Exposure to Airborne Particulate Matter: An Additional Risk Factor for Metabolic Syndrome in Saudi Arabia

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Abstract. Metabolic syndrome is a serious problem in Saudi Arabia. It has been attributed mainly to life style. Exposure to airborne particulate matter is a subject of concern in Jeddah. The present study aimed to find a possible association of metabolic syndrome prevalence with levels of particulate matter and their elemental constituents. The study was conducted in two districts of Jeddah, Al Nuzlah and Al Rehab. PM₁₀ and PM_{2.5} were measured in each district as well as their elemental composition. Metabolic syndrome was defined by the presence of three components: hyperglycemia, hypertension and obesity. Al Nuzlah district showed higher prevalence of metabolic syndrome, together with higher levels of PM_{2.5}, nickel and cadmium. It can be concluded that exposure to particulate matter may be considered as an additional risk factor for metabolic syndrome.

Keywords: Particulate Matter, Metabolic Syndrome, Jeddah, Elemental Composition, Risk Factors.

Introduction

The combination of interrelated metabolic abnormalities predisposing individuals to cardiovascular diseases is usually referred to as metabolic syndrome (MetS) (Lindsay and Howard, 2004; Alberti, *et al.*, 2005 and Suzuki, *et al.*, 2008). Presence of any three of five risk factors (abdominal obesity, elevated triglycerides, reduced high-density lipoprotein cholesterol, elevated blood pressure and elevated fasting glucose) constitutes a diagnosis of MetS (Albert, *et al.*, 2009). MetS is a risk factor not only for cardiovascular diseases, but also, for various cancers mainly endometrial (Rosato, *et al.*, 2011) and colorectal (Pelucchi, *et al.*, 2010) cancers.

Increased oxidative stress, through increased reactive oxygen species (ROS) levels, was found to play a central role in metabolic syndrome and its component pathologies (Hutcheson and Rock, 2012): obesity (Furukawa, *et al.*, 2004 and Montero, *et al.*, 2012), hyperglycemia (De Mattia, *et al.*, 2008), dyslipidemia (Zelzer, *et al.*, 2011), and hypertension (Ward, *et al.*, 2004 and Wang, *et al.*, 2009).

Association between exposure to airborne particulate matter (PM) and health is well established. Particle size: fine particles (PM_{2.5}) and ultrafine particles (PM_{1.0}), and their metal content (Ni, V, Br, Cr, As, Mn), were found to play a critical role in the PM

toxicity (Araujo and Nel, 2009, Zanobetti, *et al.*, 2009 and Bell, 2012).

PM exposure was found to promote the development of the metabolic syndrome (Hutcheson and Rock, 2012), or its components: diabetes (Gonzalez, *et al.*, 2013 and Chen, *et al.*, 2013a) and hypertension (Chen, *et al.*, 2013b), increased oxidative stress being the fundamental mechanism (Chuang, *et al.*, 2007 and Ghio, *et al.*, 2012). Metal-containing inhalable nanoparticles can penetrate the alveolar-septal barrier and generate oxidative stress both via activation of alveolar macrophage and systemic vascular oxidases including NAD(P)H, mitochondrial and xanthine oxidases (Zanobetti, *et al.*, 2009). Moreover, metals directly support electron transport to generate oxidants and also diminish levels of antioxidants (Ghio, *et al.*, 2012). Some metals contribute to MetS through their endocrine-disrupting properties (De Coster and van Laberecke, 2012).

People with MetS exposed to particulate matter (PM) showed greater susceptibility to PM-associated cardiac effects. Autonomic dysfunction (Chen and Schwartz, 2008) and inflammatory responses (Park, *et al.*, 2010) were two suggested mechanisms.

The prevalence and characteristics of MetS in Saudi Arabia was studied as early as 2002. These studies reported different prevalence depending on different definitions: World Health Organization (WHO), National Cholesterol Education Program (NCEP), Adult Treatment Panel III (ATP III), and International Diabetes Federation (IDF). The overall MetS prevalence ranged from 16.7% to 40% (Akbar, 2002; Al-Qahtani and Imtiaz, 2005; Al-Nozha, *et al.*, 2005; Al-Qahtani, *et al.*, 2006; Barrimah, *et al.*, 2009; Al-Daghri, *et al.*, 2010, Al-Zahrani, *et al.*, 2012; Bahijri, *et al.*, 2013 and Bahijri and Al-Raddadi, 2013).

The most common factors were hypertension, low HDL cholesterol, and abdominal obesity.

Exposure to PM₁₀ collected from Jeddah, Saudi Arabia, was found to induce cholesterol and lipid metabolism genes both in vitro (Sun, *et al.*, 2012) and in vivo (Brocato, *et al.*, 2014). This is the first study trying to point out that in addition to the classical risk factors, air pollution is an important additional risk factor for MetS.

Materials and Methods

Study Population

Due to the anticipated differences in the socioeconomic and pollution levels between South and North Jeddah, the present study was carried out in two districts, Al Nozlah district representing South Jeddah, and Al Rehab district representing North Jeddah. This study was conducted by interviewing individuals visiting one mega-mall in each district. A team was present in each mall during weekends' nights, from June 2011 to September 2011. Participants were selected based on their willingness. The only criterion for exclusion was living in the area (north or south) for less than 15 years. Before interviewing, one of the researchers explained the purpose of the study and the content of the questionnaire, which did not require the participant to be identified by name. Therefore, confidentiality was strictly maintained in all the completed questionnaires. An informed verbal consent was obtained from each participant. Participants were informed about the results of their examination in situ.

The questionnaire included age, occupation, home address, past history of diabetes, hypertension and any other chronic diseases, smoking habits, physical activity and vegetables and fruits consumption. After the interview, the participant's body weight and height were recorded in light clothes and no

shoes. Body mass index (BMI) was calculated according to the formula: $BMI = \text{mass (kg)} / (\text{height (m)})^2$. Concerning the smoking history, Indrayan's smoking index was calculated. It accounts for different characteristics like cigarettes smoked per day, duration of smoking, passive smoking, smoking of filter cigarettes or water pipes, age at start and duration elapsed since quitting by ex-smokers (Aslam, et al., 2011).

An accurate blood pressure measurement was done. Each participant was asked to sit comfortably for 5 min prior to the examination, during which his back was fully supported. Three measurements were taken with 5 minutes interval and their mean recorded. Random capillary blood sugar levels were measured by finger pricks. Participants reporting use of anti-hypertensive drugs were considered hypertensive regardless of their blood pressure reading. The same was applied to diabetic patients.

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Metabolic syndrome cases were subjects having all three metabolic syndrome components, i.e., Capillary blood sugar: > 130 , systolic blood pressure: > 130 &/or diastolic blood pressure: > 85 , BMI: for males > 29.0 and for females: > 29.9 . Free subjects were those having none of the aforementioned MetS components.

Air Sample Collection

Two sampling sites were selected, one located in Al Nozlah district representing south Jeddah, the other in Al Rehab district in north Jeddah. They were set at a height of 9 meters above the ground level on the roof of a building in each district. Using $PM_{2.5}$ and PM_{10} samplers (Automated Cartridge

Collector Unit (ACCU) Sampler), the samples were collected using a calibrated vacuum pump (Gast, USA) to draw air at a rate of 10 L/min, and daily 24 hour samples were collected on Teflon filters (GelmanTeflo, 37 mm, 0.2 μm pore-size) from midnight to midnight. The flow rates of the vacuum pump were calibrated before and after each sampling session. Samples were collected from June 2011 to September 2011 at a rate of three times per week, once on a weekend day and twice on weekdays.

Gravimetric and Elemental Analysis

The detailed description for gravimetric and elemental analysis of samples via energy dispersive X-ray fluorescence (ED-XRF) is provided in Maciejczyk and Chen (2005). In short, filter masses were measured on a microbalance (model MT5, Mettler-Toledo Inc., Highstown, NJ), and the samples were subsequently analyzed for 12 elements by nondestructive XRF (model EX-6600-AF, Jordan Valley) using two secondary fluorescers (Ti and Ge), and spectral software XRF2000v3.1 (U.S. EPA and ManTech Environmental Technology, Inc.). Concentrations of elements above detection limit were defined as 3 times of the uncertainty of the measurements (3σ).

Statistical Analysis

We first conducted χ^2 tests to compare differences in distribution of selected population characteristics for the free subjects and the MetS cases between the two districts. Then, we applied the Wilcoxon-Mann-Whitney test for testing the significance when the median of the concentration of PM_{10} and their elemental constituents were compared. Significance was accepted at $p < 0.05$, $p < 0.01$. All analyses were completed using SAS (V.9.3; SAS Institute Inc, Cary, North Carolina, USA).

Results

Table 1 shows the distribution of metabolic syndrome cases and free subjects by selected population characteristics. The percentage of cases with metabolic syndrome was significantly higher ($P < 0.01$) in Al Nuzlah

districts reaching 49.0% versus 18.6% in Al Rehab district. There were no significance differences in sex, age, BMI, smoking, educational level, regular exercise performing and vegetable and fruit consumption between the two studied districts.

Table 1. Distribution of metabolic syndrome cases and free subjects by selected population characteristics in the two districts. (Al Nuzlah: n=100, Al Rehab: n=145).

		Free subjects		MetS cases	
		Al Nuzlah	Al Rehab	Al Nuzlah	Al Rehab
		n (%)	n (%)	n (%)	n (%)
Total		51 (51.0%)	118 (81.4%)	49 (49.0%)**	27 (18.6%)
Sex	Male	57 (70.4%)	48 (64.9%)	15 (78.9%)	37 (52.1%)
	Female	24 (29.6)	26 (35.1%)	4 (21.1%)	34 (25.4%)
Age (years) (Mean $\pm$ SD)		24.06 $\pm$ 6.23	27.45 $\pm$ 5.76	41.21 $\pm$ 9.87	40.23 $\pm$ 11.36
BMI (Kg/m²) (Mean $\pm$ SD)		23.02 $\pm$ 2.16	24.12 $\pm$ 2.82	33.55 $\pm$ 2.99	34.17 $\pm$ 3.16
Smoking	Non Smokers	70 (86.4%)	60 (81.1%)	12 (63.2%)	43 (60.6%)
	Smokers	11 (13.6%)	14 (18.9%)	7 (36.8%)	28 (39.4%)
Educational level	Undergraduate	53 (65.4%)	39 (52.7%)	11 (57.9%)	44 (61.9%)
	Graduate	28 (34.6%)	35 (47.3%)	8 (42.1%)	27 (38.1%)
Regular exercise	Yes	29 (35.8%)	24 (32.4%)	4 (21.1%)	18 (25.4%)
	No	52 (64.2%)	50 (67.6%)	15 (78.9%)	53 (74.6%)
Vegetable and fruit consumption	< 5 servings/ day	75 (92.6%)	65 (87.8%)	16 (84.2%)	61 (85.9%)
	5+ servings/day	6 (7.4%)	9 (12.2%)	3 (15.8%)	10 (14.1%)

**p<0.01

The concentration of PM₁₀ and their elemental constituents ($\mu\text{g}/\text{m}^3$) in the two districts, Al Nuzlah and Al Rehab are presented in Table 2. When the medians were

compared, no statistically significant differences could be detected between the median levels of total PM₁₀ or their elemental constituents, between the two districts.

Table 2. Concentration of PM₁₀ and their elemental constituents (µg/m³) in the two districts, Al Nuzlah and Al Rehab.

PM₁₀						
	Al Nozlah			Al Rehab		
µg/m ³	Mean	SD	Median	Mean	SD	Median
Total	73.5140	10.1338	71.7015	68.9484	20.4789	60.2780
Ti	0.1538	0.0280	0.1622	0.1977	0.0790	0.1862
V	0.0326	0.0096	0.0383	0.028	0.0058	0.0226
Cr	0.0066	0.0011	0.0071	0.0059	0.0023	0.0053
Co	0.0285	0.0058	0.0284	0.0252	0.0058	0.0266
Ni	0.0099	0.0027	0.0111	0.0065	0.0025	0.0065
Ga	0.0013	0.0007	0.0016	0.0026	0.0021	0.0026
Ge	0.0005	0.0005	0.0005	0.0024	0.0017	0.0022
As	0.0041	0.0044	0.0035	0.0100	0.0159	0.0029
Se	0.0028	0.0003	0.0028	0.0036	0.0017	0.0039
Rb	0.0025	0.0004	0.0026	0.0030	0.0014	0.0027
Sr	0.0217	0.0034	0.0218	0.0232	0.0150	0.0183
Cd	0.0766	0.0160	0.0741	0.0848	0.0272	0.0731
Pb	0.0399	0.0445	0.0214	0.1005	0.1503	0.0197

The concentration of PM_{2.5} and their elemental constituents (µg/m³) in the two districts, Al Nuzlah and Al Rehab are presented in Table 3. Comparing the medians revealed that the levels of total PM_{2.5}, nickel

and cadmium were significantly higher ($p < 0.05$) in Al Nozlah district. The rest of the elements did not show any significant difference between both districts.

Table 3. Concentration of PM_{2.5} and their elemental constituents (µg/m³) in the two districts, Al Nuzlah and Al Rehab.

PM _{2.5}						
	Al Nozlah			Al Rehab		
µg/m ³	Mean	SD	Median	Mean	SD	Median
Total	29.10	14.12	23.30*	18.04	3.95	17.12
Ti	0.0112	0.0027	0.0119	0.0173	0.0143	0.0147
V	0.0291	0.0098	0.0331	0.0150	0.0038	0.0147
Cr	0.0018	0.0008	0.0014	0.0015	0.0010	0.0017
Co	0.0054	0.0002	0.0054	0.0058	0.0023	0.0059
Ni	0.0071	0.0023	0.0074*	0.0042	0.0009	0.0042
Ga	0.0002	0.0002	0.0001	0.0020	0.0019	0.0013
Ge	0.0007	0.0004	0.0006	0.0020	0.0017	0.0015
As	0.0022	0.0019	0.0024	0.0078	0.0106	0.0025
Se	0.0025	0.0007	0.0025	0.0031	0.0013	0.0024
Rb	0.0016	0.0003	0.0016	0.0011	0.0006	0.0012
Sr	0.0021	0.0007	0.0022	0.0018	0.0020	0.0014
Cd	0.0044	0.0037	0.0039*	0.0007	0.0010	0.0007
Pb	0.0366	0.0487	0.0146	0.0863	0.1435	0.0120

*p<0.05

Discussion

The association between exposure to PM exposure and the individual components of MetS such as: Hyperglycemia, hypertension, high triglycerides, obesity and low HDL has been well documented in literature (Li, et al., 2013; Roberts, et al., 2014; Rizzo, et al., 2014; Wang, et al., 2014; Fleisch, et al., 2014 and Pope, et al., 2015) . However, studies relating MetS per se with PM exposure are scarce. The 28.3% overall prevalence of MetS in Saudi Arabia was attributed to risk factors including males, increasing age, lower education, higher

income, smoking, and sedentary life style (Aljohani, 2014).

In the present study, MetS was found to be significantly more prevalent among Al Nuzlah subjects reaching 49.0%. The role of usual risk factors for MetS seems to be minimal, since no significant differences could be detected in age, obesity, smoking, educational level, sedentary life style, and food consumption between the two populations studied. The higher levels of total PM_{2.5} and not PM₁₀ in Al Nuzlah support the idea of a possible role of PM exposure in the onset of MetS. It has been

suggested that PM_{2.5} is more harmful to health than PM₁₀, because they can penetrate deeper in lungs (Churg and Brauer, 2000). Recent literature reported a positive association between exposure to PM and MetS (Eze, et al., 2015 and Brook, et al., 2016).

The toxicity of PM depends largely on its components. As endocrine disrupting chemicals, heavy metals and metalloids were found to play a role in the onset of MetS. Genetic factors and mitochondrial dysfunction could be the underlying mechanism (Sun, et al., 2012; Brocato, et al., 2014 and Kim and Lee, 2014). Moreover, a synergistic effect of a mixture of metals on the prevalence of MetS in the general population has been detected (Moon, 2014). The present study revealed significantly higher levels of nickel and cadmium in the PM of Al Nuzlah district, where MetS was more prevalent.

Nickel as being a key player in the adverse health effects associated with PM exposure has long been reported. Cardiovascular disease (Ying, et al., 2013 and Bell, et al., 2014), insulin resistance (Xu, et al., 2012) and MetS have been associated with nickel exposure (Yang, et al., 2014). It was proved that exposure to nickel and PM from Saudi Arabia at the same dose dysregulated the same MetS-genes (Brocato. et al., 2014, 2015).

Recent studies showed an association of blood cadmium concentration with MetS (Lee and Kim, 2013, 2015 and Han, et al., 2015). The pathological mechanism by which cadmium exposure may lead to MetS remains uncertain. Insulin resistance (Kawakami, et al., 2010) and heme catabolism (Satarug and Moore, 2012) were suggested as underlying characteristics of cadmium-associated MetS.

In conclusion, the present study adds more evidence that besides the role of life style, exposure to particulate matter must be

considered an additional risk factor in the development of MetS.

The author acknowledges some limitations. The study is cross sectional in nature and hence causal relationships could not be ascertained. Self-reporting bias in lifestyle practices such as diet, smoking habits and physical activity may have affected the results.

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التعرض للجسيمات المحمولة في الهواء: عامل خطر إضافي لمتلازمة الأيض في السعودية

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المستخلص. تشكل متلازمة الأيض مشكلة خطيرة في السعودية. ونسبت المشكلة إلى نمط الحياة. يعتبر التعرض للجسيمات المحمولة في الهواء في جدة موضوعاً مثيراً للاهتمام. وقد هدفت الدراسة الحالية إلى إيجاد علاقة محتملة بين انتشار متلازمة الأيض ومستويات الجسيمات والعناصر المكونة لها. تم إجراء الدراسة في حي النزلة وحي الرحاب بجدة. تم قياس مستويات الجسيمات الأقل من ١٠ ميكرون والجسيمات الأقل من ٢,٥ ميكرون والعناصر الموجودة فيها. وقد اشترط لتعريف متلازمة الأيض تواجد الثلاث عناصر التالية: زيادة نسبة السكر في الدم، وارتفاع ضغط الدم، والبدانة. وقد أظهر حي النزلة ارتفاعاً معنوياً في انتشار متلازمة الأيض، مع ارتفاع مستويات الجسيمات الأقل من ٢,٥ ميكرون، والنيكل والكاديوم. ويمكننا أن نستنتج من هذه النتائج أنه يمكن اعتبار التعرض للجسيمات عامل خطر إضافي للإصابة بمتلازمة الأيض.