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FROM THE EDITOR



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This is the last issue this year that has papers from Turkey, Nepal, Libya, Australia and Lebanon

Paudel S et al, conducted a cross-sectional study was conducted in School of Nursing and Midwifery at Patan Academy of Health Sciences, Lalitpur, Nepal. A total of 331 nursing students participated in the study. HPLP behavior was evaluated using Walker's Health Promoting Lifestyle Profile (HPLP). Data were analyzed using independent t-test and analysis of variance test by SPSS Version 16 package with significance level of $p < 0.05$. The mean age of the participants was 22.86 ± 5.80 years (range 16 - 54). The BMI of respondents revealed that 69.8% had normal weight, 15.4% underweight and 14.8% overweight. The mean of the total health promoting behaviors were 2.74 ± 0.41 out of a score of four. The HPLP score of Bachelor of Nursing (BN) was

highest (2.83 ± 0.49), whereas it was lowest (2.70 ± 0.37) for the Proficiency Certificate Level (PCL) Nursing. Out of six sub categories of HPLP, Spiritual Growth (3.05 ± 0.49) and Interpersonal Relationship (3.04 ± 0.56) showed high scorers, while Physical Activities (2.32 ± 0.60) and Nutrition (2.58 ± 0.49) had low scorers throughout the all the level of students. The authors concluded that the physical activity and nutrition level of students was inadequate in general among all. It was expected that nurse would show more health-promoting behaviors than the general public. The hectic schedule of academic work as well as their societal orientation about life and living might have contributed toward such divergence. Low exercise score indicated the need for intervention programs for the nurses.

Mehmet R. H et al tried to understand whether or not smoking-induced endothelial injury triggers plasma triglycerides. Patients with plasma triglycerides lower than 60 mg/dL were put into the first, lower than 100 mg/dL into the second, lower than 150 mg/dL into the third, lower than 200 mg/dL into the fourth, and 200 mg/dL or greater into the fifth groups, respectively. The study included 875 cases (370 males). Although the mean age increased just up to plasma triglycerides value of 200 mg/dL, male ratio and smoking increased parallel to increased plasma triglycerides values, continuously. Interestingly, the most significant increase of smoking was seen just after plasma triglycerides value of 200 mg/dL, and there was no significant effect of aging or excess weight on this step. The authors concluded that plasma triglycerides may behave as acute phase reactants indicating disseminated endothelial injury and atherosclerosis. There may be significant associations between male gender, smoking, aging, excess weight, and plasma triglycerides values. FPG, LDL, WCH, HT, DM, COPD, CHD, and CRD were all deteriorated parallel to the increased male ratio, smoking, mean age, BMI, and plasma triglycerides values.

A paper from Libya looked at the skin humiliation/ degrading/ trauma/ disturbance.

Skin- is our protective layer against the eternal world, and our reflective mirror. It is basically the biggest organ of our body, and yet still being humiliated, manipulated, and degraded by different styles and tools application. There are certain practices which are harmful to the skin and pose risks as a whole and generally speaking. Some would think it is merely a decoration to the skin; however, some people went too far and pierced it, painted it, tattooed it, just to stand out as an ornament. Sometimes, you would only perceive a tiny island of a normal skin within different coloured paints of different massive forms. The authors suggested however; an alternative way, henna tattoo, cheap, easy to apply and it fades out in few days. It can be designed in different forms to the different taste as well as the likings in different places. Additionally, we tend to like changes across the time.

To conclude, it is wise to think carefully before having such colourful patterns on the skin, in different parts of the body. It would make sense, considering a job in the future, whereby many official jobs won't accept such a thing until a tattoo has been removed or made invisible.

A paper from Australia looks at the issues of Nursing and Climate Change. Climate Change brings many challenges for Nursing Staff and Carers generally as it will exacerbate problems of human health particularly in the elderly and those with chronic disease.

Nurses globally have also rallied politically to stress the need for a healthy environment to avoid the health consequences of climate change and its direct effect on health along with increased numbers of natural disasters such as floods, fires, famines and hurricanes.

A position statement was announced by Annette Kennedy, ICN President at the International Council of Nurses (ICN) Regional Conference in Abu Dhabi. As the global voice of nursing, ICN's position is that nurses have a shared responsibility to sustain and protect the natural environment from depletion, pollution, degradation and destruction."

LOW DENSITY LIPOPROTEINS ACT AS NEGATIVE ACUTE PHASE PROTEINS IN THE METABOLIC SYNDROME

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Abstract

Background: We tried to understand whether or not low density lipoproteins (LDL) act as negative acute phase proteins (APP) in the metabolic syndrome.

Methods: Patients with plasma triglycerides values lower than 60 mg/dL were collected into the first, lower than 100 mg/dL into the second, lower than 150 mg/dL into the third, lower than 200 mg/dL into the fourth, and 200 mg/dL and greater into the fifth groups, respectively.

Results: The study included 875 cases (370 males and 505 females), totally. Although the mean age, male ratio, smoking, body mass index (BMI), fasting plasma glucose (FPG), white coat hypertension (WCH), hypertension (HT), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), and chronic renal disease (CRD) increased parallel to the increased plasma triglycerides values, continuously ($p < 0.05$ nearly in all steps), the mean LDL values increased just up to plasma triglycerides values of 200 mg/dL, but then decreased, significantly (137.5 versus 129.0 mg/dL, $p = 0.020$).

Conclusions: The increased plasma triglycerides values may be one of the most sensitive parameters of the metabolic syndrome that is characterized with disseminated endothelial damage, inflammation, fibrosis, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. Although the mean age, male ratio, smoking, BMI, FPG, WCH, HT, DM, COPD, CHD, and CRD increased parallel to the increased plasma triglycerides values, continuously, LDL was the only metabolic parameter that increased just up to the plasma triglycerides values of 200 mg/dL but then decreased, significantly. So LDL acts as negative APP in the metabolic syndrome.

Key words: Low density lipoproteins, triglycerides, acute phase proteins, metabolic syndrome

Introduction

Chronic endothelial damage may be the most common sort of vasculitis, and the leading cause of early aging and premature death in the human being (1-4). Much higher blood pressure (BP) of the afferent vasculature may be the major underlying mechanism by inducing recurrent injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are predominantly involved in the process. Therefore the term of venosclerosis is not as famous as atherosclerosis in the medical literature. Because of the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic nature which reduces blood flow to terminal organs, and increases 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), rheumatologic disorders, chronic infections, and cancers for the development of terminal endpoints including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, early aging, and premature death (5-10). Although early withdrawal of the predisposing factors may delay terminal consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, and aging, endothelial changes cannot be reversed completely due to their fibrotic nature. Up to now, the predisposing factors and terminal endpoints were researched under the titles of metabolic syndrome, aging syndrome, or accelerated endothelial damage syndrome in the medicine, extensively (11-14). Although its normal limits could not be determined clearly yet, increased plasma triglycerides may be one of the most sensitive parameters of the metabolic syndrome (15-17). Due to the growing evidence 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 (18, 19). Although ATP II determined the normal plasma triglycerides value as lower than 200 mg/dL in 1994 (19), World Health Organisation in 1999 (20) and ATP III in 2001 reduced their normal limit as lower than 150 mg/dL (18). Although these cutpoints are usually used to define limits of the metabolic syndrome, there are still suspicions about the safest value of plasma triglycerides in the medical literature (16, 17). Though the absolute sensitivity of plasma triglycerides in the metabolic syndrome, role of low density lipoproteins (LDL) is suspicious (21). We tried to understand whether or not LDL act as negative acute phase proteins (APP) in the metabolic syndrome.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients at and above the age of 15 years were included. Their medical histories including HT, DM, COPD, and already used medications were learned, and a routine check up procedure including fasting plasma glucose (FPG), triglycerides, and 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 (22, 23). 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 (18). Cases with an overnight FPG value of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics (18). 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 (18). CRD is diagnosed with a persistently elevated serum creatinine level of 1.3 mg/dL in males and 1.2 mg/dL in females. 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 (24). 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 (24). An exercise electrocardiogram is performed just in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken just for the exercise electrocardiogram positive cases. So CHD is diagnosed either angiographically or with the Doppler echocardiographic findings as the already developed movement disorders in the cardiac walls. 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% (25). Eventually, patients with plasma triglycerides values 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 and higher into the fourth groups, respectively. The male ratio, mean age, BMI, FPG, triglycerides, and LDL, and prevalence

of smoking, WCH, HT, DM, COPD, CHD, and CRD 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 875 cases (370 males and 505 females), totally. Although the mean age, male ratio, smoking, BMI, FPG, WCH, HT, DM, COPD, CHD, and CRD increased parallel to the increased triglycerides values, continuously ($p < 0.05$ nearly in all steps), the mean LDL values increased just up to plasma triglycerides values of 200 mg/dL but then decreased, significantly (137.5 versus 129.0 mg/dL, $p = 0.020$) (Table 1 - next page).

Discussion

Excess weight may lead to both structural and functional abnormalities of many organs of the body. Adipose tissues produce leptin, tumor necrosis factor- α , plasminogen activator inhibitor-1, and adiponectin-like cytokines acting as acute phase reactants in the plasma (26, 27). Excess weight-induced chronic low-grade vascular endothelial inflammation may play a significant role in the pathogenesis of accelerated atherosclerosis in the whole 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 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. Combination of these cardiovascular risk factors will eventually terminate with increased left ventricular stroke work and risks of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the prevalence of CHD and stroke increased parallel to the increased BMI values in the other studies (28, 29), and risk of death from all causes including cancers increased throughout the range of moderate to severe weight excess in all age groups (30). The relationship between excess weight, elevated BP, and plasma triglycerides is described in the metabolic syndrome (15), and clinical manifestations of the syndrome include obesity, dyslipidemia, HT, insulin resistance, and proinflammatory and prothrombotic states (13). 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 the other study (31). On the other hand, the prevalence of increased LDL cases were similar both in the hypertriglyceridemia (200 mg/dL and higher) and control groups (18.9% versus 16.3%, $p > 0.05$, respectively) in the above study (31). Similarly, plasma LDL values increased just up to the plasma triglycerides values of 200 mg/dL but then decreased significantly in the present study, too ($p < 0.05$ for all).

Smoking may be found among one of the most common causes of vasculitis all over the world. It causes a chronic inflammatory process on the vascular endothelium, probably depending on the concentration of smoke that terminates with an accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. Therefore smoking has to be included among the major components of the metabolic syndrome. Strong and terminal atherosclerotic effects of smoking are the most obviously seen in Buerger's disease (thromboangiitis obliterans). It 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. Although the well-known strong atherosclerotic effects of smoking, smoking in the human being and nicotine administration in animals may be associated with decreased BMI values (32). Evidence revealed an increased energy expenditure during smoking both on rest and light physical activity (33), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (34). According to an animal study, nicotine may lengthen intermeal time and decrease amount of meal eaten (35). Additionally, the mean BMI seems to be the highest in the former, the lowest in the current and medium in never smokers (36). Smoking may be associated with a postcessation weight gain (37). Similarly, although 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 (38). The result may show both the strong atherosclerotic and weight decreasing roles of smoking (39). Similarly, the incidence of a myocardial infarction is increased six-fold in women and three-fold in men who smoke 20 cigarettes per day (40). In another definition, smoking may be more dangerous for women probably due to the associated higher BMI and its consequences in them. Parallel to the above results, the proportion of smokers is consistently higher in men in the literature (23). So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite. Smoking-induced weight loss may be related with the smoking-induced chronic vascular endothelial inflammation all over the body, since loss of appetite is one of the main symptoms of the disseminated inflammations in the body. Physicians can even understand healing of the 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 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 (34-36). After smoking cessation, normal appetite comes back with a prominent weight gain but the returned weight is the patients' physiological weight, actually.

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

Variable	Lower than 60 mg/dL	p- value	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 of cases	84		207		235		148		201
Age (year)	<u>35.6 ± 16.4</u> (17-79)	<u>0.000</u>	<u>43.6 ± 17.5</u> (16-83)	<u>0.009</u>	<u>47.7 ± 15.3</u> (16-82)	<u>0.018</u>	<u>51.2 ± 12.6</u> (19-82)	Ns*	<u>49.8 ± 12.3</u> (19-88)
Male ratio	<u>30.9%</u>	<u>0.05></u>	<u>39.1%</u>	Ns	<u>40.4%</u>	Ns	<u>43.9%</u>	<u>0.05></u>	<u>51.2%</u>
Smoking	<u>16.6%</u>	Ns	<u>21.7%</u>	Ns	<u>26.3%</u>	Ns	<u>23.6%</u>	<u>0.001></u>	<u>38.3%</u>
BMI† (kg/m²)	<u>24.6 ± 5.3</u> (16.7-45.9)	<u>0.002</u>	<u>27.1 ± 5.9</u> (16.7-49.3)	<u>0.000</u>	<u>29.4 ± 6.1</u> (18.4-51.0)	Ns	<u>29.9 ± 4.8</u> (19.2-49.0)	Ns	<u>30.0 ± 5.0</u> (21.0-51.1)
FPG‡ (mg/dL)	<u>96.5 ± 35.3</u> (71-377)	<u>0.016</u>	<u>106.6 ± 48.7</u> (59-400)	Ns	<u>106.8 ± 35.1</u> (71-335)	<u>0.006</u>	<u>117.3 ± 47.8</u> (68-386)	Ns	<u>124.3 ± 55.3</u> (74-392)
Triglyceride (mg/dL)	<u>51.0 ± 7.5</u> (27-59)	<u>0.000</u>	<u>78.3 ± 10.8</u> (60-99)	<u>0.000</u>	<u>122.2 ± 14.5</u> (100-149)	<u>0.000</u>	<u>174.1 ± 14.2</u> (150-199)	<u>0.000</u>	<u>325.8 ± 160.4</u> (200-1,350)
LDL§ (mg/dL)	<u>98.6 ± 23.3</u> (56-161)	<u>0.000</u>	<u>114.6 ± 33.0</u> (31-269)	<u>0.000</u>	<u>131.1 ± 31.7</u> (56-228)	<u>0.033</u>	<u>137.5 ± 32.4</u> (50-237)	<u>0.020</u>	<u>129.0 ± 40.8</u> (10-239)
WCH	<u>17.8%</u>	<u>0.05></u>	<u>24.1%</u>	<u>0.05></u>	<u>31.0%</u>	Ns	<u>35.1%</u>	Ns	32.3%
HT**	<u>8.3%</u>	<u>0.001></u>	<u>15.9%</u>	<u>0.05></u>	<u>21.2%</u>	Ns	<u>22.2%</u>	Ns	<u>26.3%</u>
DM***	<u>2.3%</u>	<u>0.001></u>	<u>11.1%</u>	Ns	<u>13.6%</u>	Ns	<u>18.2%</u>	<u>0.05></u>	<u>24.3%</u>
COPD****	<u>4.7%</u>	<u>0.01></u>	<u>9.1%</u>	<u>0.01></u>	<u>14.0%</u>	Ns	12.8%	<u>0.05></u>	<u>18.4%</u>
CHD*****	<u>4.7%</u>	<u>0.001></u>	<u>10.1%</u>	Ns	<u>11.4%</u>	Ns	<u>14.8%</u>	Ns	11.9%
CRD*****	0.0%	Ns	1.9%	Ns	<u>0.4%</u>	<u>0.01></u>	<u>2.0%</u>	<u>0.01></u>	<u>4.9%</u>

*Nonsignificant (p>0.05) †Body mass index ‡Fasting plasma glucose §Low density lipoproteins

||White coat hypertension **Hypertension ***Diabetes mellitus ****Chronic obstructive pulmonary disease

*****Coronary heart disease *****Chronic renal disease

Although the several negative effects of excess weight on health, nearly three-quarters of cases above the age of 30 years have excess weight (41). The prevalence of excess weight increases by decades, particularly after the third decade, up to the eighth decade of life (41). So 30th and 70th 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 and 150 mg/dL, respectively here. So smoking remained as the solitary 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 (18), much lower limits may provide additional benefit for health (16, 17). 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 metabolic syndrome. The mean age, male ratio, smoking, BMI, FPG, WCH, HT, DM, COPD, CHD, and CRD increased parallel to the plasma triglycerides values from the first towards the fifth groups, continuously. In our opinion, significantly increased plasma triglycerides values by aging may be secondary to aging-induced decreased physical and mental stresses; those eventually terminate with onset of excess weight and many associated health problems. Interestingly, the mean age increased just up to the plasma triglycerides values of 200 mg/dL in the present study. Similarly, the mean BMI values increased just up to the plasma triglycerides values of 150 mg/dL, significantly. These trends may be due to the fact that although the borderline high triglycerides values (150-199 mg/dL) is 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 (18). 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, COPD, and CRD were the highest in the highest triglycerides having group in the present study. Eventually, although some authors reported that lipid assessment can be simplified as the measurements of total cholesterol and high density lipoproteins (HDL) values alone (42), the present study and most of the others indicated significant relationships between plasma triglycerides and LDL values and terminal consequences of the metabolic syndrome (43).

APP are a class of proteins whose plasma concentrations increase (positive APP) or decrease (negative APP) as a response to inflammation, infection, and tissue damage (44-46). In case of inflammation, infection, and tissue damage, local inflammatory cells (neutrophils and macrophages) secrete several kinds of cytokines into the blood, most notable of which are the interleukins. The liver responds by producing many positive APP. At the same time, production of many proteins is reduced. Therefore these proteins are called negative APP. Some of the well-known negative APP are albumin, transferrin, retinol-binding protein, antithrombin, and transcortin. The decrease of such proteins is also used as an indicator of inflammation. The physiological role of decreased synthesis of such proteins is generally to save amino acids for producing positive APP more effectively. Due to the decreased production of some proteins in liver during severe inflammatory conditions, production of LDL may also be suppressed. Similarly, although the mean triglycerides, fibrinogen, C-reactive protein, and glucose values were significantly higher in cases with ischemic stroke, the oxidized LDL values did not correlate with age, stroke severity, and outcome in the other study (47). Additionally, significant alterations occur in lipid metabolism and lipoprotein composition during infections, and triglycerides increase whereas HDL and LDL decrease in another study (48). Furthermore, a 10 mg/dL increase of LDL was associated with a 3% lower risk of hemorrhagic stroke in another study (49).

As a conclusion, increased plasma triglycerides values may be one of the most sensitive parameters of the metabolic syndrome that is characterized with disseminated endothelial damage, inflammation, fibrosis, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. Although the mean age, male ratio, smoking, BMI, FPG, WCH, HT, DM, COPD, CHD, and CRD increased parallel to the increased plasma triglycerides values, continuously, LDL was the only metabolic parameter that increased just up to the plasma triglycerides values of 200 mg/dL but then decreased, significantly. So LDL act as negative APP in the metabolic syndrome.

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HIGH AND LOW DENSITY LIPOPROTEINS MAY BE NEGATIVE ACUTE PHASE PROTEINS OF THE METABOLIC SYNDROME

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Abstract

Background: We tried to understand whether or not high density lipoproteins (HDL) and low density lipoproteins (LDL) may be negative acute phase proteins (APP) of the metabolic syndrome.

Methods: Patients with plasma HDL values lower than 40 mg/dL were collected into the first group, and then age and gender matched patients with plasma HDL values 40 mg/dL and greater were collected into the second group, and compared in between.

Results: There were 75 patients in the first and 118 patients in the second groups. Smoking (34.6 versus 31.3%), body mass index (BMI) (27.2 versus 26.7 kg/m²), fasting plasma glucose (119.4 versus 113.0 mg/dL), white coat hypertension (25.3 versus 32.2%), hypertension (10.6 versus 16.1%), and chronic obstructive pulmonary disease (14.6 versus 18.6%) were similar in both groups ($p > 0.05$ for all). Although triglycerides (162.7 versus 125.4 mg/dL, $p < 0.001$), diabetes mellitus (DM) (21.3 versus 12.7%, $p < 0.05$), and coronary heart disease (CHD) (20.0 versus 11.0%, $p < 0.05$) were higher, LDL (105.3 versus 126.2 mg/dL, $p < 0.000$) and HDL (34.1 versus 50.0 mg/dL, $p < 0.000$) were lower in patients with plasma HDL values lower than 40 mg/dL.

Conclusions: Although the similar mean age, gender distribution, smoking, and BMI in both groups, triglycerides, DM, and CHD were higher whereas LDL and HDL were lower in patients with plasma HDL values lower than 40 mg/dL. So HDL and LDL may be negative APP of the metabolic syndrome.

Key words: High density lipoproteins, low density lipoproteins, triglycerides, acute phase proteins, metabolic syndrome

Introduction

Chronic endothelial damage may be the most common kind of vasculitis, and the leading cause of early aging and premature death in the human being (1-4). Much higher blood pressure (BP) of the afferent vasculature may be the major underlying mechanism by inducing recurrent injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are predominantly involved in the process. Therefore the term of venosclerosis is not as famous as atherosclerosis in the medical literature. Because of the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic nature that reduces blood flow to terminal organs, and increases 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), rheumatologic disorders, chronic infections, and cancers for the development of terminal endpoints including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, early aging, and premature death (5-10). Although early withdrawal of the predisposing factors may delay terminal consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, and aging, endothelial changes cannot be reversed completely due to their fibrotic nature. Up to now, the predisposing factors and terminal endpoints were researched under the titles of metabolic syndrome, aging syndrome, or accelerated endothelial damage syndrome in the medicine, extensively (11-14). Although its normal limits have not been determined clearly yet, increased plasma triglycerides may be one of the most sensitive parameters of the metabolic syndrome (15-18). Due to the growing evidence 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 (19, 20). Although ATP II determined the normal plasma triglycerides value as lower than 200 mg/dL in 1994 (20), World Health Organisation in 1999 (21) and ATP III in 2001 reduced their normal limit as lower than 150 mg/dL (19). Although these cutpoints are usually used to define limits of the metabolic syndrome, there are still suspicions about the safest value of plasma triglycerides in the medical literature (16-18). Although the absolute sensitivity of plasma triglycerides in the metabolic syndrome, roles of high density lipoproteins (HDL) and low density lipoproteins (LDL) are suspicious (22). We tried to understand whether or not HDL and LDL may be negative acute phase proteins (APP) of the metabolic syndrome

the age of 15 years were included. Their medical histories including HT, DM, COPD, and already used medications were learned, and a routine check up procedure including fasting plasma glucose (FPG), HDL, LDL, and triglycerides was performed. Current daily smokers with six pack-months and cases with a history of three pack-years were accepted as smokers. Due to the very low prevalence of alcoholism in Turkey (23), we did not include regular alcohol intake into the study. 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 (24, 25). 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 (19). Cases with an overnight FPG value of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics (19). 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 (19). 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 (26). 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 (26). An exercise electrocardiogram is performed just in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken just for the exercise electrocardiogram positive cases. So CHD is diagnosed either angiographically or with the Doppler echocardiographic findings due to the already developed movement disorders in the cardiac walls. 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% (27). Eventually, patients with plasma HDL values lower than 40 mg/dL were collected into the first group, and then age and gender matched patients with plasma HDL values 40 mg/dL and greater were collected into the second group, respectively. Smoking, BMI, FPG, triglycerides, LDL, HDL, WCH, HT, DM, COPD, and CHD 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.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients at and above

Results

There were 75 patients in the first and 118 patients in the second groups. The mean age (45.4 versus 47.9 years) and male ratio (53.3 versus 53.3%) were similar in both groups ($p>0.05$ for both). Smoking (34.6 versus 31.3%), BMI (27.2 versus 26.7 kg/m²), FPG (119.4 versus 113.0 mg/dL), WCH (25.3 versus 32.2%), HT (10.6 versus 16.1%), and COPD (14.6 versus 18.6%) were similar in

both groups, too ($p>0.05$ for all). Although the mean triglycerides (162.7 versus 125.4 mg/dL, $p<0.001$), DM (21.3 versus 12.7%, $p<0.05$), and CHD (20.0 versus 11.0%, $p<0.05$) were higher, LDL (105.3 versus 126.2 mg/dL, $p<0.001$) and HDL (34.1 versus 50.0 mg/dL, $p<0.001$) were lower in patients with plasma HDL values lower than 40 mg/dL, significantly (Table 1).

Table 1: Characteristic features of the study cases according to the plasma high density lipoproteins values

Variable	Lower than 40 mg/dL	p-value	40 mg/dL and higher
Number of cases	75		118
Mean age (year)	45.4 ±15.2 (16-79)	Ns*	47.9 ±14.6 (19-77)
Male ratio	53.3%	Ns	53.3%
Smoking	34.6%	Ns	31.3%
BMI† (kg/m ²)	27.2 ±4.5 (18.4-39.9)	Ns	26.7 ±5.0 (17.8-42.4)
FPG‡ (mg/dL)	119.4 ±48.4 (76-287)	Ns	113.0 ±54.2 (63-400)
<u>Triglycerides (mg/dL)</u>	<u>162.7 ± 92.8 (43-470)</u>	<u><0.001</u>	<u>125.4 ± 73.2 (27-410)</u>
<u>LDL§ (mg/dL)</u>	<u>105.3 ± 33.1 (10-211)</u>	<u><0.000</u>	<u>126.2 ± 29.5 (54-202)</u>
<u>HDL (mg/dL)</u>	<u>34.1 ± 3.8 (22-39)</u>	<u><0.000</u>	<u>50.0 ± 9.1 (40-91)</u>
WCH**	25.3%	Ns	32.2%
HT***	10.6%	Ns	16.1%
<u>DM****</u>	<u>21.3%</u>	<u><0.05</u>	<u>12.7%</u>
COPD*****	14.6%	Ns	18.6%
<u>CHD*****</u>	<u>20.0%</u>	<u><0.05</u>	<u>11.0%</u>

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

Discussion

Excess weight may lead to both structural and functional abnormalities of many organs of the body. Adipose tissues produce leptin, tumor necrosis factor- α , plasminogen activator inhibitor-1, and adiponectin-like cytokines acting as acute phase reactants in the plasma (28, 29). Excess weight-induced chronic low-grade vascular endothelial inflammation may play a significant role in the pathogenesis of accelerated atherosclerosis in the whole 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 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. Combination of these cardiovascular risk factors will eventually terminate with increased left ventricular stroke work and risks of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the prevalence of CHD and stroke increased parallel to the increased BMI values in the other studies (30, 31), and risk of death from all causes including cancers increased throughout the range of moderate to severe weight excess in all age groups (32). The relationship between excess weight, elevated BP, and plasma triglycerides is described in the metabolic syndrome (15), and clinical manifestations of the syndrome include obesity, dyslipidemia, HT, insulin resistance, and proinflammatory and prothrombotic states (13). 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 the other study (33). On the other hand, the prevalence of increased LDL cases were similar both in the hypertriglyceridemia (200 mg/dL and higher) and control groups (18.9% versus 16.3%, $p > 0.05$, respectively) in the above study (33). Similarly, although the significantly higher triglycerides ($p < 0.001$), plasma LDL and HDL values were lower in cases with plasma HDL levels lower than 40 mg/dL in the present study ($p < 0.000$ for both).

Smoking may be found among one of the most common causes of vasculitis all over the world. It causes a chronic inflammatory process on the vascular endothelium, probably depending on the concentration of smoke that terminates with an accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. Therefore smoking has to be included among the major components of the metabolic syndrome. Strong and terminal atherosclerotic effects of smoking are the most obviously seen in the Buerger's disease (thromboangiitis obliterans). It 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. Although the well-known strong atherosclerotic effects of smoking, smoking in the human being and nicotine administration in animals may be associated with decreased BMI values (34). Evidence revealed an increased energy expenditure

during smoking both on rest and light physical activity (35), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (36). According to an animal study, nicotine may lengthen intermeal time and decrease amount of meal eaten (37). Additionally, the mean BMI seems to be the highest in the former, the lowest in the current and medium in never smokers (38). Smoking may be associated with a postcessation weight gain (39). Similarly, although CHD was detected with similar prevalences in both genders, prevalence of smoking and COPD were higher in males against the higher BMI, LDL, triglycerides, WCH, HT, and DM in females (40). Similarly, the incidence of a myocardial infarction is increased six-fold in women and three-fold in men who smoke 20 cigarettes per day (41). In another definition, smoking may be more dangerous for women probably due to the associated higher BMI and its consequences in them. Parallel to the above results, the proportion of smokers is consistently higher in men in the literature (25). So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite (42). Smoking-induced weight loss may be related with the smoking-induced chronic vascular endothelial inflammation all over the body, since loss of appetite is one of the major symptoms of the disseminated inflammations in the body. Physicians can even understand healing of the 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 (36-38). After smoking cessation, normal appetite comes back with a prominent weight gain but the returned weights are the patients' physiological weights, actually.

Although ATP III reduced the normal limit of plasma triglycerides as lower than 150 mg/dL in 2001 (19), much lower limits may provide additional benefit for health (16-18). In the above study (17), 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 metabolic syndrome. The mean age, male ratio, smoking, BMI, FPG, WCH, HT, DM, and COPD increased parallel to the plasma triglycerides values from the first towards the fifth groups, continuously (17). In our opinion, significantly increased plasma triglycerides values by aging may be secondary to aging-induced decreased physical and mental stresses, those eventually terminate with onset of excess weight and many associated health problems. Although the borderline high triglycerides values (150-199 mg/dL) is 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 (19). 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 above study (17). Eventually, although some authors reported that lipid assessment can be simplified as the measurements of total cholesterol and HDL values alone (43), the present study and most of the others indicated significant relationships between plasma triglycerides, HDL, and LDL values and terminal consequences of the metabolic syndrome (44).

Cholesterol, triglycerides, and phospholipids are the major lipids of the body. Cholesterol is an essential structural component of animal cell membrane, bile acids, adrenal and gonadal steroid hormones, and vitamin D. Triglycerides are fatty acid esters of glycerol, and they are the major lipids transported in the blood. The bulk of our body's fat tissue is in the form of triglycerides. Phospholipids are triglycerides that are covalently bound to a phosphate group. Phospholipids regulate membrane permeability, remove cholesterol from the body, provide signal transmission across the membranes, act as detergents, and help in solubilization of cholesterol. Cholesterol, triglycerides, and phospholipids do not circulate freely in the plasma, instead they are bound to proteins, and transported as lipoproteins. There are five major classes of lipoproteins including chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), LDL, and HDL. Chylomicrons carry exogenous triglycerides from intestine to liver via the thoracic duct. VLDL are produced in liver, and carry endogenous triglycerides from the liver to the peripheral organs including adipocytes and muscle tissue. In the capillaries of adipocytes and muscle tissue, 90% of triglycerides is removed by a specific group of lipases. So VLDL are converted into IDL by removal of triglycerides. Then IDL are degraded into LDL by removal of more triglycerides. So VLDL are the main source of LDL in the plasma. LDL deliver cholesterol from the liver to the parts of body. Although the liver removes majority of LDL from the circulation, a small amount is uptaken by scavenger receptors on macrophages that may migrate into arterial walls, where they become the foam cells of atherosclerotic plaques. HDL removes fats and cholesterol from cells, including within artery wall atheroma, and carry the cholesterol back to the liver and steroidogenic organs such as adrenals, ovaries, and testes for excretion, re-utilization, and disposal. All of the carrier lipoproteins in the plasma are under dynamic metabolic control, and are readily affected by diet, illnesses, drugs, and BMI. Thus lipid analysis should be performed during a steady state. But the metabolic syndrome alone is an abnormal condition with a low grade inflammatory process on vascular endothelium all over the body. Thus the metabolic syndrome alone may be a cause of abnormal lipoproteins levels in the plasma. On the other hand, although HDL are commonly called as 'the good cholesterol' due to their

roles in removing excess cholesterol from the blood and protecting the arterial walls against atherosclerosis (45), recent studies did not show similar results, and low plasma HDL levels may alert searching of additional metabolic and inflammatory pathologies in the body (46-48). Normally, HDL may show various anti-atherogenic properties including reverse cholesterol transport and anti-oxidative and anti-inflammatory features (46). However, HDL may become 'dysfunctional' in pathological conditions which means that relative composition of lipids and proteins, as well as the enzymatic activities of HDL are altered (46). For instance, properties of HDL are compromised in patients with DM due to the oxidative modification and glycation of HDL, as well as the transformation of HDL proteomes into proinflammatory proteins. Additionally, neither niacin, fibrates, nor cholesteryl ester transfer protein inhibitors, three highly effective agents about increasing HDL levels, reduced all cause mortality, CHD mortality, myocardial infarction, or stroke in patients treated with statins (49). While higher HDL levels are correlated with cardiovascular health, no medication used to increase HDL has been proven to improve health (49). In other words, while high HDL levels may correlate with better cardiovascular health, specifically increasing one's HDL may not increase cardiovascular health (49). So they may actually be just indicators instead of the main actors of the process. Beside that, HDL particles that bear apolipoprotein C3 are associated with increased, rather than decreased, risk for CHD (50). Similarly, although the similar mean age, gender distribution, smoking, and BMI in both groups, DM and CHD were significantly higher in patients with plasma HDL values lower than 40 mg/dL in the present study.

APP are a class of proteins whose plasma concentrations increase (positive APP) or decrease (negative APP) as a response to inflammation, infection, and tissue damage (51-53). In case of inflammation, infection, and tissue damage, local inflammatory cells (neutrophils and macrophages) secrete several kinds of cytokines into the blood, most notable of which are the interleukins. The liver responds by producing many positive APP. At the same time, productions of many proteins are reduced. Therefore these proteins are called as negative APP. Some of the well-known negative APP are albumin, transferrin, retinol-binding protein, antithrombin, and transcortin. The decrease of such proteins is also used as an indicator of inflammation. The physiological role of decreased synthesis of such proteins is generally to save amino acids for producing positive APP, effectively. Due to the decreased production of some proteins in liver during severe inflammatory conditions, production of HDL and LDL may also be suppressed. By this way, although the similar mean age, gender distribution, smoking, and BMI in both groups, the higher triglycerides, DM, and CHD against the lower HDL and LDL values in patients with plasma HDL values lower than 40 mg/dL can be explained in the present study. Similarly, although the mean triglycerides, fibrinogen, C-reactive protein, and glucose values were significantly higher in cases with

ischemic stroke, the oxidized LDL values did not correlate with age, stroke severity, and outcome in the other study (54). Additionally, significant alterations occurred in lipid metabolism and lipoprotein composition during infections, and triglycerides increased whereas HDL and LDL decreased in another study (55). Furthermore, a 10 mg/dL increase of LDL was associated with a 3% lower risk of hemorrhagic stroke in another study (56).

As a conclusion, although the similar mean age, gender distribution, smoking, and BMI in both groups, triglycerides, DM, and CHD were higher whereas LDL and HDL were lower in patients with plasma HDL values lower than 40 mg/dL, significantly, so HDL and LDL may be negative APP of the metabolic syndrome.

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THE BENEFITS OF HAVING ONCOLOGY NURSE NAVIGATORS WITH IMPLICATIONS FOR QATAR: A LITERATURE REVIEW

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Abstract

Background: The number of cancer patients is increasing in Qatar. Thus, there is need for oncology nurse navigators to deal with trajectories of cancer care, which in turn aligns with the National Cancer Strategy. Oncology nurse navigators support patients, families, and caregivers, which eliminates barriers to their care. It is asserted that Oncology nurse navigators provide streamlined care aimed at mitigating the cost of healthcare.

Aim: To explore oncology nurse navigators' roles and implications of these roles in Qatar.

Method: A review of the literature was conducted using databases such as CINAHL, Academic Search Complete and MEDLINE. This literature review included ten articles published between 2008 and 2018 that focused on the benefits of oncology nurse navigators' roles for cancer care. The quality of studies was assessed using Mixed Method Appraisal Tool and a matrix table was used to categorize and analyze the data.

Result: Data analysis revealed themes related to the benefit of oncology nurse navigators such as: patient satisfaction, self-management, and care coordination. Oncology nurse navigators increase patients' satisfaction because they provide education, information, and emotional support for patients. They also help patients to increase self-management

because they empower patients toward symptom management. Finally, oncology nurse navigators increase care coordination because they facilitate communication and reduce barriers to care.

Key words: oncology nurse navigators, cancer care, oncology patients

Introduction

Cancer currently causes 10% of the deaths in Qatar and the occurrence of new cancer cases will double by the year 2030 as the Qatari population ages [1]. The risk of having cancer is higher and may lead to increased complications for patients with advanced age. For this reason, the National Cancer Strategy aims to have nurses who specifically specialize in oncology and can further navigate the healthcare system; such nurses would be known as Oncology Nurse Navigators (ONNs). Oncology nurse navigators have skills and knowledge to deal with the complexity of the trajectory of cancer care for patients [2]. Oncology nurse navigators would be seen as beneficial in order to meet the demands of the oncology patients as they navigate their way through the course of cancer care in Qatar. The role of ONNs has been defined as professional registered nurses with “oncology specific clinical knowledge who offer individualized assistance to patients, families, and caregivers to help overcome health care barriers” [3]. Oncology nurse navigators provide all types of care to patients. This may encompass such things as psychological support, guidance, and education about various facets of the oncology department [4]. They counsel patients so they may know what to expect during and after their appointments and about care needs. Oncology nurse navigators have extensive knowledge of the cancer system where they work and thus are able to provide information to both inpatients and outpatients [5]. Oncology nurse navigators provide a holistic model of cancer care for individuals in order that they may have a better quality of life and care services, because they provide social, physical, and psychological support [2]. For these reasons, ONNs are needed to meet patient needs. Oncology nurse navigators require specialization of all departments within the oncology department with a focus on getting patients where they need to be and ensuring they are aware of treatment schedules, and what to do if side effects occur after treatment regimens [3]. Nurses who take on this role require specialized knowledge to be able to fulfill the needs of these patients. For this reason, additional training is needed for nurses to navigate the complex care of patients with cancer.

Patient navigators have evolved in their role which now in most cases, is highly specialized. In the cases where cancer is the diagnosis, these nurses are known as oncology nurse navigators (ONN) and thus play an important role for patients and their families. The word cancer and what it connotes creates real fear; most people think that having cancer means the end of life for them [6]. Although for some that may be true, there is still the need to be able to navigate through the system to receive both support and treatment. Patients and their families will face the biggest challenges of their life as they negotiate complex cancer care [7]. For this reason, ONNs are seemingly required to ensure care services are seamless and patients will receive the required services [8]. They are also pivotal owing to the prevention of complications from noncompliance. Oncology nurse navigators have been shown to be successful for breast

cancer patients and in fact has proven to increase survival rates [9]. Nurse navigation programs have become a global need in many oncology centers as stakeholders attempt to optimize patient care and services for people who have cancer [10]. These programs have become popular in most health care centers for many people who seek cancer care worldwide. Moreover, another benefit of this program may be that patients with cancer and their carers will be better equipped to enable self-care while at home; this is due to the teaching provided by these ONNs [11]. Patients who have been seen by ONNs and have received teaching related to their illness are also said to have a decrease in emergency room visits and readmission, therefore reducing inpatient care costs [12].

Qatar has clinical nurse pathway coordinators; however, their roles are limited and do not encompass the actual role ONNs may play. The role of ONNs is currently not well defined nor used in Qatar. Thus, the purpose of this literature review was to explore roles associated with having ONNs who are nurses, with implications for Qatar.

Method

To understand the benefits and important services that are provided by ONNs, a literature review was conducted using Cronin, Ryan and Coughlan's framework. This framework includes determining a review topic, searching the literature, analyzing and synthesizing literature, and writing the review, including adding references [13].

Literature Search

The following databases were used for this literature review: CINAHL, Academic Search Complete, and MEDLINE. The key search terms used were patient navigat*, nurse navigator*, patient navigation, oncology, cancer care, hospital*, and inpatient*. The initial search resulted in 232 articles. Of these 232 articles, 192 articles remained after applying limiters. The limiters were peer-reviewed articles published in English between 2008 and 2018.

Data Evaluation

The 192 articles were evaluated for inclusion in this review. The titles of these 192 articles were reviewed for inclusion based on inclusion and exclusion criteria. The inclusion criteria were (a) studies which focused on oncology care; (b) studies conducted in hospitals; (c) studies which focused on the oncology nurse navigator; (d) study designs restricted to primary studies that included qualitative, quantitative, and mixed method studies. Exclusion criteria included (a) studies that are grey literature; (b) studies done in the community; (c) studies that focus on non-cancer patients; (d) studies focused on navigators that did not include nurses; and (e) studies published before 2008. After reviewing titles, 92 articles were further excluded based on inclusion and exclusion criteria. The remaining 100 articles were reviewed for potential inclusion. After

reviewing abstracts, 50 articles were removed based on the above criteria. The remaining 50 articles were further reviewed for duplication. Duplicate articles were removed ($n = 25$). After full text review of 25 articles, 15 articles were excluded because these articles did not focus on nurse navigators but focused on social workers as navigator. Ten articles were found to be appropriate for inclusion in this literature review: five qualitative and five quantitative.

Data Appraisal

Five qualitative and five quantitative studies were appraised for methodological quality. Qualitative studies included one phenomenological, one case study, and three descriptive qualitative studies. Quantitative studies included two non-randomized trials, two randomized control trials and one descriptive quantitative type study. The Mixed Method Appraisal Tool (MMAT) was used to appraise the studies [14]. This tool has two steps. The first step is to answer two questions to evaluate all types of studies. The second step is to answer five questions related to the specific type of studies. The responses are yes, no, or cannot tell. Each of the five qualitative articles met the criteria of both the first and second stage of the MMAT which included looking at research question, data analysis, data collection and reporting. Four of the quantitative articles also met the above criteria. However, one quantitative article was noted to have a high attrition but met all other outlined criteria.

Data Extraction

After critical appraisal, the data were extracted using a literature review matrix. The approach for matrix designs is based on the topic and the purpose of the research study (Cronin et al., 2008). The matrix developed for this review contained the following information: (a) author and country, (b) aim (c) method, (d) sample size, (e) findings, and (e) limitations.

Findings

Of the ten articles included in this review, five were qualitative and five were quantitative and all were published between 2008 and 2018. These studies were conducted in various countries such as the United States ($n = 4$), Canada ($n = 3$), Korea ($n = 2$), and Denmark ($n = 1$). There were five qualitative studies with different types of designs. These included three descriptive, one case study and one phenomenology. In the descriptive study, Gotlib et al. (2017) [15] examined the experiences of patients regarding navigation services. In another descriptive study, Jeyathevan et al. (2017a) [16] explored the role of ONNs in enhancing patient empowerment. In another descriptive study, Korber et al. (2011) [17] identified perspectives of participants in the navigation program. In the case study, Horner et al. (2013) [18] compared the patients in the navigation program with patients receiving usual care. In the phenomenological study, Jeyathevan et al. (2017b) [19] explored the role of ONNs in facilitating continuity of care for adults with lung cancer. The quantitative studies

were two non-randomized control trials, one descriptive study and two randomized control trials. Three studies Lee et al. (2017) [20], Park et al. (2017) [21], and Mertz et al. (2017) [22], examined the effects of ONNs on patient satisfaction. In another study Koh et al. (2011) [23], examined the effectiveness of the patient navigation program. One study by Wagner et al. (2014) [24] sought to determine whether nurse navigation intervention improves quality of life and patients' experiences.

Several benefits of ONNs' roles were identified in the ten articles included in this review. These benefits impacted on patient experiences and health outcomes. The impact of the roles of ONNs of these studies are categorized into three overarching themes such as patient satisfaction, care coordination, self-management and were further broken down to five sub themes: providing information and education, providing emotional support, facilitation of communication, eliminating barriers to care, and personalized symptom management.

Discussion

Present in the literature was evidence that patients with cancer were especially satisfied because ONNs provide information and education for them, which enabled them to have better access to care due to guidance through the medical system [15-18-21-23-24]. The findings from this literature review are congruent with a quantitative study conducted by Hook et al. in 2012 [25]. This study's findings demonstrated that the majority of patients (97%) were satisfied with ONNs because ONNs helped these patients to learn new information about their care management and cancer stages. This same study showed that information provided by ONNs improved patients' perception of their cancer experiences. A further study conducted by Trevillion et al. (2015) [26] demonstrated that 94 % of participants understood the information provided by ONNs and 85.2% of participants were satisfied with the amount of information and guidance in navigating the health care system. Information and education that is provided by ONNs to patients with cancer empowers them to make decisions regarding care that is informed and best able to meet their needs.

Literature also highlights that patients were satisfied because ONNs provided emotional support [18-22]. A qualitative study conducted by Hebert and Fillion (2011) [27] showed patient satisfaction were increased when ONNs provided emotional support for patients. This study went on to demonstrate that patients were able to cope with disease because ONNs were aware of the emotional and psychological needs of these patients. Patients in this study reported that ONNs helped them deal with difficult situations during their treatment. One patient went on to say "she {ONN} brings us emotional security... and you know that you can count on her" [27]. Similarly, in the study of Mertz et al. (2017) [22], satisfaction was increased because ONNs provided options and interventions for patients to decrease distress. Comparably, Harding

(2015) [28] showed that women with breast cancer were more satisfied with care of ONNs and reported less distress. In this study, women who were cared for by ONNs had lower distress scores than non – navigated women.

The finding of this literature review showed that ONNs were actively involved in supporting patients in self-management, which helped patients to cope with their cancer.

Patients in this review understood specific self-efficacy enhancing techniques to cope with cancer related symptoms [15-17-18-19]. Similarly, Fillion et al. (2012) [29] showed that ONNs were actively involved in helping patients to have self-management, and they used a variety of specific efficacy-enhancing techniques to help patients cope with disease. In this study, patients with cancer felt an increase in self-efficacy when dealing with health problems and symptom management. Fillion et al. (2012) [29] showed that ONNs monitored patients' symptoms by providing and facilitating symptom management. In addition, ONNs reinforced self-care behavior and assisted patients and their families in following individualized treatment, and care plans. In this study, ONNs worked toward educating, modeling, and coaching to facilitate patients' and their families' behavioral changes toward patient centered care. Another study conducted by Wilcox and Bruce (2010) [30] identified that ONNs helped patients with cancer to develop tools to cope with their difficulties and patients felt more empowered. This helped patients to decrease their anxieties during their treatment. Oncology nurse navigators in this study were seen as advocates in empowering patients with cancer to cope with diseases.

Care coordination is vital to eliminating barriers to effective care management [16-24]. This finding highlighted the role of ONNs in improving care coordination for cancer patients, which helped these patients to have better access to care. Similarly, Bailey, et al. (2018) [31] underscored the fact that care coordination is one of the necessary competencies needed in the role of ONNs. This competency helped ONNs to facilitate well-organized delivery of healthcare services and to serve as a key contact to promote optimal outcomes while delivering patient centered care. In this study, ONNs identified barriers to care and facilitated referrals, as appropriate, to mitigate barriers in order to coordinate care. However, Yatim et al. (2017) [32] showed different findings related to care coordination activities. These authors identified five categories of ONNs' coordination activities for patients with cancer. These categories were monitoring patients, helping patients to navigate through clinical pathways, managing technical problems, collecting data, and transmitting patient data. All of these coordination activities for ONNs helped patients to have better access to care and work toward eliminating obstacles.

ONNs play an important role in care coordination by facilitating communication and discussion with members of the multidisciplinary team [17-18-20]. These findings emphasize that ONNs need to act as liaisons between patients, families, and caregivers to improve patients' outcome. Similarly, another study showed that communication was one of the competencies of ONNs that helped to coordinate patient care [33]. Oncology nurse navigators in this study demonstrated intrapersonal communication that allows an exchange of ideas and information with patients and patients' families. In this study, ONNs ensured that communication is culturally sensitive, and they facilitated communication among members of the team to prevent delays in care that can affect patient outcomes.

Conclusion

The aim of this paper was to explore the benefits of having ONNs and implications of these roles in Qatar. Oncology nurse navigators play important roles in providing streamlined care to cancer patients based on the retrieved research findings. Most articles showed the benefits of having ONNs in increasing patient satisfaction, increasing self-management, and improving care coordination. This literature review highlighted that patient satisfaction increased because ONNs provide education and information and emotional support for patients with cancer. This review also demonstrated that ONNs empower patients with cancer to increase self-management. It further showed that care coordination can be improved due the facilitation of communication and elimination of barriers to care. For these reasons, the role of ONNs should be introduced to Qatar to benefit the population which in turn aligns with the Cancer National Strategy.

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HOSPICE CARE AND THE ISLAMIC FAITH: A NARRATIVE REVIEW

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Abstract

Having care delivered that is culturally relevant and in keeping with one's own philosophy of a good death is something that is seen to some as important. While there is a vast number of people with different cultural mores and beliefs, it is more apparent now than ever for healthcare providers to keep current with the cultural preferences of patients who wish to die at home. Islam is a faith that is practiced not only in Muslim countries but is widespread throughout the world. As such, it is unique in its facets. Having a skilled, knowledgeable healthcare workforce that is familiar with these facets is required in order to facilitate a good death at home. This is one where

the patient feels valued and is enabled to die with dignity and be cared for by healthcare providers who are familiar with their beliefs and practices. This narrative review seeks to embrace and enlighten those healthcare providers who wish to become familiar with the preferences of patients of the Islamic faith who wish to die at home.

Key words: Hospice, Muslim, Cultural Relevance

Introduction

According to Salman et al. (2010) [1], nearly one quarter of the world's population is comprised of people from the Islamic and Muslim faith. Due to this, it is more important than ever to have nurses who are culturally proficient when it comes to providing hospice care. Abudari et al. (2016)[2] reported that healthcare providers from different religious and cultural backgrounds such as non-Muslim nurses at King Faisal specialist hospital in the Kingdom of Saudi Arabia faced challenges when providing end of life care for terminally ill Muslim patients. Salman et al.'s (2010) [1] study demonstrated that the provision of culturally appropriate care is an important aspect of end of life care, which should be acknowledged and adopted by healthcare providers. Similarly, Lovering (2012)[3] reported that healthcare providers who utilize the crescent model of nursing care to provide spiritual support allowing family members to practice religious beliefs is an important aspect of culturally relevant care. This can be in the form of using such things as ZamZam [holy water] while giving medication and providing personal care. Tayeb et al. (2010) [4] stated that there are essential aspects to be considered when delivering end of life care. Essential features recommended by the Muslim society should be understood by healthcare providers in delivering care that is culturally relevant. These features include religious faith and beliefs, self-esteem and body image, and concerns about family security. Salman et al. (2010) [1] found that the acknowledgment of religious beliefs and cultural traditions facilitates the provision of spiritual and psychosocial support to patients and their families, which contributes to the reduction of suffering. This is in part due to the belief that Muslims live their lives according to cultural and philosophical beliefs of the Islamic religion, which is a unique feature amongst the cultural and philosophical underpinnings of their tradition. In Qatar, the majority of people are Muslims; however, the healthcare workforce includes nurses who originate from over 70 different countries worldwide and possess different cultural and religious backgrounds. Thus, it is imperative that these nurses and other healthcare providers be equipped with knowledge to provide culturally relevant end of life care, enabling them to support terminally ill patients and their families in their last days of life [5]. The purpose of this narrative review is to highlight the history of hospice care and the effect it may have on the Islamic faith. This narrative review is built on the notion that knowledge is constructed by drawing conclusions from the literature [6].

History of Hospice Care

In medieval times, the term hospice meant hospitality [7]. It was a place where refugees lived and/or exhausted travellers rested from long journeys. In 1948, the term hospice was adopted by the physician Dame Cicely Saunders and used for specialized care for dying patients. The first modern hospice care center was established in a residential suburb of London, which was known as St. Christopher's Hospice in 1971 [7]. Croson et al. (2018) [8] defined hospice as a service delivery system that focuses

on caring not curing by providing comprehensive and compassionate supportive care for the families and the patients suffering from life threatening illness. According to the National Hospice and Palliative Care Organization as cited by Croson et al. (2018) [8], hospice care supports patients' needs by providing holistic care that helps to fulfil the desires of people in the last days of life. Therefore, the Islamic and Muslim perspective about hospice care needs to be understood in order to facilitate delivery of end of life care services in countries where Muslims are the predominant population.

A Good Death

Libon-on et al. (2017) [9] reported that a good death in nurses' perception is 'one that involves dignity, comfort, freedom from pain and the ability of patients to spend quality time with their family before passing' (p. 66). Literature states that most people with a terminal disease would prefer to die in the comfort of their home. It has been reported that about 50% to 83% of people with advanced cancer in seven European countries prefer to die at home [10]. In one such study in Qatar, it was reported that most people with cancer prefer to die at home even though the majority of deaths occurred in the hospital due to the lack of alternative palliative care models that could be available at the community level [11]. In Qatar, palliative care only provides symptom management and end of life care for cancer patients inside the hospital. This service has not been able to fulfil the wishes and demands of patients and their families with the rising number of cancer patients in Qatar [11]. Therefore, health care systems in Qatar are required to develop or adopt a model of hospice care that could be provided to patients who wish to die at home. This specialized approach to care could target patients within the community and include a specialized model of hospice care. Home health care is a unit that delivers care at the community level for patients with acute or chronic illness and disability. However, this unit lacks nurses with the expertise and the competencies who can provide end of life care and symptom management for life threatening illness at the community level [12]. The home hospice model of care may provide services that are beneficial to patients, families, and organizations. Hospice care is a potential option that can fill the gap between these two services and fulfil the wishes and demands of patients and their families with the rising number of cancer cases.

Islam and Hospice Care

According to Mendieta et al. (2017) [13], Islam is a religion that encourages principles of caregiving, faith, and family, which are similar to universal principles. These principles could be a good start for working toward hospice services in Muslim communities. For this to be successful, healthcare providers need to have a deep understanding of Muslims' perceptions of health, illness, and treatment. Muslims believe health is a blessing from Allah while illness and suffering is an atonement of one's sins [14]. Ahmed (2018)[15] reported that Muslim beliefs are adopted from the Qur'an and Sunnah [the Prophetic Tradition] that

guide decision making about terminal illnesses and end of life care. This author also reported that the Qur'an, Sunnah, and a consensus of Ulama or Council of Senior Scholars are forms of guidance that can facilitate the implementation of hospice palliative care services in the Muslim community. These services provide physical and spiritual care services at the end of life. At the end of life, spirituality and religion play a significant role in giving strength to ill people in their suffering and facilitate decision making about end of life issues. Ahmed further noted that spirituality is the way of people expressing their worship of and connection to their creator Allah and religiosity is 'participation in beliefs, rituals and activities of one of the traditional religions' (p. 66). This set of beliefs and rituals are adopted from the Qur'an and Sunnah that provide guidelines that facilitate the work of healthcare providers to provide spiritual support within the context of end of life care. The Qur'an itself is referred to as the book of healing. The Holy Qur'an 17:82 reads, 'And We send down of the Qur'an that which is healing and mercy for the believers, but it does not increase the wrong doers except in loss.' The Qur'an is a treatment for the diseases of chest and heart: 'O mankind, there has to come to you instruction from your Lord and healing for what is in the breasts and guidance and mercy for the believers' (10:57). In the area of health and medicine, the Prophet Muhammad had a lot of sayings and works which led to the development of a discipline known as al-Tibb al-Nabawi [the advice given by Prophet Muhammad with regards to sickness, treatment, and hygiene]. For example, prophetic statements such as 'There is no disease that Allah has created, except that he also has created its treatment' [16:582:7] provides a strong impetus for Muslim scholars to undertake medical investigations.

Ghaly et al. (2018) [17] showed that there are two main forms of Ulama consensus that are known as al-ijtihād al-fardī and al-ijtihād al-jamāī which guide patients, families, and healthcare providers in decision making related to end of life issues. These authors define al-ijtihād al-fardī as an individual Muslim religious scholar's effort and perspectives of ethical-legal reasoning. They also interpret al-ijtihād al-jamāī as a collective that lends itself to Muslim religious scholars and biomedical scientists' development of ethical-legal reasoning. These scholars are the part of the Islamic Organization for Medical Sciences (IOMS) who work together with other institutions on bioethical issues related to medical treatment from the Islamic perspective. Islam has modes of medical treatment known as tadawi that has five branches such as prevention and curative care. Palliative care is an advanced branch in tadawi. Many arguments and discussions have ensued related to palliative care services such as end of life care. Muslim religious scholars have given various opinions regarding end of life treatments such as life-sustaining treatments (LSTs; e.g. mechanical ventilation and cardiopulmonary resuscitation) and pain management medication in life-limiting illnesses. The vast majority of scholars have given priority to withdrawing instead of withholding LSTs. The collective decision of Islamic scholars was to accept withdrawing of LSTs in terminal illness on the condition

that if the physician nearly asserts that recovery is not possible, there is no need to prolong patient suffering by keeping Patient in a vegetative state. On the other hand, some scholars have stated that withdrawing LSTs is forbidden, considering it as intentional homicide and the sanctity and preservation of human life as an obligation imposed by God. They explained that Muslims should be optimistic especially for believers who believe in the Omnipotent God. It is challenging for healthcare providers to provide end of life care for these believers as they believe that illness and wellness are God's will, which is truth [18]. These believers seek religious practices as a way of treatment, such as prayer and reading the holy Quran, to cope with life threatening illnesses while Islam encourages seeking medical treatment.

The Islamic perspectives regarding benefits attained in pain management by using pain medication is limited because Muslims have faith that bearing pain will be rewarded by Allah. There is religious misconception related to receiving opioids and treating pain. Khader (2017) [18] stated that 'In Islam, tolerating pain can be rewarded from God and expiate sins. But Islam encourages seeking treatment and pain relievers such as narcotics' (p. S70). Islam gives permission to use analgesics for controlling unbearable pain provided it does not affect the level of patient consciousness to the point where they are unable to perform religious rituals, such as prayer. The intentional suppression of one's consciousness is categorically forbidden. However, Islam allows those practices of forbidden actions in the case of anaesthesia that is required for some surgeries. Muslim scholars have an objection to giving terminal sedation to gasping patients who are near death. Patients during this period have to be coherent enough to say the formula of shahada [declaring belief in the oneness of God and acceptance of Muhammad as God's prophet] as a part of religious duty. These Islamic perspectives can be used by healthcare providers while providing end of life care to patients at the time of hospice care. Care needs to take into consideration the context of patients' beliefs and religious rituals. These improve the quality of life of dying persons by fulfilling the spiritual, faith, and psychological needs of dying persons.

Conclusion

It is apparent from the literature that healthcare workers require educational programs to increase their knowledge and skill related to integration of Islamic beliefs while providing end of life care. These programs would help nurses to have a better understanding about traditional Islamic medicine as most of the nurses in particular in Qatar are Christian in their belief. It is impossible to understand all the cultural mores of every patient; however, when one lives and works in a Middle Eastern country, it is imperative one is equipped with the knowledge and education to care for patients at the end of life especially if they have a culture unlike their own.

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