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Comparison of blood constituents related to metabolic syndrome in different *Mizaj*es (Temperaments)

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ABSTRACT

Background: According to Canon, illness could be without any established disease and without any manifested changes in measurable parameters. Therefore, it is possible to assume metabolic syndrome as an illness. *Objectives:* The aim of this study is try to answer this question if the blood constituent's profile, within normal limits, related to metabolic syndrome, differs in persons with various normal temperament profiles. *Methods:* A descriptive study performed on 400 healthy subjects of either sex with ranging in age from 20 to 40 years. The participants' mizaj was determined using questionnaire. Measurement was carried out by blood cell counter Sysmex KX21N and auto-analyzer Erba XL 600 using Pars Azmoon Company's Quantitative Detection Kit. SPSS16 was used for data analysis. *Results:* There was a statistically significant difference in glucose (p=0.007) and triglycerides (p=0.004) of females with warmness-wetness and warmness-dryness. The highest average values of FBS and cholesterol as well as the lowest average value of HDL-C were in males with coldness-wetness Mizaj. The highest mean of triglycerides was in males with warmness-wetness. Those who sorted into dryness group have an average glucose, triglycerides and cholesterol concentration lower and HDL-C, amylase and lipase concentration higher than wetness individuals. There was a negative correlation between lipase and glucose (r=-0.25, p=0.001), triglycerides (r=-0.18, p=0.047). *Conclusion:* The wetness Mizaj could be a predictable Mizaj of prone to metabolic syndrome.

Keywords: Mizaj, Metabolic Syndrome, Blood constituents, Persian traditional medicine

1. INTRODUCTION

The blood constituents profile even in normal limits varies according to different factors such as races, gender, and in the same person under various conditions. This profile is based on biochemical reactions which affect and are also affected by the changes in the body and impart a certain Mizaj (temperament) to the body as well (Akbar, 2012). In the Canon, Avicenna states "Mizaj" is that quality which results from the mutual interaction and impression of the four contrary primary qualities, namely heat, cold, moisture, dryness residing within the (imponderable) elements (Avicenna, 1973). In Persian traditional medicine, Mizaj have divided into nine categories including medium and four simple Mizajes warm, cold, moist, and dry and four combined Mizajes warm and moist, warm and dry, cold and moist, cold and dry (Mojahedi et al., 2014). The normal population Mizaj, which is basically the upper and lower limits of normal range, is the narrowest of Mizaj (Abu-Asab et al., 2013). The imbalance in body Mizaj and humors is the trigger for increasing susceptibility to illness or leads to the onset of disease condition (Abu-Asabet al., 2013; Rezaeizadeh et al., 2009). Humors are the soluble substances produced from food and drink by the digestive stages, including blood, phlegm, yellow bile, and black bile. Thus, humors are referring to classes of biochemical compounds in the human body. Based on Persian traditional medicine, the various digestive processes, in order of the food materials passageway, includes a certain amount of digestion during the act of mastication, true digestion in the stomach by reason of the heat of the enveloping members, yielding "chyle", the digestive function of the liver, the vessels digestion, and finally, the tissues bath (Avicenna, 1973; Abu-Asab et al., 2013).

The metabolic syndrome is a cluster of conditions includes obesity, hyperglycemia, dyslipidemia, and hypertension. Component features include insulin resistance, fasting hyperglycemia, raised blood pressure, raised triglycerides, low HDL-cholesterol concentrations, and obesity (in particular, abdominal obesity). The presence of these clinical conditions is associated with increased risk of cardiovascular disease and of developing diabetes (Burtis et al., 2012; Alberti et al., 2005).

The discussion about a healthy person could be focused on normal temperament and element composition of the blood. According to Canon, illness could be without any established disease and without any manifested changes in measurable parameters and result from simple disturbance of temperament without the involvement of any humors. Ill used for conditions which have not been diagnosed, and yet may prove (Akbar, 2012; Abu-Asab et al., 2013; Sina, 1997). Therefore, it is possible to assume metabolic syndrome as an illness. Now, the question is, does the study of Mizaj and humor in relation to the modern blood and serum parameters arrives us at early signs of illness, diagnose, and treat? The aim of this study is try to answer this question if the blood constituent's profile, within normal limits, related to metabolic syndrome, differs in persons with various normal temperament profiles. With the results of this study, the potential for developing a metabolic syndrome in virtue of Mizaj type could be predictable.

2. METHODS AND MATERIAL

The QUMS (Qazvin University of Medical Sciences) committee approved our study (Ethical Code: IR.QUMS.REC.1396.82). A descriptive study performed on 400 healthy subjects of *either sex* with ranging in *age* from 20 to 40 years. For participation in the study, the adequate information delivered to the volunteers by written consent form. Demographic forms were fulfilled. Exclusion criteria were current evidence history of any clinically significant disease or any chronic disease, pregnancy, taking any drug or medication, smoking, alcohol ingestion and vegetarian. The participants' mizaj was determined using questionnaire that traditional medicine researchers of Shahed University of medical science had previously found its satisfactory reliability and validity.
All participants were asked to fast for 8 to 12 hours before blood taking. Venous whole blood samples were collected using anticoagulant ethylene diamine tetraacetic acid (EDTA) for analysis of platelets and without the use of anticoagulants in order to test the serum constituents. Platelets were immediately measured with blood cell counter Sysmex KX21N (Sysmex Corporation, Kobe, Japan). Serum obtained by centrifugation (150 g for 5 min) of 3 ml coagulated whole blood. Measurement of biochemical analytes FBS, triglycerides, cholesterol, HDL-C, LDL-C, alpha-amylase, lipase was performed using the Pars Azmoon Company's Quantitative Detection Kit (Iran) and by auto-analyzer Erba XL 600 (Mannheim, Germany).

Statistical analysis

Software of SPSS16 (SPSS, Chicago, IL, USA) was used for data analysis. The obtained data were analyzed by statistical tests of means ± SD, ANOVA, and independent samples t-test and Pearson correlation coefficient. A p- value of <0.05 was the chosen significant level.

3. RESULTS

We studied four hundred volunteers with a mean age of 28.7±7.6 (range 20-40) years. The subjects were 177 males (44.2%) and 223 females (55.8%). Regardless of the gender, the percentage of the participant individuals, which falls on five sectors of combined mizajes, included coldness-wetness, coldness-dryness, warmness-wetness, and warmness-dryness were 21.75%, 10.75%, 22.75%, 11.5% respectively. In addition, the total estimated frequencies of four simple mizajes were coldness 32.5%, warmness 34.25%, wetness 44.5% and dryness 22.25%. The rest of these sectors are medium mizaj with frequency of 33.25% in the totality of subjects. The frequencies of warmness-wetness in males and coldness-wetness in females were more common among different combined mizajes.

The observed analyte values with typical reference intervals or at recommended normal cut-off points in adults have been included in this study. Lowest or highest values was considered an outlier and therefore omitted from all further analyses. Analysis of blood constituents levels of FBS, triglycerides, cholesterol, HDL-C, LDL-C, amylase, lipase and platelet in different groups have been shown in tables 1 to 5. In general, the outcome of the comparison study of analytes, by gender, displayed that HDL-C and platelet value averages were higher in women than in men, which only the latter was significant (p=0.004). The mean of four others including FBS, triglycerides, cholesterol, and amylase, were higher in men than women but not statistically significant (p>0.05). Pairwise comparisons among combined mizajes by gender showed that a statistically significant difference exists in FBS (p=0.007) and triglycerides (p=0.004) of females with warmness-wetness and warmness-dryness.In addition, in women with coldness-wetness to coldness-dryness Mizaj was significantly more mean values of HDL-C (p=0.04) and lipase (p=0.02).

The results showed that the highest average values of FBS (96.9±6.1 mg/dl) and cholesterol (183.6±32.1 mg/dl) as well as the lowest average value of HDL-C (45±8.1 mg/dl) were in males with coldness-wetness Mizaj (table 1-5). In addition, the lowest average values of FBS (85.6±6.1 mg/dl), triglycerides (67.6±21.5 mg/dl) and cholesterol (162.6±27.3 mg/dl) found in females with warmness-dryness mizaj. Besides, the highest mean of triglycerides (101.3±37.6 mg/dl) was in males with warmness-wetness.

When two opposite simple Mizajes in total subjects are compared, there are a statistically significant difference between dryness and wetness Mizajes for FBS (p=0.001), triglycerides (p=0.0001), cholesterol (p=0.02), HDL-C (p=0.02), lipase (p=0.01) and amylase (p=0.03). Those who sorted into dryness group have an average FBS, triglycerides and cholesterol concentration lower and HDL-C, amylase and lipase concentration higher than wetness individuals. In general, simple Mizajes with coldness or wetness have higher mean amount of triglycerides, cholesterol, and LDL-C.

Correlation analysis revealed no association between amylase and FBS or lipids (p>0.05) except for HDL-C (r=0.144, p=0.026). There was a negative correlation between lipase and FBS (r=-0.25, p=0.001), triglycerides (r=-0.18, p=0.047), and no association with cholesterol (r=-0.044, p=0.541), LDL-C (r=0.045, p=0.472), and HDL-C (r=0.045, p = 0.52). Regarding LDL-C and platelet profile, although, the results of mizaj groups had not statistically significant difference in LDL-C and platelet, but the highest mean of those was observed in coldness-wetness men and coldness-dryness women, respectively.

Table 1 Comparison of fasting blood sugar levels between temperament indices

Sex	Indices		Fasting blood sugar levels (mg/dl)				
			Min	Max	Mean	±SD	P value
Male	Coldness	Wetness	82	100	96.9	8.1	0.067
		Dryness	70	99	90.5	10.5	
	Warmness	Wetness	80	100	93.6	7.6	0.159
		Dryness	82	97	90.5	5.2	
	Medium		70	97	91.7	10.7	
	Total		70	100	92.6	9.5	
Female	Coldness	Wetness	71	100	89.5	9.2	0.441
		Dryness	76	96	87.2	10.4	
	Warmness	Wetness	76	100	92.2	9.4	0.007
		Dryness	76	96	85.6	6.1	
	Medium		70	99	87.7	10.3	
	Total		70	100	88.4	10.2	
Total	Coldness		70	100	90.6	10.1	0.48
	Warmness		70	100	90.9	9.1	
	Wetness		70	100	92.3	9	0.001
	Dryness		70	99	87.8	8.7	
	Medium		67	110	89.5	9.8	

Table 2 Comparison of lipids levels between temperament indices

Sex	Indices		Triglycerides levels (mg/dl)					Cholesterol levels (mg/dl)				
			Min	Max	Mean	±SD	P value	Min	Max	Mean	±SD	P value
Male	Coldness	Wetness	36	142	95.9	32.9	0.34	134	228	183.6	32.1	0.08
		Dryness	40	138	81.2	33.3		137	217	169.8	24.6	
	Warmness	Wetness	42	149	101.3	37.6	0.56	105	236	178.3	30.1	0.39
		Dryness	45	147	87.2	30.8		113	238	170.5	37.7	
	Medium		34	145	87.6	28.2		115	241	178.2	30.6	
	Total		34	149	99.3	34.4		105	241	176.0	31.3	
Female	Coldness	Wetness	33	148	92.7	35.6	0.21	117	238	174.3	28.4	0.39
		Dryness	47	131	83.5	25.3		124	224	169.2	29.6	
	Warmness	Wetness	38	148	92.3	31.1	0.004	132	236	175.9	27.3	0.06
		Dryness	42	115	67.6	21.5		123	208	162.6	27.3	
	Medium		37	146	83.5	31.2		96	237	168.5	31.2	
	Total		33	148	92.3	39.3		96	238	169.9	29.2	
Total	Coldness		33	148	97.9	34	0.72	117	238	174	28.6	0.70
	Warmness		42	149	96	31.2		105	238	172.5	31.3	
	Wetness		38	149	105	34	0.0001	105	238	176.4	29.2	0.02
	Dryness		42	147	82	25		113	238	166.7	28.8	
	Medium		65	110	85.8	30.9		96	241	171.5	32.1	

Table 3 Comparison of lipoproteins levels between temperament indices

Sex	Indices		LDL-C levels (mg/dl)					HDL-C levels (mg/dl)				
			Min	Max	Mean	±SD	P value	Min	Max	Mean	±SD	P value
Male	Coldness	Wetness	71	98	86	12.7	0.49	30	62	45	8.1	0.70
		Dryness	36	100	79.7	22.5		33	72	47.7	17.8	

	Warmness	Wetness	22	93	81.7	18.3	0.67	31	90	46.3	12.2	0.41
		Dryness	76	100	85.4	11.2		41	63	51.2	8.4	
	Medium		66	97	85.1	10.9		37	73	48.7	9.5	
	Total		22	100	83.9	15.7		30	90	47.7	10.4	
Female	Coldness	Wetness	59	100	83.9	12.4	0.91	35	69	50.6	8.5	0.04
		Dryness	64	99	83.5	12.2		39	76	55.6	10.1	
	Warmness	Wetness	69	89	84.2	9.4	0.56	43	74	55.2	7.9	0.77
		Dryness	63	100	81.8	12.8		33	74	54.3	11.3	
	Medium		49	100	82.9	13.3		31	70	53.2	10.8	
	Total		49	100	83	12.4		31	76	52.9	9.7	
Total	Coldness		36	100	83.9	13.4	0.35	30	76	50.5	10.2	0.83
	Warmness		22	100	81.7	14.5		31	90	50.9	10.5	
	Wetness		22	100	83.1	13.5	0.83	30	90	49.7	9.7	0.02
	Dryness		36	100	82.6	13.6		33	76	53.5	11.2	
	Medium		49	100	84.5	10		30	90	51.1	10	

Table 4 Comparison ofdigestive enzymes levels between temperament indices

Sex	Indices		Amylase levels (mg/dl)					Lipase levels (mg/dl)				
			Min	Max	Mean	±SD	P value	Min	Max	Mean	±SD	P value
Male	Coldness	Wetness	29	101	67.7	18.4	0.81	19	76	41.5	23.4	0.50
		Dryness	42	110	65.5	21.7		0.6	50	32.7	16.6	
	Warmness	Wetness	37	119	62.1	21.1	0.40	0.9	75	31.2	14.2	0.94
		Dryness	60	82	70.4	9.4		21.3	38.3	30.7	7.8	
	Medium		39	105	65.6	15		10.5	72	31.8	16.3	
	Total		29	119	67.2	19.2		0.6	72	33.2	19.2	
Female	Coldness	Wetness	28	96	59.5	14.6	0.12	3.9	101.5	31.2	11.2	0.02
		Dryness	24	96	66.5	19.1		5.4	87.6	41.3	18.5	
	Warmness	Wetness	5	88	58.1	19.1	0.12	5.4	87.6	34.2	17.5	0.36
		Dryness	44	98	66.4	19		21.9	92.5	41.6	20.3	
	Medium		35	86	70.4	23.5		9.4	93.7	37.6	19.4	
	Total		5	98	63.3	19.5		3.9	101.5	36.6	19.7	
Total	Coldness		24	110	62.8	17.2	0.78	0.6	101.5	36.3	17.1	0.27
	Warmness		5	119	62.0	19.2		0.9	92.5	39.9	20.9	
	Wetness		5	119	60.3	17.1	0.03	0.9	101.5	33.2	14	0.01
	Dryness		24	110	66.9	17.7		0.6	92.5	40.7	19.5	
	Medium		34	107	66.3	17		10	99	36.9	17.9	

Table 5 Comparison of Platelet levels between temperament indices

Sex	Indices		Platelet levels (mg/dl)				
			Min	Max	Mean	±SD	P value
Male	Coldness	Wetness	170	295	216.1	35.5	0.27
		Dryness	143	255	201.4	34.4	
	Warmness	Wetness	110	303	206.4	42.7	0.29
		Dryness	144	260	193	35.2	
	Medium		111	330	210.5	47.7	
	Total		111	330	207.2	42.1	

Female	Coldness	Wetness	109	392	222.5	54.2	0.23
		Dryness	153	300	237.7	41.2	
	Warmness	Wetness	163	420	252	57.3	0.12
		Dryness	161	331	228	49.5	
	Medium		231	432	224	62.4	
	Total		109	432	222.8	51.2	
Total	Coldness		109	392	221.9	48.6	0.90
	Warmness		110	420	222.6	51.6	
	Wetness		109	420	224.5	51.7	0.30
	Dryness		143	331	217.3	45.1	
	Medium		111	432	223.5	53.7	

4. DISCUSSION

The most of studied subjects fall into wetness mizaj. A criterion of this mizaj is muscular or fatty that the latter in combined with coldness temperament may progress to obesity which is considered to be a feature of the metabolic syndrome (Mojahedi et al., 2014; Burtis et al., 2012).

In addition, in wetness subjects have been found, on the one hand, a significantly higher mean of FBS, cholesterol, and triglycerides, and, on the other hand, lesser of HDL-C than dryness individuals. Moreover, the highest average values of FBS, cholesterol, and LDL-C, as well as the lowest average value of HDL-C were in males with coldness-wetness mizaj. Considering that the abnormal of those analytes (i.e., increased fasting glucose, triglycerides, cholesterol, LDL-C and decreased HDL-C) in a defining level are criteria for clinical identification of metabolic syndrome (Burtis et al., 2012), one could speculate that men with wetness mizaj especially in combined with coldness may be prone to this condition.

These results are consistent with those reports that impaired fasting glucose and central (visceral) obesity, associated with the development of type 2 diabetes, was observed more frequently in men. Impaired fasting glucose typically being 1.5–3 times higher in men in nearly all age groups. Besides, visceral fat accumulation leading to increased triglycerides, low HDL-C, contributes to the individuals meeting a diagnosis of metabolic syndrome.

In traditional medicine, the fat and the oil are coldness and moist constituents of the body. According to *Avicenna*, in chapter of urinalysis of The Canon of medicine , Serous or phlegmatic humor, which is an also caused by cold and moist humor, the diabetes, and the raw humors (undigested food)are comorbid and are significances of whiteness urine (Avicenna, 1973; Sina, 1997).

In contrast, the association of warmness-dryness mizaj in females with the lowest average values of FBS, triglycerides, cholesterol and LDL-C suggests that the dryness, leading to skinny due to reduction in body fat or muscles, when combined with warmness, might be associated with a decreased risk of metabolic syndrome. Given that individuals with warmness mizaj are muscular, it is perhaps relevant that, diminishing the serum levels of glucose and lipids could be attributed at least in part to better metabolized in mitochondria's muscles. Interestingly, we observed that the levels of essential digestive enzymes amylase and lipase are higher in dryness than wetness mizajes inversely with FBS, lipids and HDL-C.

Total Serum amylase contains an approximately equal proportion of salivary and pancreatic isoenzymes; therefore it have endocrine functions as well; its physiological secretory function could be both digestive or nondigestive (Skrha & Stěpán, 1987; Des Gachons & Breslin, 2016). It has been observed that digestive enzymes (amylase) reduce post-prandial hyperglycaemia (Pierzynowski et al., 2017). A correlation between low serum amylase and type 1 and 2 diabetes, metabolic syndrome, and also increased risk of cardio-metabolic disorders in asymptomatic adult populations has been reported (Des Gachons & Breslin, 2016;Nakajima, 2016). In addition, due to the role of insulin in the synthesis and secretion of amylase, the decrease in the amount of serum amylase in inadequate pancreatic insulin secretion as well as insulin resistance has been found (Nakajima, 2016; Schneeman et al., 1983). Serum amylase (and lipase) levels can be raised in individuals unrelated to pancreas. Increased amylase activity has been observed in various conditions such as dyslipidemia and anorexia nervosa (Borovickova et al., 2016). Moreover, in a classification of healthy, non obese individuals based on the amount of blood amylase as high (HA) or low amylase (LA) has been observed that HA individuals have significantly lower postprandial blood glucose and more AMY1 gene copies within their genomes than the LA individuals (Mandel & Breslin, 2012).

We found that lipase have a strong and weak negative correlation with FBS and triglycerides, respectively, but no correlation with cholesterol or LDL-C and HDL-C. These observations led us to speculate that lipase could be involved in the metabolisms of both glucose and lipids. These results are in agreement with some findings of studies in which diabetic 2 patients have been manifested

lower mean serum amylase and lipase levels than healthy subjects (Lamarche & Paradis, 2007). Srihardyastutie A. et al., found that the increased serum lipase activity is a positively correlated with plasma glucose, but did not correlate with lipid profile (Cholesterol, Triglyceride, HDL and LDL), in Indonesian diabetic 2 patients (Srihardyastutie et al., 2015). Nevertheless, our results were unlike to those reported by Adedeji et al. in diabetes mellitus which lipase activity is elevated at increased concentrations of glucose and lipids (Adedeji et al., 2007).

Given that, there are various lipases, the role that each of them plays in development of metabolic syndrome is a controversial issue. Based on the Miyashita and Shirai study, lipoprotein lipase (LPL) mass is low in type 2 diabetes mellitus and is inversely proportional to the amount of serum triglyceride and directly proportional to the HDL-C, consistent with our results. Also, there was a significant lower LPL in individuals with metabolic syndrome and coronary atherosclerosis (Miyashita & Shirai, 2005). However, unlike LPL, endothelial lipase (EL) that effectively hydrolyzes HDL phospholipids is associated with lower HDL-C and might play a role in progress of atherosclerosis in individuals with overweight and metabolic syndrome (Badellino etal., 2005; Miksztowicz et al., 2014).

Inhibition or decreased synthesis of lipoprotein or hepatic lipases increases plasma triglyceride. In addition, maldigestion of the fat and hyperglycemia have been observed in pancreatic lipase deficiency. Besides, in Persian traditional medicine the existence of oily substance in blood, the diabetes or anorexia could be due to abnormal digestion, raw humors or dominant phlegmatic humor (Emtiazy et al., 2012). Furthermore, the higher of FBS and lipids levels in wetness mizajes might be attributable in part to less observed normal activity of amylase and lipase than dryness.

Our results showed that a mildly high LDL-C and platelets in men with coldness-wetness Mizaj. Diet-induced hyperlipidemia can potently activates human platelets via oxidized LDLs (Relou et al., 2003). Oxidized HDLs, on the contrary, can inhibit platelet aggregation (Valiyaveettil et al., 2008). Thus, it has been reported that platelet hyper reactivity in response to elevated levels of oxidized LDL contribute to atherogenesis, diabetes, and the metabolic syndrome (Pravenec & Kurtz, 2002).

5. CONCLUSION

People with different normal Mizajes indicate different mean value of some blood and serum parameters, within normal limits, related to metabolic syndrome. As expected, the wetness Mizaj individuals have higher mean normal levels of FBS and lipids, especially when combined with coldness Mizaj in men. Thus, this could be a predictable Mizaj of prone to metabolic syndrome. In addition, it appears that metabolic role of digestive enzymes such as amylase and lipase, which are less value in wetness than dryness Mizajes, influences on progress to metabolic syndrome.

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