE III - Correlation (*r* values) between the rate of cigarette smoking and some of the studied markers in cigarette smokers

	Rate (Cig/day)	Hb (g/dl)	Hct (%)	WBC ($x10^9$/L)	MetHb (%)	VAI	2-hr GT (mg/dl)
Rate (Cig/day)		0.329*	0.501*	0.155*	0.191*	0.091	0.160*
Hb (g/dl)	0.329*		0.576*	0.075	-0.178*	-0.187*	-0.146
Hct (%)	0.501*	0.576*		0.174*	-0.131	-0.075	-0.074
WBC ($x10^9$/L)	0.155*	0.075	0.174*		-0.133	-0.036	-0.186*
MetHb (%)	0.191*	-0.178*	-0.131	-0.133		0.441*	0.837*
VAI	0.091	-0.187*	-0.075	-0.036	0.441*		0.461*
2-hr GT (mg/dl)	0.160*	-0.146	-0.074	-0.186*	0.837*	0.461*	

* significant difference (P<0.05); BMI: body mass index; Hb: hemoglobin; Hct: hematocrit; WBC: white blood cells; MetHb: methemoglobin; VAI: visceral adiposity index; GT: glucose tolerance.

TABLE IV - Correlation (*r* values) between duration of water-pipe smoking and some of the studied markers in the water-pipe smokers

	Duration (year)	Hb (g/dl)	Hct (%)	WBC ($x10^9$/L)	MetHb (%)	VAI	2-hr GT (mg/dl)
Duration (year)		0.613*	0.423*	0.114	0.806*	0.282*	0.539*
Hb (g/dl)	0.613*		0.726*	0.030	0.514*	-0.169*	0.141
Hct (%)	0.423*	0.726*		-0.031	0.381*	-0.256*	0.143
WBC ($x10^9$/L)	0.114	0.030	-0.031		0.042	0.345*	0.062
MetHb (%)	0.806*	0.514*	0.381*	0.042		0.176*	0.640*
VAI	0.282*	-0.169*	-0.256*	0.345*	0.176*		0.446*
2-hr GT (mg/dl)	0.539*	0.141	0.143	0.062	0.640*	0.446*	

* significant difference (P<0.05); BMI: body mass index; Hb: hemoglobin; Hct: hematocrit; WBC: white blood cells; MetHb: methemoglobin; VAI: visceral adiposity index; GT: glucose tolerance.

TABLE V - Correlation (*r* values) study between the rate of water-pipe smoking and some of the studied markers in water-pipe smokers

	Rate (session/day)	Hb (g/dl)	Hct (%)	WBC ($x10^9$/L)	MetHb (%)	VAI	2-hr GT (mg/dl)
Rate (session/day)		0.574*	0.387*	0.171*	0.598*	-0.055	0.162*
Hb (g/dl)	0.574*		0.726*	0.030	0.514*	-0.169*	0.141
Hct (%)	0.387*	0.726*		-0.031	0.381*	-0.256*	0.143
WBC ($x10^9$/L)	0.171*	0.030*	-0.031		0.042	0.345*	0.062
MetHb (%)	0.598*	0.514*	0.381*	0.042		0.176*	0.640*
VAI	-0.055	-0.169*	-0.256*	0.345*	0.176*		0.446*
2-hr GT (mg/dl)	0.162*	0.141	0.143	0.062	0.640*	0.446*	

* significant difference ($P<0.05$); BMI: body mass index; Hb: hemoglobin; Hct: hematocrit; WBC: white blood cells; MetHb: methemoglobin; VAI: visceral adiposity index; GT: glucose tolerance.

DISCUSSION

The results of the present study showed that both cigarette and water-pipe smoking have remarkable effects on the anthropometric parameters (body weight, BMI, and WC), and water-pipe smoking demonstrates significantly higher impact compared with cigarette smoking. In line with our findings, a cross-sectional study from Syria reported that water-pipe smoking was correlated with a high risk of obesity (Ward *et al*., 2015). In both types of smoking habits, this significant increase in body weight and adiposity can be correlated with the submaximal exercise capacity, which is found to be more prevalent in water-pipe smokers (Ben Saad *et al*., 2010). Moreover, current smokers had a higher craving for a high-fat diet, and great difficulties in bodyweight reduction and changing their dietary habits (Chao *et al*., 2017).

In the present study, both cigarette and water-pipe smokers had significantly higher levels of Hb, Hct, and WBC compared with non-smokers, and water-pipe smokers showed significantly higher values of Hb and Hct compared with the CS group. In this regard, previous reports did not show consistent results, since Hb and WBC levels were not affected during chronic exposure of rats to WP smoke, while associated with a significant increase in Hct value (Miri-Moghaddam *et al*., 2014). Meanwhile, a case-control study from Sudan showed that WPS had significantly higher levels of Hb, Hct, and WBC (Nadia, Shamseldein, Sara, 2015). Moreover, the present data revealed a significant increase of MetHb levels in both types of smokers compared with non-smokers, with the higher influence of WPS over CS in this regard. This may be attributed to the significant increase of oxidative stress markers and attenuation of the antioxidant defense systems in both CS and WPS groups (Szulińska *et al*., 2013; Yalcin *et al*., 2017).

The present study showed that CS and WPS significantly increased SBP and DBP compared with non-smokers. These results are consistent with many previous reports that demonstrate immediate effects smoking on BP and found to be correlated with the duration and rate of smoking, with more significant influence of WPS in this respect (Eissenberg, Shihadeh, 2009; Cobb *et al*., 2012; Layoun *et al*., 2014). The greater significant effects of WPS on health risks compared with CS can be related to that WP smokers inhale more tobacco smoke than cigarette smokers and the large volume of inhaled smoke during one smoking session that may last more than one hour. Additionally, charcoal is used as a source of heat to burn WP tobacco, which can be associated with the release of high amounts of potentially toxic chemicals including carbon monoxide and heavy metals

(Chan, Murin, 2011). The present study demonstrated the significant negative impacts of WPS and CS on TG and HDL-C levels compared with non-smokers, which explain the reported elevation of the abdominal adiposity marker (VAI) of the smokers. This significant increase in abdominal obesity, which is positively associated with the duration of smoking, could be related to the nicotine-induced activation of the hypothalamus-pituitary-adrenal axis and the associated elevation of serum cholesterol levels (Rohleder, Kirschbaum, 2006). Moreover, nicotine-induced catecholamine release induces lipolysis and increased serum TG levels and HDL-C metabolism (Zhu *et al*., 2011). In the present study, we showed that active WPS and CS was associated with increased levels of 2-hr GT compared with non-smokers and positively associated with VAI and duration of smoking. To our knowledge, this is the first cross-over study to show the association of rate and duration of WP smoking with the glycemic tolerance in healthy WP smokers and compared that with cigarette smokers. Currently, few studies have demonstrated the association between cigarette and WP smoking and increased risks of glycemic intolerance and type 2 diabetes mellitus. A meta-analysis study indicated that active smokers had an elevated risk of type 2 diabetes mellitus compared with non-smokers (Willi *et al*., 2007). However, the extent to which smoking habits impair the glycemic tolerance of healthy smokers was not fully elucidated with inconsistent results and the results. Some data mentioned that active smoking was associated with higher HbA1c levels (Baggio *et al*., 2002; Nilsson *et al*., 2004), whereas others did not (Anan *et al*., 2006; Wang *et al*., 2019). In the present study, active CS and WPS were associated with higher 2hr-GT levels, supporting the idea of positive association. Taken together, these results may support the benefit of smoking cessation for healthy subjects to avoid impaired glucose tolerance, insulin resistance, and type 2 diabetes mellitus. Various pathophysiologic mechanisms are suggested to explain the effect of smoking on glycemic control. Smoking is associated with insulin resistance (Sultana *et al*., 2019) and elevated levels of systemic inflammation, oxidative stress markers (Khan *et al*., 2019), and sympathetic activity (Moheimani *et al*., 2017). These factors may contribute to insulin resistance. Furthermore, elevated levels of WC despite lower BMI in current smokers (Canoy *et al*., 2005), may partly contribute to increased insulin resistance. Another possible mechanism that mediates this relationship may be the deteriorated β-cell function (Xu *et al*., 2018) as an outcome of chronic pancreatic inflammation (Xiang *et al*., 2017). There are some limitations in the present study including the exclusion of the presence of passive smoking habit, which may influence the studied parameters. Therefore, the possibility of influence by passive smoking cannot be ignored. Additionally, the current study enrolled only male participants due to the very low prevalence of CS and WPS among Iraqi females attributed to the local cultural background. Finally, the cross-sectional design of the present work does not allow for predicting any cause-and-effect relationships, while there may be other confounding factors besides those evaluated in the present study.

CONCLUSION

The present study suggests that both cigarette and water-pipe smoking have significant deleterious effects on body fat distribution, glucose tolerance, and hematological markers. There was a positive association between the rate of smoking and obesity, glycemic intolerance in both groups.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in this work.

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