ECRONICON OPEN ACCESS

EC CLINICAL AND MEDICAL CASE REPORTS
Research Article

Smoking May Not Prevent Overweight or Obesity

Mehmet Rami Helvaci[1]*, Ayse Ceylan[2], Yasemin Kayabasi[2], Huseyin Sencan[1], Abdulrazak Abyad[3], Lesley Pocock[4]

[1]Specialist of Internal Medicine, MD, Turkey
[2]Manager of Writing and Statistics, Turkey
[3]Middle-East Academy for Medicine of Aging, MD, Lebanon
[4]Medi-WORLD International, Australia

***Corresponding Author:** Mehmet Rami Helvaci, S*pecialist of Internal Medicine, MD, Turkey.*
E-mail: *mramihelvaci@hotmail.com* **Phone:** *00-90-506-4708759*

Received: November 22, 2022; **Published:** January 27, 2023

Abstract

Background: We tried to understand whether or not there is a long term effect of smoking on prevention of overweight or obesity.

Method: Patients between the ages of 35 and 70 years were studied to be able to see the long term effects of smoking on prevention of overweight and obesity, and to avoid debility induced weight loss in elders. The study included consecutive cases with the normal weight, and age and sex-matched cases with overweight and obesity. Current daily smokers with a period of one pack-year and cases with a history of five pack years were accepted as smokers.

Results: There were 270 cases in each of the normal weight, overweight, and obesity groups. Mean ages of them were 47.1, 46.3, and 48.9 years, respectively ($p > 0.05$ between them). The female ratio was 53.7% in the three groups. Prevalences of smoking were similar in the three groups (35.9%, 32.9%, and 33.7%, respectively, $p > 0.05$ between all). Whereas prevalences of HT were 8.1%, 13.7%, and 21.8%, and prevalences of DM were 9.6%, 20.0%, and 28.5% in them, respectively ($p < 0.001$ between all). Similarly, prevalences of dyslipidemia were 19.2%, 32.5%, and 40.3% in them, respectively ($p < 0.01$ between all).

Conclusion: Prevalences of smoking were similar in the normal weight, overweight, and obesity groups, although the absence of any significant difference according to the mean age and gender distribution between the groups. On the other hand, prevalences of HT, DM, and dyslipidemia increased gradually and significantly from the normal weight towards the overweight and obesity groups.

Keywords: *Smoking; Normal Weight; Overweight; Obesity; Hypertension; Diabetes Mellitus; Dyslipidemia*

Introduction

The endothelium is a monolayer of endothelial cells that builds up the inner lining of artery, vein, capillary, and lymphatics. It may be the major player in the blood fluidity, platelets aggregation, and vascular tone. It may be the chief actor in the immunology, inflammation, and angiogenesis. It may also be significant in the endocrinology. The endothelial cells control vascular tone and blood flow by synthesizing and releasing nitric oxide, metabolites of arachidonic acid, and reactive oxygen species. They are also important in generation of vasoactive hormones such as angiotensin II. An endothelial dysfunction linked to an imbalance between the synthesis and release of these endothelial factors may explain the initiation of several cardiovascular pathologies including hypertension (HT) and atherosclerosis. On

the other hand, overweight, obesity, smoking, alcohol, chronic inflammation, prolonged infection, and cancers are well-known causes of chronic endothelial inflammation terminating with an accelerated atherosclerosis-induced end-organ insufficiencies all over the body [1,2]. Chronic endothelial damage may be the major underlying cause of aging and death by causing end-organ insufficiencies in the human being. Much higher blood pressures (BP) of the afferent vasculature may be the major accelerating factor by causing recurrent endothelial injuries. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Therefore, the term of venosclerosis is not as famous as atherosclerosis in the literature. Due to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood supply to the terminal organs, and increase systolic and decrease diastolic BP further. Some of the well-known accelerating factors of the inflammatory process are physical inactivity, animal-rich diet, overweight, obesity, smoking, alcohol, chronic inflammation, prolonged infection, and cancers for the development of irreversible consequences including obesity, HT, diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, and finally early aging and premature death [3]. Although early withdrawal of the accelerating factors may delay such irreversible consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, and aging, endothelial changes can not be reversed completely 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]. We tried to understand whether or not there is a long term effect of smoking on prevention of overweight or obesity in the present study.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between January and October 2006. Consecutive patients with the normal weight, and age and sex-matched patients with overweight and obesity were included. Patients between the ages of 35 and 70 years were studied to be able to see the long term effects of smoking on prevention of overweight and obesity, and to avoid debility induced weight loss in elders. Their medical histories including smoking habit and already used medications were learnt, and a routine check up procedure including hemogram, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), fasting plasma glucose (FPG), total cholesterol, 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 an abdominal ultrasonography were performed just in case of requirement. Current daily smokers with a period of one pack-year and cases with a history of five pack years in the past were accepted as smokers. Cigar or pipe smokers were excluded. Cases with regular alcohol consumption (one drink a day) with at least one year and patients with inflammatory, infectious, or devastating disorders including eating disorders, malignancies, acute or chronic renal failure, cirrhosis, COPD, hyper- or hypothyroidism, and heart failure were excluded. Body mass index (BMI) was calculated by measurements of the Same Physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared, and obesity is defined as a BMI of 30.0 kg/m^2 and higher, overweight as 25.0 - 29.9 kg/m^2, and normal weight as 18.5 - 24.9 kg/m^2 [6]. Cachexia cases with a BMI value of lower than 18.5 kg/m^2 were excluded, too. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases after a 10-minute education about proper BP measurement techniques [7]. The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest for a period of 5-minute in the seated position before the measurements. HT is defined as a mean BP of 135/85 mmHg or higher on average HBP measurements [8]. Cases with an overnight FPG level of 126 mg/dL or higher on two occasions were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 125 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level of 200 mg/dL or higher is DM [6]. Additionally, patients with

dyslipidemia were detected by using the National Cholesterol Education Program Expert Panel's recommendations for defining dyslipidemic subgroups [6]. Dyslipidemia is diagnosed if the plasma LDL value is 160 mg/dL or higher and/or triglycerides value of 200 mg/dL or higher and/or HDL value of lower than 40 mg/dL [6]. Prevalences of smoking, HT, DM, and dyslipidemia were detected in the normal weight, overweight, and obesity groups, and results were compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

There were 270 cases in each of the normal weight, overweight, and obesity groups. Mean ages of them were 47.1, 46.3, and 48.9 years, respectively ($p > 0.05$ between them). The female ratio was 53.7% in the three groups. Prevalences of smoking were similar in the three groups (35.9%, 32.9%, and 33.7%, respectively, $p > 0.05$ between all). Whereas prevalences of HT were 8.1%, 13.7%, and 21.8%, and prevalences of DM were 9.6%, 20.0%, and 28.5% in them, respectively ($p < 0.001$ between all). Similarly, prevalences of dyslipidemia were 19.2%, 32.5%, and 40.3% in them, respectively ($p < 0.01$ between all) (Table 1).

Variables	Normal weight	p-value	Overweight	p-value	Obesity
Number	270		270		270
Female ratio	53.7%		53.7%		53.7%
Mean age (year)	47.1 ± 6.3 (35-70)	Ns*	46.3 ± 5.4 (35-70)	Ns	48.9 ± 6.7 (35-70)
Smoking	35.9%	Ns	32.9%	Ns	33.7%
HT†	8.1%	< 0.001	13.7%	< 0.001	21.8%
DM‡	9.6%	< 0.001	20.0%	< 0.001	28.5%
Dyslipidemia	19.2%	< 0.001	32.5%	< 0.01	40.3%

Table 1: *Comparison of cases with normal weight, overweight, and obesity.*

**Nonsignificant (p > 0.05); †Hypertension; ‡Diabetes mellitus.*

Discussion

Excess weight may be the most common causes of vasculitis all over the world [9,10]. Obesity may be an irreversible consequence of the metabolic syndrome, since it usually starts to develop just after infancy [11]. Due to the long period of development, pharmaceutical and nonpharmaceutical approaches provide little benefit either to heal obesity or to prevent its consequences. Excess weight may cause a chronic low-grade inflammation on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess weight in all age groups [10]. The chronic low-grade inflammation may even cause genetic changes on the endothelial cells, and the eventual systemic atherosclerosis may even decrease clearance of the malignant cells in the body. Beside that harmful effects of excess weight on the BP were shown in the literature [12]. For example, prevalence of sustained normotension (NT) was higher in the underweight (80.3%) than the normal weight (64.0%, $p < 0.05$) and overweight groups (31.5%, $p < 0.05$) [12] and 52.8% of patients with HT had obesity against 14.5% of patients with the sustained NT ($p < 0.001$) [13]. So, the main underlying cause of the metabolic syndrome seems as weight gain, which may be the main cause of insulin resistance, hyperlipoproteinemias, impaired fasting glucose, impaired glucose tolerance, and white coat hypertension (WCH) via the prolonged low-grade inflammation on vascular endothelium all over the body [14]. Prevention of the weight gain with increased physical activity, even in the absence of a prominent weight loss, will probably result with resolution of many parameters of the metabolic syndrome [15,16]. According to our experiences, excess weight may actually be a consequence of physical inactivity instead of an excessive eating habit. Majority of obese patients may even eat less than normal weight individuals. In another definition, excess weight may actually be a problem with the burning of taken calories,

and prevention of weight gain can not be achieved by diet alone [17]. In other words, if you can burn, you can eat as much as you want. On the other hand, limitation of excess weight as an excessive fat tissue around the abdomen under the heading of abdominal obesity may be meaningless. Actually, it should be defined as overweight or obesity via the BMI since adipocytes function as an endocrine organ wherever they found, and they release leptin, tumour necrosis factor (TNF)-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines into the plasma [18]. The eventual hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with chronic endothelial inflammation, insulin resistance, and elevated BP. Similarly, Adult Treatment Panel III reported that most of the overweight individuals with larger muscular masses have additional excessive fat tissue predisposing to the irreversible consequences of the metabolic syndrome [6].

Smoking may be the second common cause of vasculitis all over the world. It is one of the major risk factors for the atherosclerotic end-organ insufficiencies [19]. 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 artery and veins, and it has never been reported in the absence of smoking in the literature. Beside the well-known atherosclerotic effects of smoking, some studies reported that smoking in human being and nicotine administration in animals are associated with lower BMI values [20]. Some evidences revealed an increased energy expenditure during smoking both on rest and light physical activity [21] and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner [22]. According to an animal study, nicotine may lengthen intermeal time, and simultaneously decrease amount of meal eaten [23]. Additionally, the BMI seems to be the highest in the former, the lowest in the current, and medium in never smokers [24]. Smoking may be associated with a postcessation weight gain, but evidences suggest that risk of the weight gain is the highest during the first year after quitting, and decreases with the following years [25]. Whereas probably due to the low-grade nature of the inflammation caused by smoking, the body weight and BMI were not suppressed in the smokers ($p > 0.05$ for both) in the other study [26]. Similarly, prevalence of smoking was similar in the normal weight, overweight, and obesity groups in the present study, although the absence of any significant difference according to the mean age and gender distribution between the groups. On the other hand, although the CHD was detected with similar prevalences in both genders, prevalences of smoking and COPD were higher in males against the higher BMI, LDL, triglycerides, WCH, HT, and DM in females [27]. Beside that, the incidence of myocardial infarction is increased six-fold in women and three-fold in men who smoked at least 20 cigarettes per day [28]. In other words, smoking may be more harmful for women about the atherosclerotic consequences probably due to the higher BMI in them. Smoking is consistently higher in men in the literature [19]. Similarly, 70.0% of the smokers were males in the above study [26]. Several toxic substances found in the cigarette smoke get into the blood circulation by means of the respiratory tract, and cause a vascular endothelial inflammation in all vascular systems of the body. For example, smoking may even cause irritable bowel syndrome (IBS) and its consequences including chronic gastritis, hemorrhoids, and urolithiasis by means of several underlying mechanisms [29]. First of all, 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 the symptoms and components of the IBS including loose stool, diarrhea, constipation, and urolithiasis. Secondly, diarrheal losses-induced urinary changes may even cause urolithiasis [30-32]. Thirdly, smoking-induced sympathetic nervous system activation may cause motility disorders in the gastrointestinal and genitourinary tracts. Finally, immunosuppression secondary to smoking-induced vascular endothelial inflammation may even terminate with gastrointestinal and genitourinary tract infections causing loose stool, diarrhea, and urolithiasis since some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits in the urine. In fact, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infections with bacteria those have the urease. Similarly, urolithiasis was detected in 17.9% of patients with the IBS, whereas this ratio was just 11.6% in cases without the IBS ($p < 0.01$) [30].

An acute phase response develops in case of infection, infarction, foreign body, autoimmune disorder, allergy, neoplasm, trauma, and burn-like stresses of the body. Certain mediators known as acute phase reactants (APR) are increased or decreased during the acute phase response [33,34]. These mediators are usually used in the clinical practice as indicators of acute inflammation in the body. The

terms of acute phase proteins and APR are generally used synonymously, although some APR are polypeptides rather than proteins. Plasma concentrations of the positive and negative APR increase or decrease during the acute phase response, respectively. The acute phase response is predominantly mediated by the pro-inflammatory cytokines including TNF-alpha, interleukin (IL)-1, and IL-6 secreted by immune cells. In case of inflammation, infection, and tissue damage, neutrophil and macrophages release such cytokines into the blood. The liver and some other organs respond to the cytokines by producing several positive APR. Some of the well-known positive APR are ESR, CRP, fibrinogen, ferritin, procalcitonin, hepcidin, haptoglobin, ceruloplasmin, complement proteins, and serum amyloid A. CRP is responsible for activation of the complement pathway. Serum CRP rises rapidly, with a maximal concentration reached within two days, and falls quickly once the inflammation was resolved. Measurement of CRP is a useful indicator of the inflammation in the body. It correlates with ESR, but not always sensitively. Its reason is that ESR is largely dependent upon elevation of fibrinogen with a half-life of one week, approximately. So ESR remains higher for a longer period of time despite the removal of inflammatory or infectious stimulus in the body. Whereas CRP rises with a half-life of 6-8 hours rapidly, and then returns to normal in case of a successful treatment, quickly. On the other hand, productions of the negative APR are suppressed at the same time. Some of the well-known negative APR are albumin, transferrin, retinol-binding protein, antithrombin, transcortin, alpha-fetoprotein, and hemoglobin. The suppression of such negative APR is also used as an indicator of inflammations in the body. Suppression of the synthesis of such negative APR may actually be to protect the amino acids required for the production of positive APR, sufficiently. As also shown in the above study [26], production of HDL may also be suppressed in the liver during the acute phase responses [35]. Similarly, plasma triglycerides, DM, and CHD were higher in patients with plasma HDL values of lower than 40 mg/dL, significantly [35]. So, HDL may actually behave as negative and triglycerides behave as 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 [9]. Additionally, plasma triglycerides increased whereas HDL decreased during infections [36]. On the other hand, a 10 mg/dL increase of plasma LDL values was associated with a 3% lower risk of hemorrhagic stroke in another study [37]. Similarly, the highest prevalences of HT and DM parallel to the increased values of LDL and HDL, and the highest prevalences 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 [38]. 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 [9]. The increased plasma LDL values, parallel to triglycerides, ESR, and CRP, may also be an indicator of the low-grade nature of smoking-induced inflammation in the above study [26]. Since if the smoking-induced inflammation has been severe enough, plasma LDL values had been suppressed, too. In other words, HDL and FPG may be more sensitive than LDL for suppression in the acute phase response.

Lower HDL values should alert medical professionals about searching of additional inflammatory pathologies in human being [39-41]. Normally, HDL may show various anti-atherogenic properties including reverse cholesterol transport and anti-oxidative and anti-inflammatory properties [40]. However, HDL may become 'dysfunctional' in pathologic conditions in which relative compositions of lipid and proteins, as well as the enzymatic activities of HDL are altered [40]. For example, properties of HDL are compromised in patients with DM via the oxidative modification, glycation, or transformation of HDL proteomes into proinflammatory proteins. Additionally, the drugs increasing HDL values in the plasma such as niacin, fibrates, and cholesteryl ester transfer protein inhibitors did not reduce all cause mortality, mortality of CHD, myocardial infarction, and stroke [42]. In other words, HDL may just be indicators instead of being the main actors of the human 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 [43]. Similar to the above study [26], FPG and HDL were also suppressed in the sickle cell diseases (SCD), probably due to the severe inflammatory nature of such diseases [44]. Smoking may reduce HDL via the systemic inflammatory effects on vascular endothelium. On the other hand, plasma triglycerides are the only lipids those behave as only positive APR, and they are not suppressed in pathological weight losses [45]. For example, plasma triglycerides were even increased in contrast to the suppressed body weight and BMI in the SCD [45]. Similarly, prevalences of excess weight, DM, HT, and smoking were all higher in the hypertriglyceridemia group (200 mg/dL and higher) [46]. On the other hand, the greatest number of deteriorations in the metabolic parameters was observed just above the plasma triglycerides value of 60 mg/dL [47].

Conclusion

As a conclusion, prevalences of smoking were similar in the normal weight, overweight, and obesity groups, although the absence of any significant difference according to the mean age and gender distribution between the groups. On the other hand, prevalences of HT, DM, and dyslipidemia increased gradually and significantly from the normal weight towards the overweight and obesity groups.

Bibliography

1. Helvaci MR., *et al*. "The safest value of plasma triglycerides". *World Family Medicine Journal* 17.7 (2019): 22-27.
2. Helvaci MR., *et al*. "Smoking-induced endothelial damage may increase plasma triglycerides". *World Family Medicine Journal* 17.9 (2019): 37-42.
3. Helvaci MR., *et al*. "Triglycerides may behave as acute phase reactants in the plasma". *World Family Medicine Journal* 17.11 (2019): 28-33.
4. Helvaci MR., *et al*. "White coat hypertension may be an initial sign of metabolic syndrome". *Acta Medica Indonesiana* 44.3 (2012): 222-227.
5. Helvaci MR., *et al*. "Aging syndrome". *World Family Medicine Journal* 15.3 (2017): 39-42.
6. 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* 106.25 (2002): 3143-3421.
7. O'Brien E., *et al*. "European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement". *Journal of Hypertension* 21.5 (2003): 821-848.
8. Helvaci MR and Seyhanli M. "What a high prevalence of white coat hypertension in society!" *Internal Medicine* 45.10 (2006): 671-674.
9. Helvaci MR., *et al*. "The most desired values of high and low density lipoproteins and triglycerides in the plasma". *World Family Medicine Journal* 18.8 (2020): 21-27.
10. Calle EE., *et al*. "Body-mass index and mortality in a prospective cohort of U.S. adults". *The New England Journal of Medicine* 341.15 (1999): 1097-1105.
11. Helvaci MR., *et al*. "Metabolic deterioration just after infancy". *The Middle East Journal of Internal Medicine* 6.4 (2013): 26-30.
12. Helvaci MR., *et al*. "Prevalence of white coat hypertension in underweight and overweight subjects". *International Heart Journal* 48.5 (2007): 605-613.
13. Helvaci MR., *et al*. "What is the relationship between white coat hypertension and dyslipidemia?" *International Heart Journal* 49.1 (2008): 87-93.
14. Helvaci MR., *et al*. "White coat hypertension in definition of metabolic syndrome". *International Heart Journal* 49.4 (2008): 449-457.
15. Helvaci MR., *et al*. "Treatment of white coat hypertension with metformin". *International Heart Journal* 49.6 (2008): 671-679.
16. Helvaci MR., *et al*. "Atherosclerotic effects of smoking and excess weight". *Journal of Obesity and Weight Loss Therapy* 2 (2012): 145.
17. Helvaci MR., *et al*. "Physical inactivity or an excessive eating habit". *Middle East Journal of Nursing* 12.1 (2018): 14-18.

18. Funahashi T., *et al*. "Role of adipocytokines on the pathogenesis of atherosclerosis in visceral obesity". *Internal Medicine* 38.2 (1999): 202-206.

19. Fodor JG., *et al*. "Do we diagnose and treat coronary heart disease differently in men and women?" *Wiener Medizinische Wochenschrift* 154.17-18 (2004): 423-425.

20. Grunberg NE., *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 Psychology* 11 (1992): 4-9.

21. Walker JF., *et al*. "The effect of smoking on energy expenditure and plasma catecholamine and nicotine levels during light physical activity". *Nicotine and Tobacco Research* 1.4 (1999): 365-370.

22. Hughes JR and Hatsukami DK. "Effects of three doses of transdermal nicotine on post-cessation eating, hunger and weight". *Journal of Substance Abuse Treatment* 9 (1997): 151-159.

23. Miyata G., *et al*. "Nicotine alters the usual reciprocity between meal size and meal number in female rat". *Physiology and Behavior* 74.1-2 (2001): 169-176.

24. Laaksonen M., *et al*. "Smoking status and relative weight by educational level in Finland, 1978-1995". *Preventive Medicine* 27.3 (1998): 431-437.

25. Froom P., *et al*. "Smoking cessation and weight gain". *The Journal of Family Practice* 46.6 (1998): 460-464.

26. Helvaci MR., *et al*. "Smoking may not have a long term effect on body weight". *World Family Medicine Journal* (2020).

27. Helvaci MR., *et al*. "Gender differences in coronary heart disease in Turkey". *Journal of Pakistan Medical Association* 28.1 (2012): 40-44.

28. Prescott E., *et al*. "Smoking and risk of myocardial infarction in women and men: longitudinal population study". *British Medical Journal* 316.7137 (1998): 1043-1047.

29. Helvaci MR., *et al*. "Smoking may even cause irritable bowel syndrome". *World Family Medicine Journal* 17.3 (2019): 28-33.

30. Helvaci MR., *et al*. "Irritable bowel syndrome is a multisystemic inflammatory disorder". *Advanced Research in Gastroenterology and Hepatology (ARGH)* 18.4 (2022): 555992.

31. Helvaci MR., *et al*. "A physiologic events' cascade, irritable bowel syndrome, may even terminate with urolithiasis". *Journal of Health Science* 52.4 (2006): 478-481.

32. Helvaci MR., *et al*. "Irritable bowel syndrome and chronic gastritis, hemorrhoid, urolithiasis". *The Eurasian Journal of Medicine* 41.3 (2009): 158-161.

33. Gabay C and Kushner I. "Acute-phase proteins and other systemic responses to inflammation". *The New England Journal of Medicine* 340.6 (1999): 448-454.

34. Wool GD and Reardon CA. "The influence of acute phase proteins on murine atherosclerosis". *Current Drug Targets* 8.11 (2007): 1203-1214.

35. Helvaci MR., *et al*. "High and low density lipoproteins may be negative acute phase proteins of the metabolic syndrome". *Middle East Journal of Nursing* 14.1 (2020): 10-16.

36. Pirillo A., *et al*. "HDL in infectious diseases and sepsis". *The Handbook of Experimental Pharmacology* 224 (2015): 483-508.

37. Ma C., *et al*. "Low-density lipoprotein cholesterol and risk of hemorrhagic stroke: a systematic review and dose-response meta-analysis of prospective studies". *Current Atherosclerosis Reports* 21.12 (2019): 52.

38. Helvaci MR., *et al*. "The safest values of low density lipoproteins in the plasma". *World Family Medicine Journal* 18.4 (2020): 18-24.

39. Toth PP. "Cardiology patient page. The "good cholesterol": high-density lipoprotein". *Circulation* 111.5 (2005): 89-91.

40. Femlak M., *et al*. "The role and function of HDL in patients with diabetes mellitus and the related cardiovascular risk". *Lipids in Health and Disease* 16.1 (2017): 207.

41. Ertek S. "High-density lipoprotein (HDL) dysfunction and the future of HDL". *Current Vascular Pharmacology* 16.5 (2018): 490-498.

42. Keene D., *et al*. "Effect on cardiovascular risk of high density lipoprotein targeted drug treatments niacin, fibrates, and CETP inhibitors: meta-analysis of randomised controlled trials including 117,411 patients". *British Medical Journal* 349 (2014): 4379.

43. Helvaci MR., *et al*. "What a low prevalence of diabetes mellitus between the most desired values of high density lipoproteins in the plasma". *World Family Medicine Journal* 18.7 (2020): 25-31.

44. Helvaci MR., *et al*. "Positive and negative acute phase reactants in sickle cell diseases". *World Family Medicine Journal* 20.3 (2022): 36-42.

45. Helvaci MR., *et al*. "Cholesterol may be a negative whereas triglycerides positive acute phase reactants in the plasma". *Asclepius Medical Research and Reviews* 4.1 (2021): 1-8.

46. Helvaci MR., *et al*. "What is the relationship between hypertriglyceridemia and smoking?" *The Middle East Journal of Age and Ageing* 8.6 (2011).

47. Helvaci MR., *et al*. "The safest upper limit of triglycerides in the plasma". *World Family Medicine Journal* 18.1 (2020): 16-22.

Volume 6 Issue 2 February 2023
© All rights reserved by Mehmet Rami Helvaci*., et al.*