The safest value of plasma triglycerides

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Abstract

Background: We tried to understand the safest value of plasma triglycerides according to some components of the metabolic syndrome.

Methods: Patients with plasma values of triglycerides lower than 100 mg/dL were collected into the first, lower than 150 mg/dL into the second, lower than 200 mg/dL into the third, and 200 mg/dL or higher into the fourth groups, respectively.

Results: We studied 457 cases (266 females and 191 males), totally. The female ratio decreased from the first towards the fourth groups (64.1% versus 49.4%, $p<0.01$), gradually, whereas the mean ages of the groups, body mass index (BMI), and low density lipoproteins increased just up to the plasma triglycerides value of 200 mg/dL, significantly ($p<0.05$ for all). On the other hand, the mean fasting plasma glucose and prevalence of smoking, white coat hypertension, hypertension, diabetes mellitus, and chronic obstructive pulmonary disease increased parallel to the plasma triglycerides values from the first towards the fourth groups, gradually. Interestingly, the greatest number of deteriorations (six components deteriorated, significantly) was observed just at the passage from the first into the second groups of the study cases.

Conclusions: Plasma triglycerides may actually be some acute phase reactants indicating disseminated endothelial damage, inflammation, fibrosis, and accelerated atherosclerosis with eventual end-organ insufficiencies all over the body. There may be highly significant relationships between plasma triglycerides values and aging, BMI, and smoking. Interestingly, the greatest number of deteriorations of the components of the metabolic syndrome was observed just above the plasma triglycerides value of 100 mg/dL.

Key words:
Triglycerides,
acute phase reactant,
chronic endothelial damage,
accelerated atherosclerosis,
end-organ insufficiency

Introduction

Chronic endothelial damage may be the most common sort of vasculitis, and the leading cause of aging and death in human beings (1-4). Much higher blood pressure (BP) of the afferent vasculature may be the major triggering mechanism by causing recurrent injuries on endothelium. Probably, whole afferent vasculature including capillaries are chiefly involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in medicine. Because of the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic structures which reduce blood supply to terminal organs, and increase systolic BP further. Some of the well-known components of the inflammatory process are physical inactivity, animal-rich diet, overweight, smoking, alcohol, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired fasting glucose, impaired glucose tolerance, white coat hypertension (WCH), and chronic inflammatory processes including rheumatologic disorders, chronic infections, and cancers for the development of terminal endpoints including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary heart disease (CHD), mesenteric ischemia, osteoporosis, stroke, and aging (5-9). Although early withdrawal of the triggering causes may delay terminal consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, or aging, endothelial changes cannot be reversed completely due to their fibrotic nature. Up to now, the triggering mechanisms and terminal endpoints were researched under the titles of metabolic syndrome, aging syndrome, or accelerated endothelial damage syndrome in the medical literature, extensively (10-13). Although its normal limits have not been determined clearly yet, increased plasma triglycerides values may be significant indicators of the metabolic syndrome (14). Due to the growing proof about the strong association between higher plasma triglycerides values and prevalence of CHD, Adult Treatment Panel (ATP) III adopts lower cutpoints for triglycerides abnormalities than did ATP II (15, 16). Although ATP II determined the normal plasma triglycerides value as lower than 200 mg/dL in 1994, World Health Organisation in 1999 (17) and ATP III in 2001 reduced their normal limit to as lower than 150 mg/dL (15). Although these cutoff points are usually used to define limits of the metabolic syndrome, there are suspicions about the safest value of plasma triglycerides in medicine. Beside that, smoking may be found among the most common causes of vasculitis all over the world. It is a major risk factor for the development of atherosclerotic consequences including HT, DM, CHD, PAD, COPD, cirrhosis, CRD, mesenteric ischemia, osteoporosis, stroke, and aging (18, 19). We tried to understand the safest value of plasma triglycerides according to some components of the metabolic syndrome in the present study.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients above the age of 15 years were included. Their medical histories including HT, DM, COPD, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglycerides, and low density lipoproteins (LDL) was performed. Current daily smokers with six pack-months and cases with a history of three pack-years were accepted as smokers. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Additionally, anti-hyperlipidemic drugs, metformin, and/or acarbose users were excluded to avoid their possible effects on blood lipid profiles and/or body weight (20, 21). Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (15). Cases with an overnight FPG value of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics (15). An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG value between 110 and 126 mg/dL, and diagnosis of cases with a 2-hour plasma glucose value of 200 mg/dL or greater is DM (15). Additionally, office blood pressure (OBP) was checked after a 5-minute rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in the normotensives in the office due to the risk of masked HT after a 10-minute education session about proper BP measurement techniques (22). An additional 24-hour ambulatory blood pressure monitoring was not needed due to its similar effectivity with the HBP measurements (3). Eventually, HT is defined as a mean BP of 135/85 mmHg or greater on HBP measurements, and WCH as an OBP of 140/90 mmHg or greater but a mean HBP measurement of lower than 135/85 mmHg (22). The spirometric pulmonary function tests were performed in required cases after the physical examination, and the criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (23). Eventually, patients with plasma triglycerides values of lower than 100 mg/dL were collected into the first, lower than 150 mg/dL into the second, lower than 200 mg/dL into the third, and 200 mg/dL or higher into the fourth groups, respectively. The female ratio, mean age, BMI, FPG, triglycerides, and LDL, and prevalence of smoking, WCH, HT, DM, and COPD were detected in each group and compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

We studied 457 cases (266 females and 191 males), totally. The female ratiodecreased from the first towards the fourth groups (64.1% versus 49.4%, p<0.01), gradually whereas the mean ages of the groups, BMI, and LDL increased just up to the plasma triglycerides value of 200 mg/dL, significantly (p<0.05 for all). On the other hand, the mean FPG and prevalence of smoking, WCH, HT, DM, and COPD increased parallel to the plasma triglycerides values from the first towards the fourth groups, gradually. Interestingly, the greatest number of deteriorations (six components deteriorated, significantly) was observed just at the passage from the first into the second groups of the study cases. Just three components deteriorated at the passage from the second into the third groups, significantly. Although two components including smoking and COPD deteriorated at the passage from the third into the fourth groups, the mean values of LDL decreased, significantly (140.9 versus 128.2 mg/dL, p=0.009) at the the passage, thus the number of deterioration was two minus one that was equal to one between the third and fourth groups (Table 1).

Discussion

Excess weight may lead to both structural and functional abnormalities of many organ systems of the body. Adipose tissue produces leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines which act as acute phase reactants in the plasma (24, 25). Excess weight-induced chronic low-grade vascular endothelial inflammation may play a significant role in the pathogenesis of accelerated atherosclerosis all over the body (1, 2). Additionally, excess weight may cause an increased blood volume as well as an increased cardiac output thought to be the result of the increased oxygen need of the excessive fat tissue. The prolonged increase in the blood volume may lead to myocardial hypertrophy terminating with a decreased cardiac compliance. Beside that, the mean FPG and total cholesterol increased and high density lipoproteins (HDL) decreased parallel to the increased mean BMI values (26). Combination of these cardiovascular risk factors will eventually terminate with increased left ventricular stroke work and risk of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the prevalence of CHD and stroke increased parallel to the increased BMI values

Table 1: Characteristic features of the study cases according to plasma triglycerides values

Variable	Lower than 100 mg/dL	*p*-value	Lower than 150 mg/dL	*p*-value	Lower than 200 mg/dL	*p*-value	200 mg/dL or greater
Number	159		133		78		87
Mean age	*40.6 ± 17.6 (16-83)*	*0.001*	*46.9 ± 15.9 (16-82)*	*0.014*	*51.7 ± 11.8 (23-73)*	Ns*	50.5 ± 12.3 (21-86)
Female ratio	*64.1%*	Ns	57.8%	Ns	56.4%	Ns	*49.4%*
Prevalence of smoking	*16.3%*	*0.05>*	*23.3%*	Ns	*28.2%*	*0.01>*	*42.5%*
Mean BMI†	*26.7 ± 5.6 (16.7-49.3)*	*0.000*	*29.5 ± 6.0 (18.4-50.5)*	Ns	30.0 ± 4.9 (19.2-49.0)	Ns	29.7 ± 4.7 (21.0-42.9)
Mean value of FPG‡	*102.7 ± 40.3 (59-341)*	Ns	102.7 ± 26.6 (71-244)	*0.009*	*114.6 ± 43.6 (68-320)*	Ns	*117.1 ± 42.1 (80-287)*
Mean value of triglycerides	*70.3 ± 16.4 (27-99)*	*0.000*	*120.8 ± 14.8 (100-149)*	*0.000*	*174.6 ± 14.9 (150-199)*	*0.000*	*304.8 ± 118.7 (175-1.144)*
Mean value of LDL§	*109.7 ± 33.7 (43-269)*	*0.000*	*132.1 ± 31.8 (64-228)*	*0.048*	*140.9 ± 27.7 (75-210)*	*0.009*	*128.2 ± 39.8 (10-239)*
Prevalence of WCH‖	*23.2%*	*0.05>*	*30.8%*	Ns	32.0%	Ns	*34.4%*
*Prevalence of HT***	*11.9%*	*0.001 >*	*23.3%*	Ns	25.6%	Ns	*25.2%*
*Prevalence of DM****	*8.1%*	Ns	12.7%	Ns	*16.6%*	Ns	*22.9%*
*Prevalence of COPD*****	*9.4%*	Ns	11.2%	Ns	*15.3%*	*0.001 >*	*28.7%*

*Nonsignificant (p>0.05) †Body mass index ‡Fasting plasma glucose §Low density lipoproteins ‖White coat hypertension **Hypertension ***Diabetes mellitus ****Chronic obstructive pulmonary disease

in other studies (26, 27), and risk of death from all causes including cancers increased throughout the range of moderate to severe weight excess in all age groups (28). The relationships between excess weight and elevated BP and plasma triglycerides were described in the metabolic syndrome (14), and clinical manifestations of the syndrome included obesity, dyslipidemia, HT, insulin resistance, and proinflammatory and prothrombotic states (12). Similarly, prevalence of smoking (42.2% versus 28.4%, $p<0.01$), excess weight (83.6% versus 70.6%, $p<0.01$), DM (16.3% versus 10.3%, $p<0.05$), and HT (23.2% versus 11.2%, $p<0.001$) were all higher in the hypertriglyceridemia group in another study (29). On the other hand, the prevalence of hyperbetalipoproteinemia was similar both in the hypertriglyceridemia (200 mg/dL or higher) and control groups (18.9% versus 16.3%, $p>0.05$, respectively) in the above study (29). Similarly, plasma LDL values increased up to the plasma triglycerides value of 200 mg/dL, but then decreased in the present study, too ($p<0.05$ for all). Beside that, the mean BMI increased just up to the plasma triglycerides value of 150 mg/dL ($p=0.000$), but it did not change with plasma triglycerides value of 150 mg/dL or higher, significantly ($p>0.05$).

It is a well-known fact that smoking causes a chronic inflammatory process on the vascular endothelium, probably depending upon the concentration of smoke that terminates with an accelerated atherosclerosis, end-organ insufficiency, early aging, and premature death. Thus smoking has to be included among the major components of the metabolic syndrome. Strong and terminal atherosclerotic effects of smoking are the most obvious in Buerger's disease (Thromboangiitis obliterans). It is an obliterative disease characterized by inflammatory changes in the small and medium-sized arteries and veins, and it has never been reported in the absence of smoking in medicine. Although the strong atherosclerotic effects of smoking are well known, smoking in humans and nicotine administration in animals may be associated with decreased BMI values (30). Proof revealed an increased energy expenditure during smoking both on rest and light physical activity (31), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (32). According to an animal study, nicotine may lengthen intermeal time and decrease amount of meal eaten (33). Additionally, the mean BMI seems to be the highest in former, the lowest in current and medium in never smokers (34). Smoking may be associated with a postcessation weight gain (35). Similarly, although CHD was detected with similar prevalence in both genders in the previous study (36), prevalence of smoking and COPD were higher in males with CHD against the higher mean values of the BMI, LDL, and triglycerides and higher prevalences of WCH, HT, and DM in females with CHD. This result may show both the strong atherosclerotic and weight decreasing roles of smoking (37). Similarly, the incidence of a myocardial infarction is increased six-fold in women and three-fold in men who smoke 20 cigarettes per day (38). In another definition, smoking may be more dangerous for women probably due to the higher BMI and its consequences in them. Parallel to the above results, the proportion of smokers is consistently higher in men in the literature (21). So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite. Smoking-induced weight loss may be related to the smoking-induced chronic vascular endothelial inflammation all over the body, since loss of appetite is one of the main symptoms of a disseminated inflammation in the body. Physicians can even understand healing of patients via their normalizing appetite. Several toxic substances found in cigarette smoke get into the circulation by means of the respiratory tract, and cause a vascular endothelial inflammation until their clearance from the circulation. But due to the repeated smoking habit of the individuals, the clearance process never terminates. So the patients become ill with loss of appetite, permanently. In another explanation, smoking-induced weight loss is an indicator of being ill instead of being healthy (32-34). After smoking cessation, normal appetite comes back with a prominent weight gain in the patients but the returned weights are their physiological or 'normal' weights, actually.

Despite the several negative effects of excess weight on health, nearly three-quarters of cases above the age of 30 years have excess weight (39). The prevalence of excess weight increases by decades, particularly after the third decade, up to the eighth decade of life (39). So 30 and 70 years of age may be the breaking points of life for weight, and aging may be the major determiner factor of excess weight. Probably, partially decreased physical and mental stresses after the age of 30 years and debility and comorbid disorders-induced restrictions after the age of 70 years may be the major causes for the changes of BMI values at these ages. Interestingly, the mean age and BMI increased just up to the plasma triglycerides values of 200 mg/dL, significantly, in the present study. So smoking remained as the major causative factor for the hypertriglyceridemia after the plasma triglycerides values of 200 mg/dL in the present study.

Although ATP III reduced the normal limit of plasma triglycerides values as lower than 150 mg/dL in 2001 (15), whether or not much lower limits provide additional benefits for health is unclear. In the present study, prevalence of smoking was the highest in the highest triglycerides having group which may also indicate inflammatory roles of smoking in the metabolic syndrome, since triglycerides may actually be some acute phase reactants in the plasma. The mean FPG and prevalence of smoking, WCH, HT, DM, and COPD increased parallel to the plasma triglycerides values from the first towards the fourth groups, gradually. In our opinion, significantly increased mean age by the increased plasma triglycerides values may be secondary to aging-induced decreased physical and mental stresses, which eventually terminates with onset of excess weight and other components of the metabolic syndrome. Interestingly, although the mean age increased from the lowest triglycerides having group towards the triglycerides value of 200 mg/dL, it then decreased. A similar trend was also seen with the mean LDL and BMI values. These trends may be due to the fact that although the borderline high triglycerides values (150-199 mg/dL) are seen together with

physical inactivity and overweight, the high triglycerides (200-499 mg/dL) and very high triglycerides values (500 mg/dL or greater) may be secondary to both genetic factors and terminal consequences of the metabolic syndrome including smoking, obesity, DM, HT, COPD, cirrhosis, CRD, PAD, CHD, and stroke (15). But although the underlying causes of the high and very high plasma triglycerides values may be a little bit different, probably risks of the terminal endpoints of the metabolic syndrome do not change in them. For example, prevalence of HT, DM, and COPD were the highest in the highest triglycerides having group in the present study. Eventually, although some authors reported that lipid assessment can be simplified by measurements of total cholesterol and HDL values alone (40), the present study and most of the others indicated a causal relationship between higher triglycerides and terminal consequences of the metabolic syndrome (41).

As a conclusion, plasma triglycerides may actually be some acute phase reactants indicating disseminated endothelial damage, inflammation, fibrosis, and accelerated atherosclerosis with eventual end-organ insufficiencies all over the body. There may be highly significant relationships between plasma triglycerides values and aging, BMI, and smoking. Interestingly, the greatest number of deteriorations of the components of the metabolic syndrome including mean age, smoking, BMI, LDL, WCH, and HT were observed just above the plasma triglycerides value of 100 mg/dL in the present study.

References

1. Widlansky ME, Gokce N, Keaney JF Jr, Vita JA. The clinical implications of endothelial dysfunction. J Am Coll Cardiol 2003; 42(7): 1149–1160.
2. Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001; 103(13): 1813–1818.
3. Helvaci MR, Seyhanli M. What a high prevalence of white coat hypertension in society! Intern Med 2006; 45(10): 671-674.
4. Helvaci MR, Kaya H, Seyhanli M, Cosar E. White coat hypertension is associated with a greater all-cause mortality. J Health Sci 2007; 53(2): 156-160.
5. Helvaci MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. Int Heart J 2007; 48(5): 605-613.
6. Helvaci MR, Kaya H, Duru M, Yalcin A. What is the relationship between white coat hypertension and dyslipidemia? Int Heart J 2008; 49(1): 87-93.
7. Helvaci MR, Kaya H, Seyhanli M, Yalcin A. White coat hypertension in definition of metabolic syndrome. Int Heart J 2008; 49(4): 449-457.
8. Helvaci MR, Kaya H, Sevinc A, Camci C. Body weight and white coat hypertension. Pak J Med Sci 2009; 25(6): 916-921.
9. Helvaci MR, Sevinc A, Camci C, Yalcin A. Treatment of white coat hypertension with metformin. Int Heart J 2008; 49(6): 671-679.
10. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365(9468): 1415-1428.
11. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004; 109(3): 433-438.
12. Tonkin AM. The metabolic syndrome(s)? Curr Atheroscler Rep 2004; 6(3): 165-166.
13. Franklin SS, Barboza MG, Pio JR, Wong ND. Blood pressure categories, hypertensive subtypes, and the metabolic syndrome. J Hypertens 2006; 24(10): 2009-2016.
14. Helvaci MR, Kaya H, Gundogdu M. Association of increased triglyceride levels in metabolic syndrome with coronary artery disease. Pak J Med Sci 2010; 26(3): 667-672.
15. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106(25): 3143-3421.
16. National Cholesterol Education Program. Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). Circulation 1994; 89(3): 1333-1445.
17. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of a WHO consultation 1999.
18. Helvaci MR, Aydin Y, Gundogdu M. Smoking induced atherosclerosis in cancers. HealthMED 2012; 6(11): 3744-3749.
19. Fodor JG, Tzerovska R, Dorner T, Rieder A. Do we diagnose and treat coronary heart disease differently in men and women? Wien Med Wochenschr 2004; 154(17-18): 423-425.
20. Helvaci MR, Kaya H, Borazan A, Ozer C, Seyhanli M, Yalcin A. Metformin and parameters of physical health. Intern Med 2008; 47(8): 697-703.
21. Helvaci MR, Aydin Y, Varan G, Abyad A, Pocock L. Acarbose versus metformin in the treatment of metabolic syndrome. World Family Med 2018; 16(5): 10-15.
22. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21(5): 821-848.
23. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013; 187(4): 347-65.
24. Funahashi T, Nakamura T, Shimomura I, Maeda K, Kuriyama H, Takahashi M, et al. Role of adipocytokines on the pathogenesis of atherosclerosis in visceral obesity. Intern Med 1999; 38(2): 202–206.
25. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol 1999; 19(4): 972–978.

26. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. Obes Rev 2002; 3(3): 147–156.
27. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. Biomed Environ Sci 2002; 15(3): 245–252.
28. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999; 341(15): 1097–1105.
29. Helvaci MR, Aydin LY, Maden E, Aydin Y. What is the relationship between hypertriglyceridemia and smoking? Middle East J Age and Ageing 2011; 8(6).
30. Grunberg NE, Greenwood MR, Collins F, Epstein LH, Hatsukami D, Niaura R, et al. National working conference on smoking and body weight. Task Force 1: Mechanisms relevant to the relations between cigarette smoking and body weight. Health Psychol 1992; 11: 4-9.
31. Walker JF, Collins LC, Rowell PP, Goldsmith LJ, Moffatt RJ, Stamford BA. The effect of smoking on energy expenditure and plasma catecholamine and nicotine levels during light physical activity. Nicotine Tob Res 1999; 1(4): 365-370.
32. Hughes JR, Hatsukami DK. Effects of three doses of transdermal nicotine on post-cessation eating, hunger and weight. J Subst Abuse 1997; 9: 151-159.
33. Miyata G, Meguid MM, Varma M, Fetissov SO, Kim HJ. Nicotine alters the usual reciprocity between meal size and meal number in female rat. Physiol Behav 2001; 74(1-2): 169-176.
34. Laaksonen M, Rahkonen O, Prattala R. Smoking status and relative weight by educational level in Finland, 1978-1995. Prev Med 1998; 27(3): 431-437.
35. Froom P, Melamed S, Benbassat J. Smoking cessation and weight gain. J Fam Pract 1998; 46(6): 460-464.
36. Helvaci MR, Kaya H, Gundogdu M. Gender differences in coronary heart disease in Turkey. Pak J Med Sci 2012; 28(1): 40-44.
37. Helvaci MR, Aydin Y, Gundogdu M. Atherosclerotic effects of smoking and excess weight. J Obes Wt Loss Ther 2012; 2: 145.
38. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998; 316(7137): 1043-1047.
39. Helvacı MR, Kaya H, Ozer C. Aging may be the major determiner factor of excess weight. Middle East J Age and Ageing 2008; 5(2).
40. Di Angelantonia E, Sarwar N, Perry P, Kaptoge S, Ray KK, Thompson A, et al. Major lipids, apolipoproteins, and risk of vascular disease. JAMA 2009; 302(18): 1993-2000.
41. Sarwar N, Sandhu MS, Ricketts SL, Butterworth AS, Di Angelantonia E, Boekholdt SM, et al. Triglyceride-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet 2010; 375(9726): 1634-1639.