# What a lower prevalence of diabetes mellitus but higher incidence of dyslipidemia in smokers

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## Abstract

Background: We tried to understand whether or not there is a relationship between smoking and diabetes mellitus (DM).

Methods: Current regular smokers for the last six months and age and sex-matched non-smokers were included. Patients with current alcohol consumption (one drink a day) and patients with malignancies or inflammatory, infectious, or devastating disorders were excluded.

Results: The study included 247 smokers and 167 non-smokers. The mean age and body mass index (BMI) of smokers were 46.2 years and 26.6 kg/m2, respectively, and 70.0% of them were male. Although the mean weight, BMI, systolic and diastolic blood pressures, and hematocrit values were similar in both groups, fasting plasma glucose (FPG) and DM were lower in the smokers (102.3 versus 111.6 mg/dL, p=0.007 and 8.9% versus 14.3%, p<0.05, respectively). Similarly, high density lipoproteins (HDL) were lower in the smokers, again (40.9 versus 44.0 mg/dL, p<0.05). On the other hand, triglycerides (163.1 versus 151.3 mg/dL, p<0.05) and low density lipoproteins (LDL) (123.8 versus 117.5 mg/dL, p<0.05) were higher in the smokers. Parallel to triglycerides and LDL, erythrocyte sedimentation rate (ESR) (10.6 versus 9.3 mm/h, p<0.05) and C-reactive protein (CRP) (2.3 versus 2.0 mg/L, p<0.05) were also higher in them.

Conclusion: Smoking-induced low-grade inflammation on vascular endothelium in whole body may terminate with the endothelial dysfunction, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. FPG and HDL may be negative whereas triglycerides, LDL, ESR, and CRP positive acute phase reactants terminating with lower prevalence of DM but higher incidence of dyslipidemia in smokers.

Key words: Smoking, fasting plasma glucose, diabetes mellitus, high density lipoproteins, triglycerides, low density lipoproteins, dyslipidemia

## Introduction

The monolayer of endothelial cells that forms the inner lining of arteries, veins, capillaries, and lymphatics is called as the endothelium. Probably, the whole endothelium all over the body may act as a separate organ that may be the largest organ in the body. It may contract vasculature of the peripheral organs while relaxing the internal ones during cold, anxiety, and depression-like stresses of the body. Because we measure the systolic and diastolic blood pressures (BP) of the arms and legs, they may not show the actual BP of the brain, heart, lung, liver, and kidney-like internal organs. The endothelium may be the main organ in the control of blood fluidity, platelets aggregation, and vascular tone all over the body. It may also be the main organ in the immunology, inflammation, angiogenesis, and endocrinology. The endothelium may control vascular tone and blood flow by releasing nitric oxide, reactive oxygen species, and metabolites of arachidonic acid into the circulation. It may also be important for synthesizing of vasoactive hormones such as angiotensin II. An endothelial dysfunction-induced accelerated atherosclerosis all over the body may be the main cause of end-organ insufficiencies, aging, and death. Such a dysfunction may also be important in the development of cancers by preventing clearance of malignant cells by the natural killers in terminal points of the circulation. Similarly, physical inactivity, animal-rich diet, excess weight, higher BP and glucose levels, chronic inflammations, prolonged infections, cancers, smoking, and alcohol may be accelerating factors of the chronic endothelial inflammation and dysfunction terminating with the accelerated atherosclerosis-induced end-organ insufficiencies (1, 2). The much higher BP of the afferent vasculature may be the major accelerating factor by inducing recurrent injuries on the vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in the medical literature. Due to the chronic endothelial damage, inflammation, edema, fibrosis, and dysfunction, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood flow to the terminal organs, and increase systolic and decrease diastolic BP further. Some of the irreversible consequences of the systemic inflammatory process are obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheric artery disease, chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, early aging, and premature death (3). Although early withdrawal of the accelerating factors may delay terminal consequences, endothelial changes can not be reversed, completely after development of the irreversible end-points due to their fibrotic natures. The accelerating factors and irreversible consequences are researched under the titles of the metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in the literature, extensively (4, 5). As some of the well-known components of the syndrome, there may be a significant relationship between smoking and DM, clinically.

## Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Current regular smokers at least for the last six months were studied. Patients with current alcohol consumption (one drink a day) and patients with inflammatory, infectious, or devastating disorders including eating disorders, malignancies, acute or chronic renal failure, cirrhosis, COPD, hyper- or hypothyroidism, or heart failure were excluded. A routine check up procedure including hemogram, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), fasting plasma glucose (FPG), triglycerides, low density lipoproteins (LDL), high density lipoproteins (HDL), albumin, creatinine, thyroid function tests, hepatic function tests, markers of hepatitis A, B, C, and human immunodeficiency viruses, a urinalysis, a posterior-anterior chest x-ray graphy, and an electrocardiogram was performed. An additional Doppler echocardiogram and/or abdominal ultrasonography were performed just in required cases. Body mass index (BMI) of each individual was calculated by measurements of the Same Physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (6). Office BP were checked after a 5-minute of rest in seated position with mercury sphygmomanometer. Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 100 and 125 mg/dL, and diagnosis of cases with a two-hour plasma glucose level of 200 mg/dL or higher is DM (6). Eventually, all smokers were collected into the first, and age and sex-matched non-smokers were collected into the second groups. The mean weight, BMI, systolic and diastolic BP, triglycerides, LDL, HDL, FPG, ESR, CRP, and hematocrit values and prevalence of DM 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

The study included 247 smokers (74 females and 173 males) and 167 (55 females and 112 males) non-smokers. The mean age and BMI of smokers were 46.2 years and 26.6 kg/m2, respectively, and 70.0% of them were male. Although the mean weight, BMI, systolic and diastolic BP, and hematocrit values were similar in both groups, FPG and DM were lower in the smokers (102.3 versus 111.6 mg/dL, $p=0.007$ and 8.9% versus 14.3%, $p<0.05$, respectively). Similarly, HDL were lower in the smokers, again (40.9 versus 44.0 mg/dL, $p<0.05$). On the other hand, triglycerides (163.1 versus 151.3 mg/dL, $p<0.05$) and LDL (123.8 versus 117.5 mg/dL, $p<0.05$) were higher in the smokers. Parallel to triglycerides and LDL, ESR (10.6 versus 9.3 mm/h, $p<0.05$) and CRP (2.3 versus 2.0 mg/L, $p<0.05$) were higher in the smokers, again (Table 1).

**Table 1: Comparison of smokers and non-smokers**

| Variables | Smokers | *p*-value | Non-smokers |
|---|---|---|---|
| Number | 247 | | 167 |
| ***Female ratio*** | ***29.9%*** | Ns* | 32.9% |
| Mean age (year) | 46.2 ± 13.4 (19-76) | Ns | 44.8 ± 15.7 (13-77) |
| Weight (kg) | 76.1 ± 13.8 (44-118) | Ns | 74.7 ± 13.0 (45-122) |
| BMI† (kg/m²) | 26.6 ± 4.4 (16.2-39.4) | Ns | 26.5 ± 4.5 (16.6-41.1) |
| Systolic BP‡ (mmHg) | 127.5 ± 23.7 (80-200) | Ns | 130.0 ± 22.6 (80-200) |
| Diastolic BP (mmHg) | 88.0 ± 12.4 (60-130) | Ns | 88.5 ± 11.9 (60-130) |
| Hematocrit (%) | 41.9 ± 4.6 (28-60) | Ns | 41.0 ± 3.7 (31-49) |
| ***FPG§ (mg/dL)*** | ***102.3 ± 25.5 (70-309)*** | ***0.007*** | 111.6 ± 37.6 (74-327) |
| ***DM‖*** | ***8.9%*** | ***<0.05*** | 14.3% |
| ***HDL** (mg/dL)*** | ***40.9 ± 9.6 (26-70)*** | ***<0.05*** | 44.0 ± 9.4 (24-70) |
| ***Triglycerides (mg/dL)*** | 163.1 ± 101.4 (40-585) | ***<0.05*** | ***151.3 ± 86.2 (20-410)*** |
| ***LDL*** (mg/dL)*** | 123.8 ± 34.3 (10-282) | ***<0.05*** | ***117.5 ± 29.0 (43-185)*** |
| ***ESR**** (mm/h)*** | 10.6 ± 10.2 (1-51) | ***<0.05*** | ***9.3 ± 8.0 (1-35)*** |
| ***CRP***** (mg/L)*** | 2.3 ± 2.6 (0-13) | ***<0.05*** | ***2.0 ± 2.5 (0-12)*** |

*Nonsignificant (p>0.05) †Body mass index ‡Blood pressures §Fasting plasma glucose ‖Diabetes mellitus
**High density lipoproteins ***Low density lipoproteins ****Erythrocyte sedimentation rate *****C-reactive protein

## Discussion

Obesity may be one of the irreversible end-points of the metabolic syndrome. Although some transient successes can be achieved, nonpharmaceutical approaches provide limited benefit to reverse the obesity, permanently. Due to the excess weight-induced chronic low-grade inflammation on the vascular endothelium all over the body, the risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess weight in all age groups (7). The chronic low-grade inflammation may even cause genetic changes of the endothelial cells, and the systemic atherosclerosis may prevent clearance of malignant cells, effectively. Similarly, the effects of excess weight on the BP were shown in the literature, extensively (8). For example, prevalences of sustained normotension (NT) were higher in the underweight than the normal weight (80.3% versus 64.0%, p<0.05) and overweight groups (80.3% versus 31.5%, p<0.001) (8), and 52.8% of patients with HT had obesity against 14.5% of patients with the sustained NT (p<0.001) (9). So the major underlying cause of the metabolic syndrome appears as weight gain that may be the main cause of insulin resistance, hyperlipoproteinemias, impaired fasting glucose, impaired glucose tolerance, and white coat hypertension (WCH) (10). Interestingly, weight gain before the development of an obvious overweight or obesity may even cause development of several components of the metabolic syndrome. For example, WCH alone may be a strong indicator of weight gain even before development of excess weight (8, 9). On the other hand, prevention of the weight gain with physical activity even in the absence of a prominent weight loss usually results with resolution of many parameters of the syndrome (11). According to our experiences, excess weight may actually be a result of physical inactivity instead of an excessive eating habit. In another words, there is a problem with burning of calories instead of getting them. Therefore prevention of weight gain cannot be achieved by diet, alone (12). On the other hand, limitation of excess weight as excessive fat tissue around the abdomen under the heading of abdominal obesity may be meaningless. Instead it should be defined as overweight or obesity via the BMI. Because adipocytes function as an endocrine organ, and they release leptin, tumour necrosis factor (TNF)-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines into the plasma (13). Eventual hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with insulin resistance, elevated BP, and chronic endothelial inflammation and dysfunction. Similarly, the Adult Treatment Panel (ATP) III reported that although some people classified just as overweight with larger muscular masses, most of them also have excess fat tissue predisposing to the irreversible end-points of the metabolic syndrome (6).

Smoking may be the second common cause of systemic vasculitis in the world. It is one of the major risk factors for the atherosclerotic end-organ insufficiencies (14). Its atherosclerotic effect is the most obvious in Buerger's disease. Buerger's disease is an obliterative vasculitis 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 the medical literature. Beside the obvious atherosclerotic effects of smoking, some studies reported that smoking in human being and nicotine administration in animals are associated with the lower values of BMI (15). Some evidence revealed increased energy expenditure during smoking, both at rest and doing light physical activity (16). Nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (17). According to an animal study,

nicotine may lengthen inter-meal time, and decrease amount of meal eaten (18). Similarly, the BMI seems to be the highest in the former, the lowest in the current, and medium in never smokers (19). Smoking may be associated with a post cessation weight gain, but the risk is the highest during the first year, and decreases with the following years (20). As the opposite findings to the above studies, the mean weight and BMI were similar both in the smokers and non-smokers, here ($p>0.05$ for both). Similarly, prevalence of smoking was similar in the normal weight (35.9%), overweight (32.9%), and obesity groups (33.7%, $p>0.05$ between all) in the other study (21). On the other hand, although the CHD was detected with similar prevalence in both genders, prevalence of smoking and COPD were higher in males against the higher BMI, LDL, triglycerides, WCH, HT, and DM in females (22). Beside that the prevalence of myocardial infarctions is increased three-fold in men and six-fold in women who smoked at least 20 cigarettes per day (23). In another words, smoking may be more dangerous for women about the atherosclerotic end-points probably due to the higher BMI and its consequences in them. Similar to the present study, smoking is consistently higher in men in the literature (14). Several toxic substances found in the cigarette smoke get into the circulation, and cause a vascular endothelial inflammation in all organ systems of the body. For example, smoking is usually reported together with depression, irritable bowel syndrome (IBS), chronic gastritis, hemorrhoids, and urolithiasis in the literature (24-26). There may be several underlying mechanisms to explain these associations in the smokers (24). First of all, smoking may have some antidepressant properties with several side effects. Secondly, smoking-induced vascular endothelial inflammation may disturb epithelial functions for absorption and excretion in the gastrointestinal and genitourinary tracts. These functional problems may terminate with urolithiasis and components of the IBS including loose stool, diarrhea, and constipation. Thirdly, diarrheal losses-induced urinary changes may even cause urolithiasis (25, 26). Fourthly, smoking-induced sympathetic nervous system activation may cause motility problems in the gastrointestinal and genitourinary tracts terminating with the IBS and urolithiasis. Eventually, immunosuppression secondary to smoking-induced vascular endothelial inflammation may even terminate with the gastrointestinal and genitourinary tract infections causing loose stool, diarrhea, and urolithiasis, because some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits in the urine. Actually, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infections with the bacteria producing urease. Parallel to the results above, urolithiasis was detected in 17.9% of cases with the IBS and 11.6% of cases without in the other study ($p<0.01$) (25).

Alcohol may be the third common cause of systemic vasculitis in the world. Alcohol is addictive to humans, and can result in alcohol use disorder (AUD), dependence, and withdrawal. Alcohol is the only drug that mostly damage the other individuals. It is causally associated with more than 200 different pathologies (27). Eventually, people hospitalized with AUD have an average life expectancy of 47-53 years in men and 50-58 years in women, and die 24-28 years earlier than the others (28). People with AUD have three-fold higher mortality in men and four-fold in women (29). Similar to the smoking, alcohol may be more dangerous for women about the atherosclerotic end-points probably due to their lower body mass induced lower capacity to metabolize alcohol and higher mass of fat in their body. A very substantial part of the Danish excess mortality and lower life expectancy compared to Sweden can be attributed to higher mortality related with the alcohol and smoking (28). Alcohol is one of the main causes of cancers all over the body (27). It may even cause unconsciousness and sudden death if taken in high amounts. Hepatic alcohol dehydrogenase is the main enzyme to metabolize alcohol that requires the cofactor, nicotinamide adenine dinucleotide (NAD). Normally, NAD is used to metabolize fats in the liver but alcohol competes with these fats for the use of NAD. Eventually, prolonged exposure of alcohol causes fatty liver. Ethanol is the only alcohol that is found in alcoholic beverages. Ethanol crosses biological membranes and blood-brain barrier by means of the passive diffusion, easily. Alcohol works particularly by increasing effects of the gamma aminobutyric acid that is the major inhibitory neurotransmitter in the brain. Alcohol induces happiness and euphoria, decreased anxiety, increased sociability, sedation, generalized depression of central nervous system, and impairment of cognitive, memory, motor, and sensory functions. It may even cause fetal disorders in pregnancy since ethanol is classified as a teratogen. Regular alcohol consumption leads to cell death in the liver, scarring, cirrhosis, and hepatocellular carcinoma. Heavy alcohol consumption may even terminate with permanent brain damage. Alcohol is a major contributing factor of elevated triglycerides, and triglycerides behave as sensitive acute phase reactants (APR) in the plasma (10). Although the regular alcohol consumers were excluded, plasma triglycerides were higher in the smokers in the present study (163.1 versus 151.3 mg/dL, $p<0.05$), indicating the inflammatory effects of smoking in the body.

The acute phase response occurs in case of infection, infarction, foreign body, autoimmune disorder, allergy, neoplasm, trauma, and burn-like inflammatory conditions of the body. Certain mediators known as APR are increased or decreased during the response (30, 31). These markers are commonly used in the clinical practice as the indicators of acute and chronic inflammations of the body. The terms of acute phase proteins and APR are usually used synonymously, although some APR are polypeptides rather than proteins. Positive and negative APR are those whose concentrations increase or decrease during the acute phase response, respectively. The response is predominantly mediated by the pro-inflammatory cytokines including TNF, interleukin-1, and interleukin-6 secreted by neutrophils and macrophages into the circulation. The liver and other organs respond to the cytokines by producing many positive APR. ESR, CRP, fibrinogen, ferritin, procalcitonin, hepcidin, haptoglobin, ceruloplasmin, complement proteins, and serum amyloid A are some of the well-known positive APR. CRP is a

useful indicator of the acute phase response, clinically. It is responsible for activation of the complement pathway. CRP reaches up to the maximum concentration within two days, and decreases with the resolution of the inflammation with a half-life of 6-8 hours, rapidly. It correlates with ESR, but not simultaneously since ESR is largely dependent upon elevation of fibrinogen with a half-life of one week, approximately. Thus ESR remains higher for a longer period of time despite the removal of the inflammatory stimulus. Similarly, white blood cells and platelet counts may also behave as some other positive APR in the body (32). On the other hand, productions of the negative APR are suppressed, simultaneously. Albumin, transferrin, retinol-binding protein, antithrombin, transcortin, alpha-fetoprotein, and hemoglobin are some of the well-known negative APR in the body. Suppressions of such negative APR are also used as the indicators of the acute phase response in the body. Suppressions of such negative APR may actually be secondary to the protection of amino acids and polypeptides required for the production of positive APR, sufficiently. As also observed in the smokers in the present study, production of HDL may also be suppressed in the liver during the acute phase response (33). Similarly, triglycerides, DM, and CHD were all higher in patients with plasma HDL values of lower than 40 mg/dL, significantly (33). So HDL may actually behave as negative whereas triglycerides positive APR in the plasma. Similarly, the highest CHD of the group with HDL values of lower than 40 mg/dL can also be explained by the same hypothesis in the other study (10). Additionally, plasma triglycerides increased whereas HDL decreased during infections (34). On the other hand, a 10 mg/dL increase of plasma LDL values was associated with a 3% lower risk of hemorrhagic stroke (35). Similarly, the highest prevalence of HT and DM parallel to the elevated values of LDL and HDL, and the highest prevalence of COPD, CHD, and CRD in contrast to the lowest values of LDL and HDL may show initially positive but eventually negative behaviors of LDL and HDL as the APR (36). Probably, HDL turns to the negative direction much earlier than LDL in the plasma. Interestingly, the most desired values were between 80 and 100 mg/dL for LDL, between 40 and 46 mg/dL for HDL, and lower than 60 mg/dL for triglycerides in the plasma (10). Parallel to ESR and CRP, plasma triglycerides and LDL may behave as positive whereas FPG and HDL negative APR in smokers in the present study. In another words, lower HDL values should alert clinicians for researching of any acute phase response in the body (37, 38).

Cholesterol, triglycerides, and phospholipids are the major lipids of the body. They do not circulate in the plasma, freely instead they are bound to proteins, and transported as lipoproteins. There are five main classes of lipoproteins in the plasma. Chylomicrons carry exogenous triglycerides to the liver via the thorasic duct. Very low density lipoproteins (VLDL) are produced in the liver, and carry endogenous triglycerides to the organs. VLDL are converted into the intermediate density lipoproteins (IDL) by removal of 90% of triglycerides by lipases in the capillaries of adipocytes and muscle tissues. Then the IDL are degraded into LDL by removal of more triglycerides. So VLDL are the main source of LDL in the plasma, and LDL deliver cholesterol from the liver to organs. Although the liver removes majority of LDL from the circulation, a small amount is uptaken by scavenger receptors of the macrophages migrating into the arterial walls, and become the foam cells of atherosclerotic plaques. HDL remove fats and cholesterol from cells including the arterial wall atheroma, and carry the cholesterol back to the adrenals, ovaries, and testes-like steroidogenic organs and liver for excretion, re-utilization, or disposal. All of the carrier lipoproteins are under dynamic control, and are readily affected by diet, drug, chronic inflammation, prolonged infection, cancer, tissue damage, smoking, alcohol, and excess weight. Thus lipid analysis should be performed during a steady state. But the metabolic syndrome alone is a low grade inflammatory process, thus the metabolic syndrome may even cause abnormal levels of lipoproteins in the plasma. For instance, HDL may normally show various anti-oxidative, anti-inflammatory, and anti-atherogenic properties including reverse cholesterol transport (39). However, HDL may become 'dysfunctional' in pathologic conditions which means that relative compositions of lipids and proteins, as well as the enzymatic activities of HDL are altered (39). For example, properties of HDL are compromised in patients with DM by means of the oxidative modification, glycation, and/or transformation of HDL proteomes into the proinflammatory proteins. Additionally, the drugs increasing HDL values such as niacin, fibrates, and cholesteryl ester transfer protein inhibitors can not reduce all cause mortality, CHD mortality, myocardial infarction, and stroke (40). In another words, HDL may just be some indicators instead of being the main actors of the health. Similarly, BMI, DM, and CHD were the lowest between the HDL values of 40 and 46 mg/dL, and the prevalence of DM was only 3.1% between these values against 22.2% outside these limits (41). Similar to the present study, HDL and FPG values were also suppressed in the sickle cell diseases (SCD), probably due to the severe inflammatory nature of the diseases (42). Smoking may reduce HDL and FPG by means of the systemic inflammatory effects on the vascular endothelium all over the body. On the other hand, triglycerides alone may be one of the most sensitive APR indicating the metabolic syndrome (43). Although ATP II determined the normal plasma triglycerides as lower than 200 mg/dL in 1994 (44), World Health Organisation in 1999 (45) and ATP III in 2001 reduced the normal limits as lower than 150 mg/dL (6). Although these cutpoints, there are still suspicions about the safest values of triglycerides in the plasma (43). Beside that triglycerides are the only lipids which were not suppressed with the pathological weight losses (46). For example, plasma triglycerides increased in contrast to the suppressed body weight and BMI in the SCD (46). Similarly, prevalences of excess weight, DM, HT, and smoking were all higher in the hypertriglyceridemia group (200 mg/dL and higher) in the other study (47). Interestingly, the greatest number of deteriorations in the metabolic parameters was observed with the triglycerides values of 60 mg/dL and higher (43).

The body's homeostatic mechanism keeps blood glucose levels within a narrow range with two groups of mutually antagonistic hormones. Glucagon, cortisol, and catecholamines are the catabolic hormones increasing the blood glucose, whereas insulin is the anabolic hormone decreasing the blood glucose levels. Glucagon is secreted from the alpha cells, while insulin is secreted from the beta cells of pancreatic islets which are the bundles of endocrine tissues. They regulate the blood glucose levels through a negative feedback mechanism together. When the blood glucose levels are too high, insulin tells muscles to take up excess glucose for storage. When the blood glucose levels are too low, glucagon informs the tissues to produce more glucose. Catecholamines prepare the muscles and respiratory system for a 'fight to fight' response. Cortisol prepares the body for the various stresses. A blood glucose level of four grams, or about a teaspoon, is critical for the normal function of millions of cells in the body (48). The four grams of glucose circulates in the blood stream of a person with the body weight of 70 kg. This amount is kept constant with a sophisticated control mechanism in the body. The constant blood glucose levels are maintained via the hepatic and muscular glycogen stores during fasting since glucose is stored in the skeletal muscles and hepatocytes in the form of glycogen. There are approximately 100 and 400 grams of glycogen stored in the skeletal muscles and liver, respectively (48). The brain consumes about 60% of the blood glucose during fasting. FPG, which is measured after a fasting period of 8 hours, is the most commonly used indication of overall glucose homeostasis. Infections, inflammations, surgical operations, depressions, alcohol, and smoking-like stresses may affect the blood glucose homeostasis. For instance, smoking was negatively associated with FPG and DM in Chinese men with the normal weight, but not in men with excess weight or in women (49). Similarly, smokers have a lower likelihood of newly-diagnosed DM in Chinese men with a lower BMI in the other study (50). Parallel to the above studies, FPG and DM were also lower in the smokers, here (102.3 versus 111.6 mg/dL, p=0.007 and 8.9% versus 14.3%, p<0.05, respectively). Although majority of the smokers were male again (70.0%), the mean BMI of the smokers was higher (26.6 kg/m2) in contrast to the above studies.

As a conclusion, smoking-induced low-grade inflammation on the vascular endothelium all over the body may terminate with the endothelial dysfunction, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. FPG and HDL may be negative whereas triglycerides, LDL, ESR, and CRP positive acute phase reactants terminating with lower prevalence of DM but higher incidence of dyslipidemia in the smokers.

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