

Acute post cessation smoking

A strong predictive factor for metabolic syndrome among adult Saudis

Nasser M. Al-Daghri, MSc, PhD.

ABSTRACT

الأهداف: تحديد تأثير التعرض للتبغ أو استنشاقه عند المصابين بالمتلازمة الأيضية (MS) من البالغين في المجتمع السعودي.

الطريقة: شملت بالدراسة 664 (305 ذكر و 359 أنثى) تراوحت أعمارهم ما بين 25-70 عاماً. وأجريت هذه الدراسة المقطعية خلال الفترة ما بين يونيو 2006م وحتى مايو 2007م، في مستشفى الملك عبد العزيز الجامعي - الرياض - المملكة العربية السعودية. تم تقسيم المشاركين في هذه الدراسة إلى: غير مدخنين، مدخنين، ومقلعين عن التدخين (أقلعوا عن التدخين قبل عام أو عامين). تم إجراء مسح لجميع المشاركين للتعرف على المتلازمة الأيضية (MS) باستخدام تعريف منظمة مرضى السكري الدولية (IDF) وجمعية القلب الأمريكية (AHA) وكذلك المعهد الوطني للقلب والرئة والدم (NHLBI) بالإضافة لتعريف منظمة الصحة الدولية (WHO).

النتائج: تبين أن المتلازمة الأيضية (MS) عند المقلعين عن التدخين هي الأعلى بغض النظر عن التعريف المستخدم. كانت نسبة حدوث الإصابة لدى المقلعين عن التدخين أعلى مرتين بالمقارنة بالغير مدخنين،

(95% CI: 2.23, 1.06-4.73) (95% CI: 2.78, 1.57-4.92) على التوالي $p=0.009$.

خاتمة: الفترة القصيرة بعد الإقلاع عن التدخين تعد مؤشر قوي للإصابة بالمتلازمة الأيضية (MS) بين الذكور والإناث العرب. لذلك ينبغي على برامج الإقلاع عن التدخين احتواء ضوابط لطريقة العيش، وكذلك الحماية الغذائية وذلك لمقاومة ازدياد المتلازمة الأيضية (MS) كناحية سلبية للإقلاع عن التدخين.

Objectives: To determine the influence of tobacco exposure in the development of metabolic syndrome (MS) in the adult Saudi population.

Methods. Six hundred and sixty-four adults (305 males and 359 females) aged 25-70 years were included in this cross-sectional study conducted at the King Abdul-Aziz University Hospital, between June 2006 and May 2007. We classified the participants into non-smokers,

smokers, and ex-smokers (defined as complete cessation for 1-2 years). All subjects were screened for the presence of MS using the modified American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI), International Diabetes Federation (IDF) and World Health Organization (WHO) definitions.

Results. Metabolic syndrome was highest among ex-smokers regardless of definition used. Relative risk for ex-smokers (95% CI: 2.23, 1.06-4.73) was more than twice in harboring MS as compared to non-smokers (95% CI: 2.78, 1.57-4.92) ($p=0.009$).

Conclusion. Acute post-cessation smoking is a strong predictor for MS among male and female Arabs. Smoking cessation programs should include a disciplined lifestyle and dietary intervention to counteract the MS-augmenting side-effect of smoking cessation.

Saudi Med J 2009; Vol. 30 (2): 267-271

From the Department of Biochemistry, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia.

Received 22nd November 2008. Accepted 20th December 2008.

Address correspondence and reprint request to: Dr. Nasser M. Al-Daghri, Department of Biochemistry, College of Science, King Saud University, PO Box 2455, Riyadh 11451, Kingdom of Saudi Arabia. Tel. +966(1)4675939. Fax. +966 (1) 4675931. E-mail: aldaghri2000@botmail.com

Cigarette smoking is the single most important preventable cause of death and illness.¹ Individuals who smoke experience a wide range of physiologic side effects that increase the risk of cardiovascular disease (CVD), insulin resistance, elevated catecholamine levels which contribute to an elevated heart rate and blood pressure, and hypercholesterolemia.² It has also been suggested to be a contributing factor in the development of metabolic syndrome (MS) in adolescents.³ In the Kingdom of Saudi Arabia like any other industrialized nations, MS is highly prevalent^{4,5} with an overall

prevalence of 39.3%.⁶ This is not a diagnosis but rather a cluster of abnormalities, which include abdominal obesity, dyslipidemia, hypertension, and hyperglycemia a common basis for the development of chronic diseases, such as atherosclerotic heart disease, and diabetes mellitus (DM). The incidence of tobacco exposure such as cigarette smoking, is exceptionally high in this country with its prevalence range of 19-21% in males and 9% in females.⁶⁻⁷ These 2 major risk factors for the development of coronary artery disease has constantly been a public health problem not only in this country, but in all industrialized nations as well. The pathogenesis of both MS and the multi-organ damage from chronic tobacco exposure and smoking has been more or less well documented. But the association of these 2 independent factors, and how they influence each other for the progression of the more deadly atherosclerotic heart disease specifically in this region needs to be elucidated further, as both pose great threat to public health. This study aims to determine the predictive powers of tobacco exposure in the development of MS in the adult Saudi population.

Methods. This is a cross-sectional study conducted at King Abdul-Aziz University Hospital, Riyadh, Kingdom of Saudi Arabia (KSA) from June 2006 to May 2007. The subject population was drawn from adult Saudi citizen volunteers, male and female aged 25-70 years old, with or without co-morbidities (DM, obesity, and other chronic medical conditions that do not require immediate attention, or considered medically stable during the time of the study). Ethical approval was obtained from the College of Medicine Research Center, King Saud University, Riyadh, KSA. Volunteers were asked to submit a written consent before participation. Six hundred and sixty-four (305 males and 359 females) subjects were recruited. All subjects underwent a full physical examination and completed the generalized questionnaire. Data on socio-demographic characteristics, personal and family medical history, and health-relevant behaviors including smoking were obtained by a standardized interview at the time of presentation. Height and weight were recorded to the nearest 0.5 cm and 0.1 kg. Waist and hip circumferences were also measured using a standardized tape measure and was recorded to the nearest 0.1 cm. The waist circumference was obtained as the minimum value between the iliac crest and the

lateral costal margin, and the hip circumference was determined as the maximum value over the buttocks. Blood pressure was measured using a standardized mercurial sphygmomanometer twice with 15 minute-interval each, and the average of the 2 readings were recorded. They were divided into 3 groups: current smoker's group, ex-smokers, and non-smoker groups. Smoker was defined as someone who has been actively smoking (cigarettes, sheesha) regardless of the quantity for >1 year prior to the inclusion. Ex-smoker is someone who has not been smoking for 1-2 years prior to the inclusion. Non-smoker is someone who has never smoked before.

Blood samples were collected after the 8-12 hours fasting for the determination of fasting blood glucose, and serum lipid profile which includes fasting total cholesterol, high density lipoprotein cholesterol (HDL-C), and triglycerides. Serum samples were stored at -70°C prior to analysis. Serum glucose, total cholesterol and triglycerides were measured using standard enzymatic methods and a fully automated analyzer (Konelab instruments, Finland). High density lipoprotein cholesterol levels were determined by phosphotungstic acid/magnesium chloride precipitation (Konelab instruments, Finland). Low density lipoprotein-cholesterol was calculated using Friedewald equation.

All participants were screened with or without MS. We used the updated guidelines of the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) in the presence of at least 3 of the following metabolic abnormalities: 1) abdominal obesity: waist circumference >102 cm (>40 in) in men and >88 cm (>35 in) in women, 2) hypertriglyceridemia: ≥ 150 mg/dl (1.7 mmol/L); 3) low HDL cholesterol: <1.04 mmol/L for men; <1.3 mmol/L in women; 4) hypertension: systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg and/or with anti-hypertensive medication; and 5) high fasting glucose: ≥ 5.6 mmol/L and/or with oral anti-diabetic medication.⁸ They were also screened for the presence of MS using other definitions such as International Diabetes Federation⁹ and World Health Organization¹⁰ for comparison purposes.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS for Windows, version 11.5). Variables that exhibited a positive skew were log-transformed in order to normalize the distribution. Data are presented as mean \pm standard deviation. Frequencies were presented as valid percentage. Analysis of variance with post-hoc analysis (Bonferroni) was carried out to compare the groups. Relative risk was computed to determine predictability of factors of interest. Significance was set at $p < 0.05$.

Disclosure. This research was funded by the Saudi Basic Industries Corporation (SABIC) grant number: SCIENCE-6-2007

Results. According to the AHA definition, MS was noted in 58.1% of males and 60.4% in females. Furthermore, according to the same criteria, obesity and dyslipidemia were also higher among females (43% versus 39.6% and 55.1% versus 45.7%); hypertension and impaired glucose tolerance on the other hand was higher among males (68.9% versus 41.8% and 84% versus 73.8%). Table 1 highlights the clinical characteristics of male subjects and revealed that the smoking group were significantly younger compared to both non- and ex-smokers (defined as complete cessation for 1-2 years). High density lipoprotein-cholesterol levels of ex-smokers were significantly decreased compared to non-smokers. The rest of the values were comparable to one another. Table 2 shows that female smokers have a significantly lower BMI compared to non-smokers. Both smokers and ex-smokers have higher total cholesterol, LDL-cholesterol, and triglycerides compared to non-smokers. High density lipoprotein-cholesterol levels of ex-smokers were significantly lower compared to non-smokers. The rest of the comparisons were unremarkable. Table 3 reveals that the relative risk for male (95% confidence interval: 2.23 [1.06-4.73]), and female (confidence interval 2.78; [1.57-4.92]) ex-smokers is more than twice as much in harboring MS as compared to non-smokers. Other conventional risk factors such as obesity, dyslipidemia, and hypertension are also significant predictors for the development in MS among men, and with the exception of obesity,

Table 1 - Clinical characteristics of male subjects according to degree of cigarette smoking exposure.

Parameter	Non-smoker (n=215)	Current smoker (n=55)	Ex-smoker (n=35)
Age (years)	52.8 ± 8.6	48.5 ± 10.0*†	53.3 ± 10.6
BMI (kg/m ²)	28.3 ± 4.1	29.0 ± 6.4	29.5 ± 6.5
Waist (cm)	110.8 ± 21.1	107.1 ± 20.8†	119.3 ± 28.8
Hips (cm)	93.9 ± 13.4	98.3 ± 15.6	97.8 ± 16.4
SBP (mmHg)	122.3 ± 23.1	121.5 ± 23.3	118.7 ± 23.7
DBP (mmHg)	89.0 ± 14.0	85.5 ± 12.3	92.2 ± 18.8
Glucose (mmol/L)	8.5 ± 3.4	8.7 ± 3.9	7.9 ± 2.8
Total cholesterol (mmol/L)	4.7 ± 1.0	5.0 ± 0.9	4.6 ± 1.0
HDL-cholesterol (mmol/L)	1.2 ± 0.5	1.0 ± 0.4	0.9 ± 0.4*
LDL-cholesterol (mmol/L)	3.0 ± 2.9	3.0 ± 1.0	2.6 ± 0.9
Triglycerides (mmol/L)	1.8 ± 1.1	1.9 ± 1.0	2.0 ± 1.1

Data presented as mean ± SD; *denotes significance compared to non-smoker; †denotes significance compared to ex-smoker ($p < 0.05$).
 BMI - body mass index, HDL - high density lipoprotein cholesterol, SBP - systolic blood pressure, DBP - diastolic blood pressure, LDL - low density lipoprotein cholesterol

also among women. Figures 1 & 2 show the dramatic increase in the prevalence of MS (>3 components) among ex-smokers as opposed to their non-smoking and smoking counterparts in both males and females. Prevalence of MS is highest among ex-smokers in both males (68.9%) and females (77.1%), and lowest among non-smokers (48.4% among males and 51.7% among females). Figure 3 reveals that the prevalence of MS is highest among ex-smokers regardless of the definition used and is highest using the AHA/NHLBI definition.

Discussion. The beneficial effects of smoking cessation have been well documented and established. Most chronic smokers agree; however, it takes exceptional determination to sustain the cessation because of withdrawal symptoms (restlessness, irritability, anxiety and confusion) secondary to nicotine addiction, as

Table 2 - Clinical characteristics of female subjects according to degree of cigarette smoking exposure.

Parameter	Non-smoker (n=197)	Current smoker (n=88)	Ex-smoker (n=74)
Age (years)	48.6 ± 8.6	48.3 ± 11.2	51.4 ± 11.7
BMI (kg/m ²)	29.4 ± 3.7	27.2 ± 4.9*	28.3 ± 4.9
Waist (cm)	100.3 ± 13.5	95.9 ± 12.9	98.3 ± 13.1
Hips (cm)	98.7 ± 11.7	98.9 ± 13.1	99.6 ± 14.7
SBP (mm Hg)	127.0 ± 19.8	122.0 ± 17.1	126.4 ± 19.1
DBP (mm Hg)	79.3 ± 11.8	78.6 ± 10.0	80.7 ± 12.1
Glucose (mmol/L)	8.8 ± 3.8	8.0 ± 4.9	8.7 ± 5.4
Total cholesterol (mmol/L)	4.8 ± 1.1	5.6 ± 1.6*	5.5 ± 1.5*
HDL-Cholesterol (mmol/L)	1.4 ± 0.6	1.1 ± 0.4	0.9 ± 0.5*
LDL-Cholesterol (mmol/L)	2.7 ± 0.8	3.6 ± 1.7*	3.6 ± 1.6*
Triglycerides (mmol/L)	1.7 ± 1.0	2.2 ± 1.1*	2.3 ± 1.2*

Data presented as mean ± SD; *denotes significance compared to non-smoker; †denotes significance compared to ex-smoker ($p < 0.05$).
 BMI - body mass index, HDL - high density lipoprotein cholesterol, SBP - systolic blood pressure, DBP - diastolic blood pressure, LDL - low density lipoprotein cholesterol

Table 3 - Relative risk (95% confidence interval) for metabolic syndrome among various risk factors among males and females

Risk factor	Male	Female
Smoker	1.26 (0.71-2.24)	1.61 (0.997-2.62)
Ex-smoker	2.23 (1.06-4.73)*	2.78 (1.57-4.92)*
Obesity	1.81 (1.18-2.77)*	1.16 (0.81-1.67)
Dyslipidemia	2.57 (2.08-3.17)*	2.14 (1.82-2.51)*
Hypertension	2.21 (1.41-3.44)*	3.28 (2.24-4.81)*

* $P = 0.009$

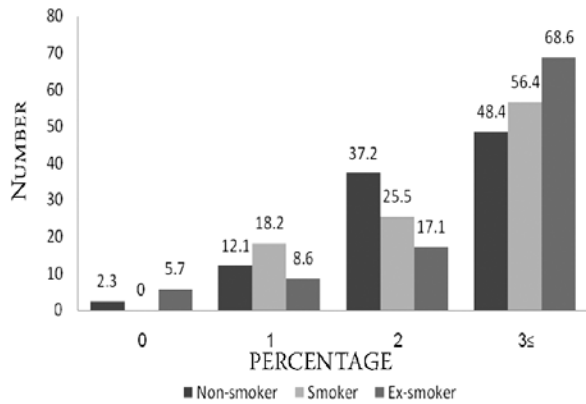


Figure 1 - Distribution of male subjects according to components of metabolic syndrome (MS) according to American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) in valid percentage (%).

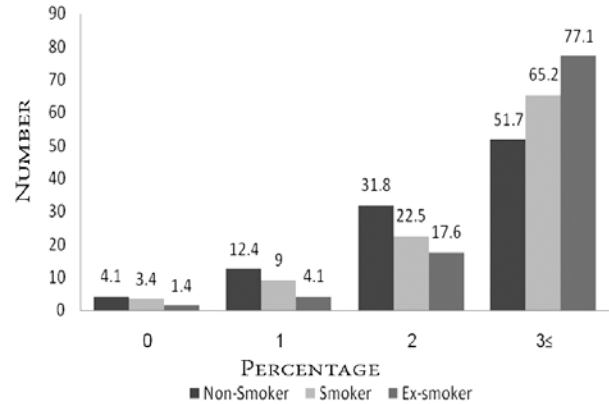


Figure 2 - Distribution of female subjects according to components of metabolic syndrome (MS) according to American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) in valid percentage (%).

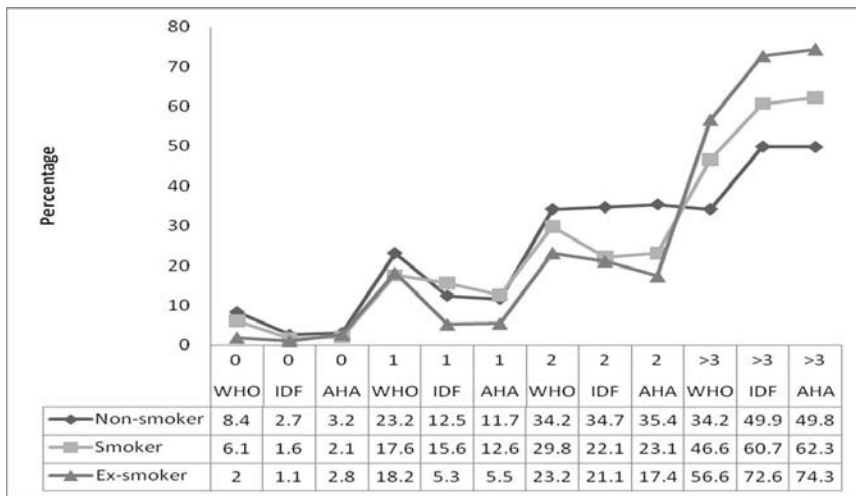


Figure 3 - Percentage (%) distribution of all subjects according to components of metabolic syndrome (MS) by various definitions. WHO - World Health Organization, IDF - International Diabetes Federation, AHA - American Heart Association

noted in almost 80% of all smokers who have attempted to quit.¹¹ In this cross-sectional study, we determined for the first time the associated risk of developing MS among adult Saudis with varying degrees of smoking exposure, and found significant increased risk among ex-smokers regardless of gender; consistent with the findings of Wada et al, who stated that the past history of smoking itself contributes to the occurrence of MS even after 20 years.¹² Our findings however, contradict the results of Chen et al,¹³ who found that ex-smokers are at insignificant risk of developing MS. One explanation aside from ethnic variation is the length of post cessation. Former smokers in this study are defined as persons who stopped smoking for 1-2 years, the time when metabolic and neurologic changes

are most evident as opposed to their definition, which was one to >20 years. Cessation of smoking has a trend to lower the risk in a year-dependent manner.¹³ In our study, the prevalence of MS is high regardless of the smoking status which can be explained by the high prevalence of subjects already harboring DM (84% males; 73.8% females). Mechanisms for acute post cessation development of MS can be explained by dissecting its components. First, we have weight gain mechanisms of which include increased the energy intake, decreased resting metabolic rate, decreased physical activity and increased lipoprotein lipase activity.¹ The decreased metabolic rate can be explained by nicotine suppression, which in turn decreases the

release of serotonin and noradrenaline, hormones that suppress appetite.¹⁴ In hypertension, not much change was noted among former smokers, whose systolic and diastolic levels were comparable to both smokers and non-smokers possibly because of the acuity of cessation. Jatoi et al¹⁵ highlighted the effects of smoking status in arterial stiffness, considered as a strong predictor of smoking-related vascular diseases. In their study, they concluded that smoking cessation would take >10 years before reversal of the deleterious effects of smoking on arterial stiffness become comparable to non-smokers.¹⁵ This in turn might explain why hypertension is not the driving component in the increased prevalence of MS among former smokers. On dyslipidemia, smoking itself affects lipid metabolism partly by its contribution to central adiposity and insulin resistance, which can alter the lipid and lipoprotein profile by interfering with fat metabolism.¹⁶ Furthermore, cigarette particulate matter alters catecholamine release which affects the very low-density lipoprotein (VLDL) and LDL concentrations to favor their accumulation in the blood, ending up in lower HDL levels and promoting atherogenesis.² Whether the dyslipidemia is present among the former smokers in this study is said to be linked to the smoking history and/or compounded by the increased caloric intake and sedentary lifestyle remains to be proven.

The duration and quantity of cigarettes smoking were not accounted for, and the definition of current smoker was based only on the time frame which is >1 year. This cross-sectional nature of studies provide limited information as to the development of MS among ex-smokers, and a follow up study is necessary to reveal if there will be a recession or improvement in the prognosis of the ex-smokers. Also, the definition used for ex-smokers (1-2 years) have certainly influenced the high prevalence of MS among ex-smokers since evidence suggested that marked improvement and down regulation of the MS components are time-dependent. Lastly, the very high prevalence of subjects with impaired glucose tolerance and DM among the cohort of adult subjects suggest that the findings might be applicable only for this group of population and another study utilizing non-diabetic subjects with varying degrees of tobacco exposure may present opposite results.

In summary, post cessation smoking in the early years is a strong predictive factor for the development of MS among male and female Arabs regardless of the definition used. Smoking cessation programs should include a disciplined lifestyle and dietary intervention among quitters to counteract the MS augmenting side-effect of smoking cessation.

Acknowledgements. *The author greatly acknowledge the contributions of Dr. Shaun Louie Sabico in the statistical analysis*

and the overall outcome of the manuscript. Many thanks to the staff and researchers of the University Diabetes Center in King Abdul-Aziz University for the subject recruitment and data collection.

References

1. Filozof C, Fernández Pinilla MC, Fernández-Cruz A. Smoking cessation and weight gain. *Obes Rev* 2004; 5: 95-103.
2. Chelland Campbell S, Moffatt RJ, Stamford BA. Smoking and smoking cessation - the relationship between cardiovascular disease and lipoprotein metabolism: a review. *Atherosclerosis* 2008; 201: 225-235.
3. Weitzman M, Cook S, Auinger P, Florin TA, Daniels S, Nguyen M, et al. Tobacco smoke exposure is associated with the metabolic syndrome in adolescents. *Circulation* 2005; 112: 862-869.
4. Godsland IF, Rosankiewicz JR, Proudler AJ, Johnston DG. Plasma total homocysteine concentrations are unrelated to insulin sensitivity and components of the metabolic syndrome in healthy men. *J Clin Endocrinol Metab* 2001; 86: 719-723.
5. Ryo M, Nakamura T, Kihara S, Kumada M, Shibazaki S, Takahashi M, et al. Adiponectin as a biomarker of the metabolic syndrome. *Circ J* 2004; 68: 975-981.
6. Al-Nozha M, Al-Khadra A, Arafah MR, Al-Maatouq MA, Khalil MZ, Khan NB, et al. Metabolic syndrome in Saudi Arabia. *Saudi Med J* 2005; 26: 1918-1925.
7. Siddiqui S, Ogbeide DO, Al Khalifa I. Smoking in a Saudi community: prevalence, influencing factors, and risk perception. *Fam Med* 2001; 33: 367-370.
8. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung and Blood Institute scientific statement: executive summary. *Circulation* 2005; 112: e285-e290.
9. International Diabetes Federation. New IDF worldwide definition of the metabolic syndrome. Proceedings of the 1st International Congress on "Pre-diabetes" and the metabolic syndrome; 2005 April 14; Berlin, Germany. Berlin (GR): International Diabetes Federation; 2005.
10. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; 15: 539-553.
11. Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry* 1986; 43: 289-294.
12. Wada T, Urashima M, Fukumoto T. Risk of metabolic syndrome persists twenty years after the cessation of smoking. *Intern Med* 2007; 46: 1079-1082.
13. Chen CC, Li TC, Chang PC, Liu CS, Lin WY, Wu MT, et al. Association among cigarette smoking, metabolic syndrome, and its individual components: the metabolic syndrome study in Taiwan. *Metabolism* 2008; 57: 544-548.
14. Nerín I, Beamonte A, Gargallo P, Jiménez-Muro A, Marqueta A. [Weight gain and anxiety levels in recent ex-smokers] *Arch Bronconeumol* 2007; 43: 9-15. Spanish.
15. Jatoi NA, Jerrard-Dunne P, Feely J, Mahmud A. Impact of smoking and smoking cessation on arterial stiffness and aortic valve reflection in hypertension. *Hypertension* 2007; 49: 981-985.
16. Kong C, Nimmo L, Elatrozy T, Anyaoku V, Hughes C, Robinson S, et al. Smoking is associated with increased hepatic lipase activity, insulin resistance, dyslipidaemia and early atherosclerosis in Type 2 diabetes. *Atherosclerosis* 2001; 156: 373-378.